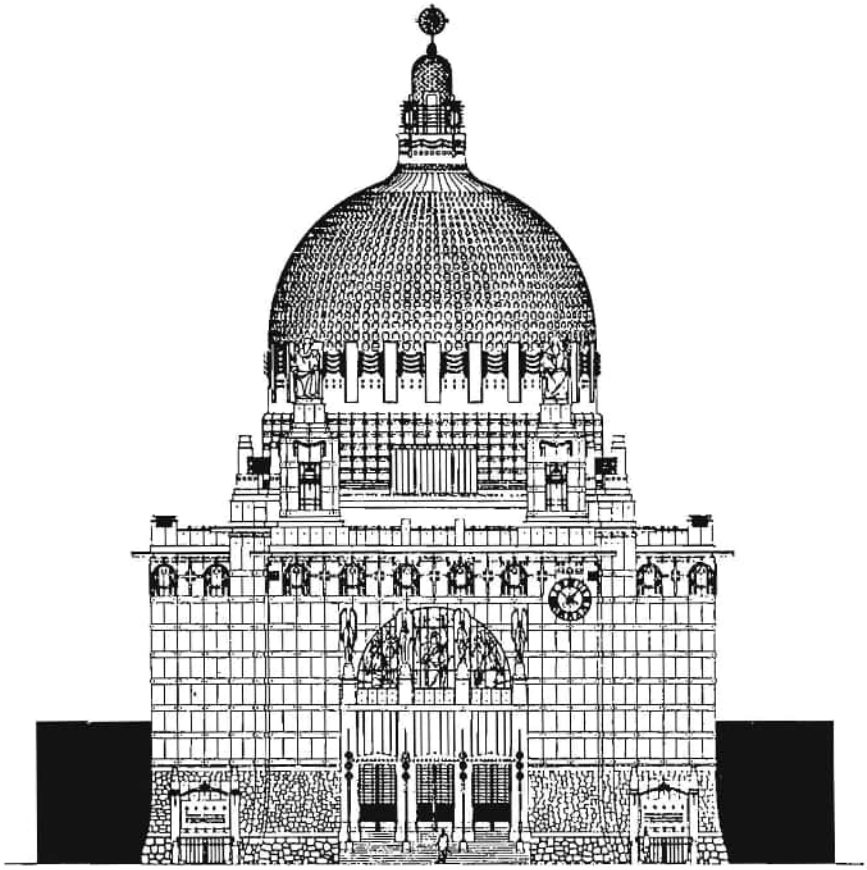
Austrian Society for Artificial Organs
Biomaterials and Medical Replacement Devices

in conjunction with the

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1st VIENNA INTERNATIONAL WORKSHOP

ON

FUNCTIONAL ELECTROSTIMULATION

BASICS, TECHNOLOGY AND APPLICATION

VIENNA (AUSTRIA), OCTOBER 19th – 22nd, 1983

PROCEEDINGS

BIOENGINEERING LABORATORY,
2nd SURGICAL CLINIC, UNIVERSITY OF VIENNA

AUSTRIAN SOCIETY FOR ARTIFICIAL ORGANS,
BIOMATERIALS AND MEDICAL REPLACEMENT DEVICES

in conjunction with the

INTERNATIONAL SOCIETY FOR ARTIFICIAL ORGANS

BIOENGINEERING LABORATORY,
2nd SURGICAL CLINIC, UNIVERSITY OF VIENNA

THE FIRST VIENNA INTERNATIONAL WORKSHOP ON FUNCTIONAL ELECTROSTIMULATION

October 19th – 22nd, 1983
at the "Jugendstil Theatre Building Baumgartner Höhe", Vienna

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I.

PRESENT AND FUTURE ASPECTS OF MICROELECTRONICS

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ABSTRACT

In part 1, the general state of the art of IC complexity, cost, and performance are pointed out. Interest is focused on CMOS technology, the most promising IC technology for low power consumption.

In part 2, the numerous stages in the design of Very Large Scale Integrated Circuits (VLSI circuits) will be described. Special attention is given to novel methods of so-called "Semicustom design", which guarantee extremly fast and relatively cheap chip realization of a complex functional specification.

The cardiac pacemaker is considered as an example of an electronic system for medical electrostimulation throughout this paper. In part 3, the attempt is made to illustrate the complexity of logic functions already possible and those which are to be expected in future systems of this kind.

In part 4, quality problems with integrated circuits, deficiency mechanisms and how to overcome them, will be discussed.

Part 1 : IC Complexity, Cost, Performance

The word "microelectronics" was coined in the early sixties, when it became possible to integrate 10 to 100 different components of a circuit (transistors, diodes, resistors and capacitors) with their electric connections on the semiconducting surface layers of a tiny silicon crystal. Since this was achieved on a surface of only a couple of square millimeters, the integrated components had to be reduced to microscopic dimensions.

The main advantages of an ever since rising level of integration in the implementation of logic systems are:

- higher reliability (e.g. less soldering joints)

- lower costs

- reduced space and power consumption

- faster switching speed (less load capacitance).

The logic system processes logical data within a certain, well-defined time frame.Data, which can arise from sensing, calculating, regulating measuring operations. In our case, the source and destination of the data is the human body.

Figure 1 depicts the development of integration density and the cost per transistor function. Please note the exponential decrease of transistor cost and the similar increase in the number of transistors on a single chip. By 1985 we will be able to integrate one million transistors on a chip of about fifty sqare millimeters. By the late eighties, this exponential behavior is expected to level off and become linear. A technological and also economical limit will be encountered in the mid nineties, when we will have ten million transistors per chip.

The present state of the art is characterized by the fact that the active part of a transistor on the surface of the IC has an area of about 1 or 2 square micrometers.

In presenting a few facts about the basic electrical properties of ICs, I will restrict myself to CMOS technology, since this technology fits very well into the needs of electrostimulation. (Figure 2)

Complementary Metal Oxide Semiconductor technology implements the logic devices (the molecules of a logic system) as connections of so-called n-conducting and p-conducting transistors, where n stands for electrons and p for electron holes. n-type transistors acquire a conducting channel if the voltage at the gate electrode exceeds the positive threshold voltage, whereas the p-type transistor starts to conduct if the gate voltage is smaller than the negative threshold voltage. The basic logic device, the inverter, is presented on the following slide. It is a series of an n-type and a p-type transistor, coupled to a positive power supply and ground. If a logical "1" (voltage equal to the power supply) is applied to the input, a few nanoseconds later a logical "0" (0 Volts) is produced at the inverter's output. If "0" is applied at the input, "1" is produced at the output.

After switching, there is only a very small leakage current of about o.5 nA, since one of the two transistors is always in a nonconducting state. Only in the transition phase a nonnegligible current is flowing. It consists of two components:

- a lateral current through both transistors

- a current which loads or unloads the output capacitance to "1" or "0".

The power consumption is proportional to the number of logical transitions per second and to the square of the voltage swing, as is depicted in the figure.

With a voltage swing of about 5 volts, we arrive at an energy of about 2 pJ per logic operation or per elementary decision.

The total power consumption of the integrated circuit therefore does not depend on the total number of transistor devices, but on the average number of switched transistors per second.

On the other hand, power consumption is a function of the square of the voltage swing, and therefore also of the supply voltage.

These considerations are very important for the design of the electronic nucleus of the cardiac pacemakers if we are to avoid a so-called "energy crisis".

Given an battery capacitance of about 5 watt hours and a battery life of 8 years, only 10 microwatts can be afforded for the pacemaker electronics. (60 microwatts are needed for atrial/ventricular stimulation).

The consequences are twofold:

- the pacemaker has to operate with a small voltage swing,
- the ICs should operate with a minimum of switching transistors per second.

The first point underlines the importance of a patient-adaptable minimal stimulation amplitude. This can be guaranteed by the Vario principle.

The second point seems to be contradictory to the structure and operation of a microprocessor, which in itself is clock-driven. Most transistors switch with the full clock frequency, giving a high power consumption on the chip. On the other hand, utilization of a microprocessor is very helpful for sophisticated operation . such as therapy of tachycardia, where individual stimulation patterns have to be programmed, according to the individual, changing needs of the patient.

The problem of the high power consumption can be overcome if additional electronics is provided to turn the microprocessor off when it is not needed (if, for instance, a phase of tachycardia has terminated).

Part two : Methods of IC Design

To stimulate ideas about new applications of integrated circuits, I will now highlight several aspects of their design; with particular reference to new and very promising strategies called "Semicustom Design". Using these strategies, it is feasible to get finished chips only a few weeks after completing their theoretical functional specification (Figure 3).

Nearly every design starts with a functional specification which has yet to be fully detailed. A part of this specification is a block diagram (Figure 4).

The blocks in this diagram are now to be expanded. This stage of development is called the logic design. The function of each block has to be detailed in terms of logic devices. A logic device is, for example, the aforementioned inverter. This process of step-by-step refinement of the design leads then to the physical representation of the logic devices: the transistor level. The realization of the logic in terms of electrical components on the surface of the IC is called the electrical design.

The final step before commencement of the photolithographic fabrication process of the IC wafer is the silicon-area-optimizing mask layout of the electric components and their interconnections.

These descending steps are accompanied by numerous aids provided by the computer. Computer Aided Design - CAD - plays an important and ever-increasing rôle in IC development for:

- analysis and simulation of all stages of the design process (function, logic, electric, layout level).

- automated synthesis of the mask layout according to the architectural or logical specification.

The synthetic CAD methods in particular make it feasible to reduce logic design time and cut expenses drastically: this can be seen from figure 3.

The basic idea is to reuse certain function units or blocks which have already been designed down to the transistor and the mask layout level.

Every function block corresponds to a mask layout block. The placement and the routing (the interconnection positioning corresponding to the block diagram) is done by the computer.

These methods of IC design are called Semicustom Design.

We use the term "Semicustom" because the design uses existing standard function blocks which are stored in a library and cannot be altered by the customer. The latter can only determine the interconnections - the netlist - of the standard blocks in line with his architectural specification.

There are two main methods of Semicustom Design:

- the Gate Array and

- the Standard Cell

approach (figure 5).

With gate arrays, design times of only several weeks and technological processing times of one week can be achived once the specification is completed.

Prefabricated IC wafers with arrays of single, unconnected transistors can be linked by aluminum wiring in one, two or three mask levels for photolithographic processing. Wiring belongs partly to the library-predefined functional blocks which are used by the customer, and partly to the customer-specific interconnections between those functional blocks.

The standard cell strategy uses mask layout cells of standard height and variable width, in line with the function blocks in the users library. These cells have to be placed and routed according to the customer's netlist.

Since the whole photolithographic process is needed for all mask levels, the production is somewhat longer than with gate arrays.

The great advantage of the gate array technique is the simple fact that it is possible to implement logic structures in silicon in a very short time. In so doing, one has to consider two main drawbacks:

- silicon area is wasted

- electrical performance can be poor.

With standard cells, the silicon area can be utilized much better since the mask layout cells are optimized with respect to area consumption and electrical performance.

The traditional full custom design gives the best results in terms of chip area and electrical behavior - it is bespoke tailoring, and therefore the worst technique as far as cost and design time are concerned.

Nowdays, ICs are often designed first as semicustom chips to implement and verify a certain custom logic in silicon. Once functionality has been validated and sufficient production volume is to be expected, an optimized fullcustom design is started.

Semicustom IC design is relatively easy to learn, even without an involvment in semiconductor electronics. Supported by the computer, the customer will be able to start the design of his very own gate array or standard cell IC after a short instruction time on the IC suppliers premises.

Part 3 : An Example of Electrostimulation: The Pacemaker

This example was already used in the context of CMOS power consumption.

25 years ago, when the electronic circuits of the first implantable cardiac pacemaker were implemented, they consisted mainly of a couple of discrete silicon transistors. Today, the CMOS IC in a programmable pacemaker contains thousands of transistors, allowing tachycardia therapy, telemetrical diagnosis and other nice features.

The state of the art in pacemaker electronics is about 4,000 transistors per chip. The next generation is expected to have 20,000 transistors, and the following 100,000.

The lifetime of one generation is about 4 years. This relatively short time urges the designer to use semicustom methods or standard microprocessor ICs in order to obtain the required turnover and market feedback.

Now, a few additional highlights concerning the future of pacemaking:

The programming facilities have to be extended. The five or ten relatively rough parameters which can be controlled individually today are felt to be insufficient. The additional intelligence which will be introduced by microprocessors gives rise to new possibilities for patient-oriented programming. The microprocessor will be able to select periods of pathological cardiac behavior according to distinct programmable criteria, and store these periods in additional memory chips. This EKG data compression will allow a long-term diagnosis. Data can be transmitted via telemetric channels.

Combinations of standard CMOS microprocessors and semicustom ICs will be very important in the future.

Parallel with and in addition to new methods of function programming, the physiological feedback channel will soon be introduced. I will only mention the well-known activities of Professor Wirtzfeld and his colleagues at the Hochschule der Bundeswehr in Neubiberg, Germany. They have constructed cardiac catheters with optical windows for analyzing the hemoglobin in order to regulate the pacemaker frequency. With the aid of a neat trick, they even seem to have managed to overcome the windshield wiper problem./1/

Part 4 : IC Quality

In the last part of my lecture I would like to give a short overview of quality problems, degrading mechanisms and long-term specifications of ICs.

In assuring the quality of MOS ICs two main groups of mechanisms have to be considered:

- Early Failures caused by random defects
- Wear Out

Risks of this kind cannot be detected by simple IC testing with customer-developed test programs. Additional measures have to be applied.

In order to detect such ICs which are prone to breakdown due to early failures, every pace is subjected to electric and thermal burn in. Typically this means that the ICs will be exposed to the specified limits of thermal and electrical conditions for one week of electrical operation.

It is an empirical fact that the failure rate in around the first 100 hours of operation is much higher than in the next 1,000 hours.

The probability of a failure as a result of random defects today lies in the range of about 10^{-7} .. 10^{-8} per hour. This would mean that of 1 million cardiac pacemakers, one device would break down every 10 to 100 hours, or in other words: over an operating period of 8 years, about 0.7 % or less of the pacemakers would break down.

Technological progress by a factor of ten seems to be feasible in the next few years.

The wear out of ICs during long-term operation is caused by irreversible deteriorations in the basic structures on the surface (electromigration, oxide punch through and other mechanisms).

In order to analyze the wear out phenomena of ICs, it is possible to make use of the fact that wear out can be accelerated by rising temperature. This acceleration by stress is based on the Arrhenius law and can therefore be determinded quantitatively.

Testing a cardiac pacemaker IC in its wear out behavior is possible by rising its normal operational temperature from 37° to 150° C. This accelerates its wear out by a factor of fifty. As a result, a 2000-hour stress test can be performed to simulate the wear out behavior over 100,000 hours of operation.

The supplier's IC tests under normal and stress conditions plus the burn in, guarantee excellent final-product quality. On the other hand, for acceptance the customer will arrange incoming inspection tests for the delivered IC lots. He will agree with the supplier upon certain acceptable quality levels (AQLs).

An AQL value of 0.1 means that only less than 0.1 % of a shipment may be deficient.

Otherwise, the acceptance of the shipment is refused by the customer.

I hope I have inspired you to look for new applications of microelectronics in the domain of electrostimulation. My opinion is that the problems in this area are not so much localized in the realization or implementation of a certain highly complicated task in silicon, but in the area of the various interfaces to the human body.

/1/ Wirtzfeldt et al.: Control of the pacemaker frequency by the central VENOUS bloud saturation. Biomed. technic 81.

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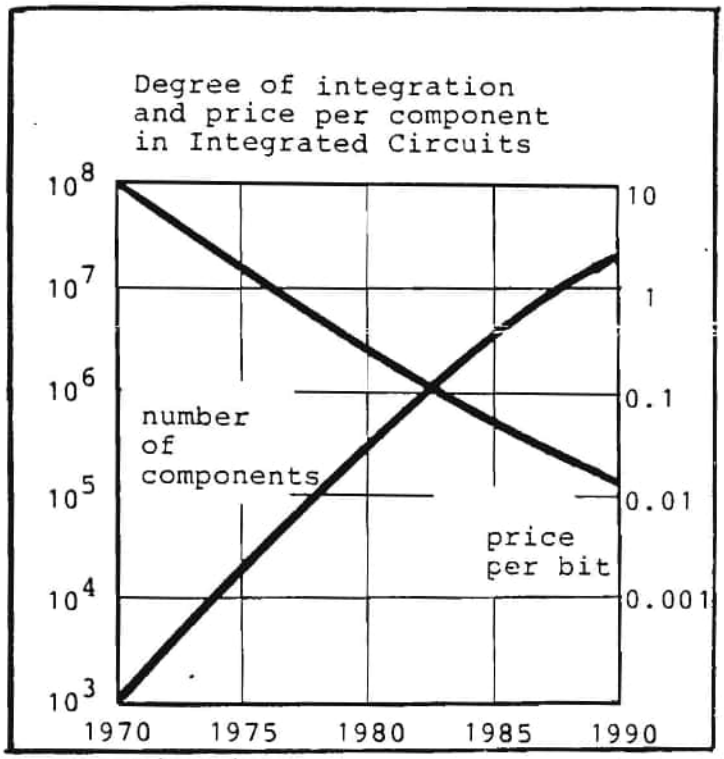


Fig. 1

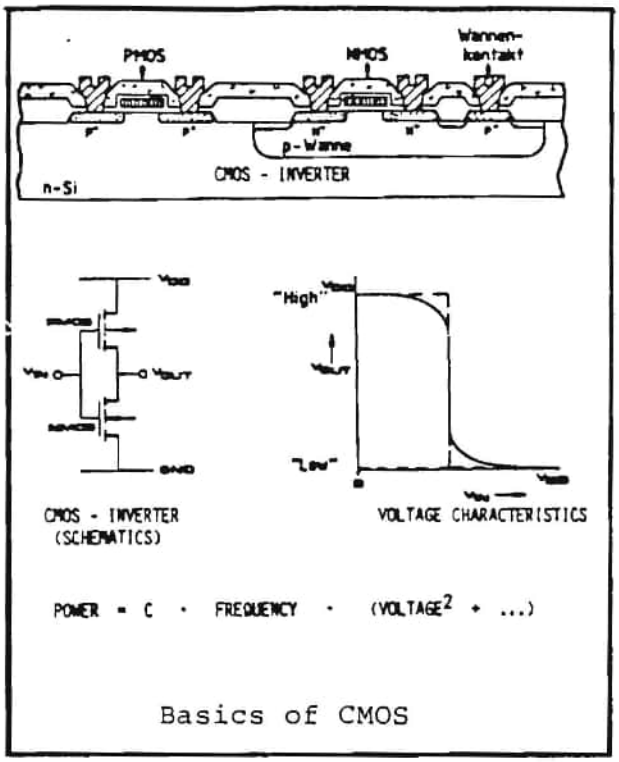


Fig. 2

Semicustom/Fullcustom
Design Characteristics

	Gate Array	Cell-Design	opt. Design (FULL CUSTOM)
RELATIVE CHIP AREA	4,0	2,7	1
RELATIVE PRICE PER CHIP	10	5	1
RELATIVE DESIGN COSTS	1	2	20
DESIGN TIME AFTER COMPLETION OF LOGIC SPECIFICATION	2,5	4	12

Fig. 3

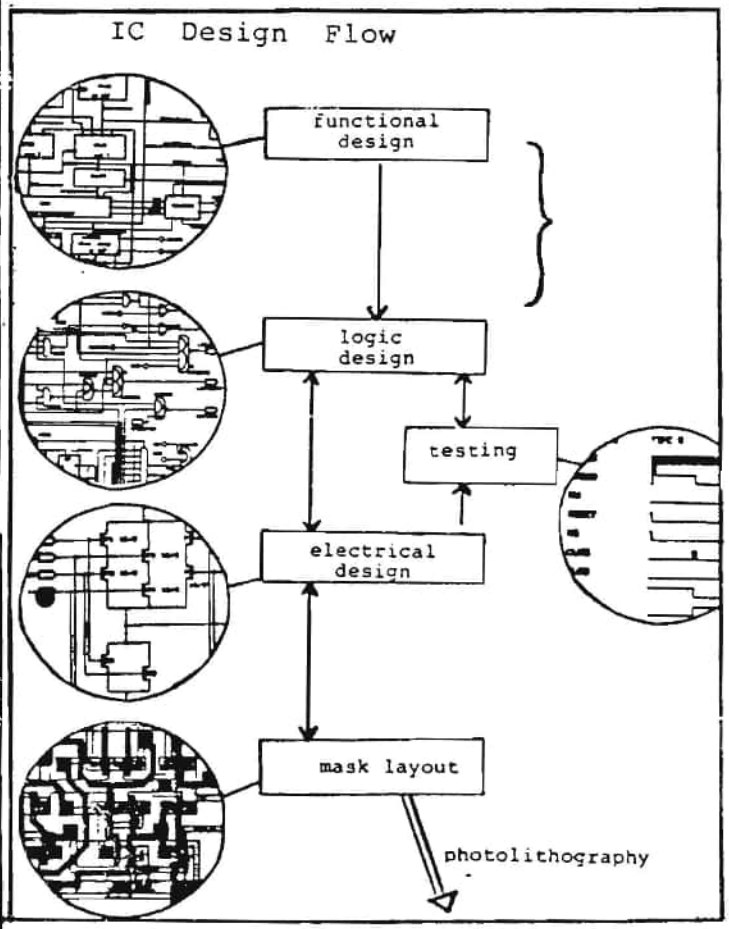


Fig. 4

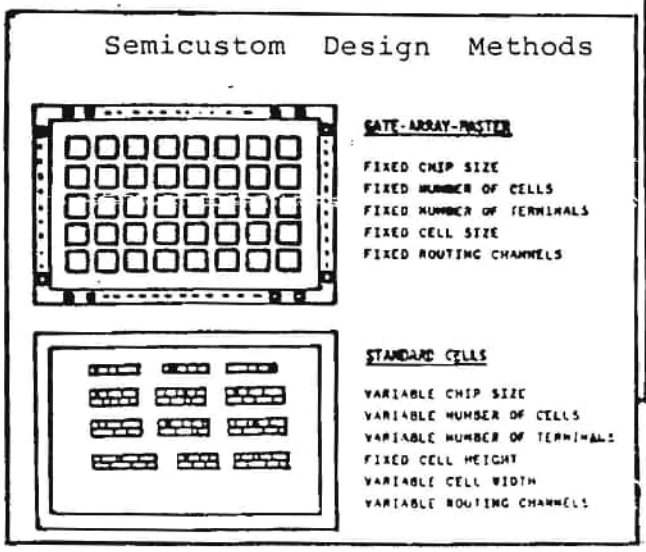


Fig. 5

II.

USEFULNES OF FUNCTIONAL ELECTRICAL STIMULATION (FES) IN REHABILITATION OF CEREBRAL PALSY CHILDREN AND CHILDREN WITH IDIOPATHIC SCOLIOSIS

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Functional electrical stimulation has been described as electrical stimulation of nerve or muscle deprived of nervous control with a view to provading muscular contraction and producing a functionally useful movement /1/. Nowadays it is widely used in the rehabilitation of persons suffering from hemiplegia, multiple sclerosis, paraparesis and in children with cerebral palsy in whom clinical manifestation and disturbances in motor functions are results of upper motor neuron lesion. Apart from this FES is useful in the treatment of children with certain deformations of the locomotor system such as idiopathic scoliosis (IS). General aims are support and acceleration of neurological recovery, development and restoration of basic reflex motor mechanisms participating in rhythmic movements organized primarily on the spinal level, prevention or correction of deformities in the locomotor apparatus resulting from insufficient postural mechanisms /2/. This knowledge of the FES influences on the organization of motor activity with carry-over effect, enables us to introduce this method in treatment of the children with retarded psychomotor development or insufficiently developed motor function. There exists an even better possibility to influence the organization and development of elementary motor mechanisms as it is the case with adult persons who have definitely developed and ten irrevesibly destroyed structures of central nervous system /3,4/. These results are observed in course of practical application of FES in spite of different possibilities of reorganization in central nervous system which was found experimentaly or based on theories as they are for instance functional reorganization of the interneuronal system, formation of alternative pathways and colateral ramifications, reactive syptogenesis, the socolled unmasking phenomenon and the changes in morphology of cells of the central nervous system resulting from an often repeated, programmed and reinforced information inflow from the periphery /5/.

Taking into account our knowledge of spinal reflex mechanism participation in gait with stimulation of peroneal nerves unilaterally or

bilaterally, tibial nerve quadriceps muscle we can control elementary mechanisms of reciprocal inhibition, flexion and extension synergies or alternating steping movements. In more than 500 children test for FES was performed. It was found positive in 79 % of tested children. Among them 77 % used the method at home or in rehabilitation instituions. The results of the treatment using FES as orthotic aid with therapeutic effect are as follow: in 20 % partially improvement of gait, in 80 % improvement of gait to the almost normal cinematic; in 35% of children long-term effect was found. As it is evident from these results, a high percent of positive results with carry-over effect is found. Quite often bilateral stimulation of peroneal nerve is applied even though the clinical picture shows hemiplegia. In some cases bilateral stimulation of peroneal nerve in swing phase and tibial nerve in stance phase was applied. Thus, the child has been helped not only walk, but also drop-foot, internal rotation, adduction and other defects of kinematics of gait have been reduced, whereas standing and errect posture in the stance phase have been also possible. Main obstacles for application of FES are contractures that do not allow dorsal flexion or strong valgus deformities. Also in the children with dyskinesia with or without dystonia or hyperkinetic hypertonic syndromes or with flaccid paralysis of central origin the FES is not recomended. For the needs of cerebral palsy children was modification of the system for FES and way of control of stimulation. This include modification of adjustment of switches in the innersole of the shoe and adaptation of different modes of sequences stimulation to the needs of each individual child. In this way there have been created ipsilateral and contralateral modes of controlling stimulation sequences, and special form of so-called contralaterally controlled alternating FES (CCA FES) /6,7/.

A special interest was paid on the use of FES in treatment of idiopathic scoliosis (progressive unphysiological lateral curving of the spine in-definite ethiology) when was recognized that neural mechanisms might be one of the possible cause, and it was confirmed with the studies of muscle activity during the loading of the spine /8,9/. Further progress was made with experiments using FES of paravertebral muscles and positive results /10,11/.

We have treated 38 children with idiopathic scoliosis in age from 8 to 17 years with different degrees of curving (from 20^{o} to 54^{o} according to Cobb).

Before starting with FES the patient had been treated by using diffe-rent conservative methods as are for instance: Cortel paris plaster,

Lyon's corset or Millwaukee brace combined with physical therapy or without it. Some of them refused recomended surgical treatment.

Functional electrical stimulation was applied over the paravertebral muscles on convex side of curvature. In double scoliosis intermitent stimulation of dorsal and lumbar muscles was used. Today FES is being used all the day in cycles of 5 s stimulation and 5 s pause.

Results of FES on diminishing of curvature may be observed in first 14 days and maximum improvement in the most cases in first 2 to 3 months of treatment was noticed. Much longer time was necessary for the changing the pattern of the muscle which is the most important result of treatment with FES. The same results were found also in the children in whom their growth was practically stopped and had severe deformation; in a few months diminishing of the curve was more than 30 % of deformation.

By using polielectromiographic analysis of paravertebral and abdominal muscles and taking in account others clinical findings (X-ray, clinical observations - if it is possible also kinetic analysis of postural mechanisms and movements of center of the gravity) we can decide for an appropriate indication for FES. In conclusion we can indicate that by using described method we not only reduced deformation or stabilised progression of deformation, but can prevent development of progression in children with bad posture or other clinical signs typical for development of deformation.

The final conclusion is that we have in our hands different possibilities of using external energy for control of man's motor functions, which can improve quality of life of the disabled people. For this purpose we must to know the basic mechanisms responsible for organization of movement as well as the changes which appear in pathological conditions. On the other side unsolved interface problem between any system used in artificial control and the body are main obstacles for clinical use, rehabilitation practice and broad use of up-today technology which is on our disposal.

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III.

TRANSFORMATION OF SKELETAL MUSCLE BY CHRONIC NERVE STIMULATION x)

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SUMMARY

An almost complete transformation of fast into slow-twitch muscle can be achieved in the rabbit by long-term, indirect stimulation. The transformation process is evident by structural, functional, and molecular changes which affect equally the three main functional systems of the muscle fibre, i.e. energy metabolism, sarcoplasmic reticulum, and contractile apparatus. The extent of these transformations depends on the duration of the stimulation. Time course studies show that the early transformations of sarcoplasmic reticulum and energy metabolism occur simultaneously and precede by far the transitions in the myosin related properties. These asynchronous changes indicate differences in the thresholds and suggest that fibre transformation is not an all or none process but must be considered as a timely ordered sequence of changes at the level of specific systems. Its basic mechanism appears to be a switch in gene expression.

MATERIAL AND METHODS

Electrode Implantation

Experiments were performed on adult, male, White New Zealand rabbits. Stimulating electrodes (5 mm long, 0.2 mm thick, coiled, stainless steel wire, soldered to an insulated, multistrand lead) were implanted in the left hindlimb parallel to and 1 mm laterally on either side of the common peroneal nerve. The 5 mm long electrodes were fixed by two sutures to the fascia of the underlying gastrocnemius muscle. The electrodes were led subcutaneously to the back of the animal and connected either to a stimulator /1/ or in the case of telestimulation /2/ to a small receiver secured to the animal's back (Fig. 1). The telestimulation system uses pulse width modulation for transmitting stimulation frequency and amplitude. Duration of the impulse is generated in the receiver.

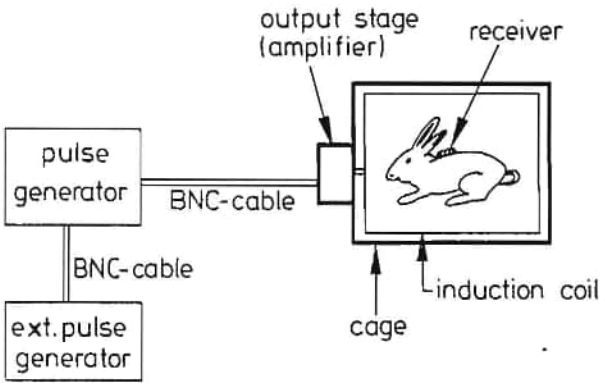


Fig. 1

Block diagram of set-up for telestimulation of caged rabbits. The system uses 5 MHz carrier frequency transmission. Pulse width modulation is used for transmitting stimulation frequency and amplitude. Duration of the stimulation impulse is generated in the receiver /2/.

x) Supported by Deutsche Forschungsgemeinschaft, Sonderforschungsbereich 138, "Biologische Grenzflächen und Spezifität".

Stimulation

Stimulation at a frequency of 10 Hz (0.15 ms pulse duration) was begun 1 wk following the electrode implantation. The amplitude was adjusted daily, following palpation of the tibialis anterior muscle (TA), to give maximum contractions without causing discomfort to the animal. Stimulation was either 12 hr intermittent (alternating periods of 1 hr stimulation and 1 hr rest) or 24 hr continuous.

Analytical Procedures

Animals were sacrificed after various periods of stimulation. Physiological, morphological and biochemical analyses were performed both on stimulated and unstimulated, contralateral tibialis anterior (TA) and/or extensor digitorum longus (EDL) muscles according to methods described in the specific references.

RESULTS AND DISCUSSION

As judged from changes in contractile parameters, chronic, indirect stimulation of fast-twitch TA and EDL muscles at a frequency naturally occurring in nerves to slow-twitch muscles, results in a progressive transformation into muscles which display typical slow-twitch characteristics (Fig. 2). This transformation affects equally the three main functional systems of the muscle fibre, i.e. energy metabolism for ATP supply, the Ca^{2+}-releasing and sequestering membranes of the sarcoplasmic reticulum, and the proteins of the contractile apparatus.

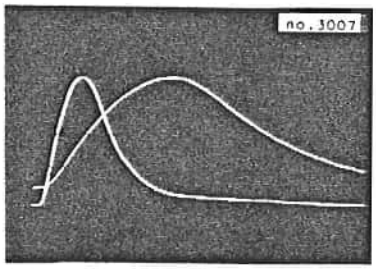


Fig. 2

Isometric twitch of control and 56 d indirectly stimulated (24 h/d) tibialis anterior muscle of a rabbit. Time to peak is 22 ms in the control and 78 ms in the stimulated muscle.

Energy Metabolism

Stimulation induces a pronounced increase in aerobic oxidative capacity as reflected by a higher capillary density /4-6/, an increase in myoglobin /7/ and in mitochondrial content /8-10/. The increase in mitochondria corresponds to elevated levels of enzymes involved in aerobic substrate end oxidation, e.g. the citric acid cycle (Fig. 3), respiratory chain, fatty acid oxidation, ketone body metabolism /7, 8, 10-14/. After prolonged stimulation, these enzymes reach levels exceeding those found in originally "red" slow-twitch muscles, e.g. soleus /8, 10/.

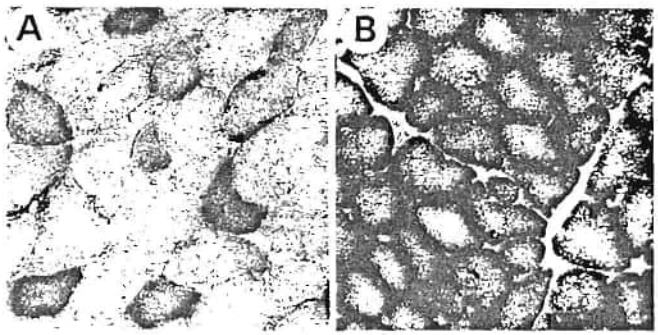


Fig. 3

Histochemical staining for mitochondrial succinate dehydrogenase in cross-sections of contralateral unstimulated (A) and 3 weeks stimulated (8 h/d) tibialis anterior of a rabbit (B).

Stimulation does not only increase the amount of mitochondria but changes their quality /7, 10/. Thus, enzymes of ketone body metabolism display relatively higher

increases than the other mitochondrial enzymes studied. Changes in the composition of mitochondrial membranes are suggested by altered proportions of two membrane-bound flavoproteins, succinate dehydrogenase and glycerolphosphate oxidase.

As stimulation increases the capacity for aerobic substrate oxidation, it decreases the capacity for anaerobic energy supply. Except for hexokinase which rises in activity, the cytosolic activities of glycolytic and glycogenolytic enzymes are markedly reduced /7, 8, 10-12/. The metabolic conversion of the muscle is further emphasized by the isozymic M to H subunit transition of lactate dehydrogenase /7, 8, 14/.

Taken together, the increases in oxygen and substrate supply and in mitochondria as well as the changes in enzyme activity and isozyme patterns signify a profound change in metabolic properties. Thus, a muscle which bases its energy-supply mainly on anaerobic metabolic pathways is turned into a "red" muscle with a high capacity for ATP supply by aerobic oxidative processes. This metabolic conversion appears to be the primary condition for sustained performance. Chronic stimulation has been shown to elicit a marked increase in resistance to fatigue /5, 11, 15, 16/ (Fig. 4).

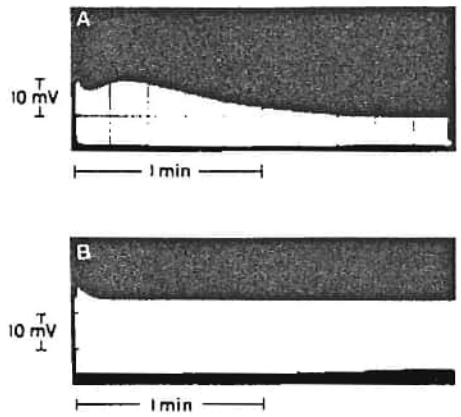


Fig. 4

Test charts of measurement of resistance to fatigue /11/. Control (A) and 3 weeks stimulated (8 h/d) tibialis anterior muscles of a rabbit were stimulated repetitively by their nerve with 330 ms lasting trains of 40 imp/s repeated every second. The developed force was recorded (ordinate). Note the progressive decrease in contractile force (fatigue) in the control muscle (A).

Sarcoplasmic Reticulum

Chronic stimulation results in a transformation of the sarcoplasmic reticulum from that of a fast-twitch into that of a slow-twitch muscle /16-22/ as is evident from marked decreases in Ca^{2+}-uptake capacity /16-19/ and a progressive reduction of the activity of Ca^{2+}, Mg^{2+}-stimulated ATPase /17-19/ (Fig. 5). The conversion of the sarcoplasmic reticulum is illustrated by a thorough rearrangement of the pattern of several intrinsic and extrinsic membrane proteins /14, 17-20/ and by changes in the phospholipid matrix of the membrane /21/. Ultrastructural studies revealed a reduced percentage volume of T-tubules /9/ and a decrease in the 7-9 µm intramembranous particles of freeze-fractured sarcoplasmic reticulum /19/. The decrease in Ca^{2+}-sequestration by the sarcoplasmic reticulum is paralleled by a reduction in the cytosolic Ca^{2+}-binding capacity. Stimulation induces a rapid decrease in parvalbumin which is no longer detectable in the chronically stimulated fast-twitch muscle after 28 d /14, 22/.

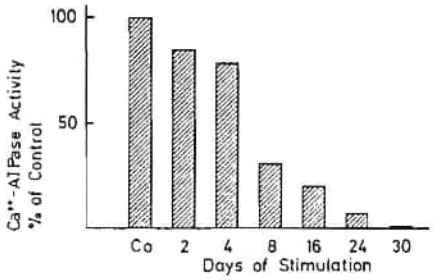


Fig. 5

Decrease in Ca^{2+}-dependent ATPase of the sarcoplasmic reticulum during increasing periods of stimulation /14/. Activities of the stimulated muscles have been referred to those of the unstimulated contralateral (Co = 100%) muscles.

Contractile Apparatus

After only a few days of stimulation changes are seen in contractile properties. There is an increase in time to peak of isometric twitch contraction and an increase in the half-relaxation time /3, 7, 11, 12, 18/. These early changes are most probably due to the above described alterations of the sarcoplasmic reticulum /12, 18/. A decrease in the maximum rate of rise of tetanic tension which is observed after prolonged stimulation /16/, is related with progressive changes in the properties of myosin, i.e. a decrease in the Ca^{2+}-activated myosin ATPase /16, 23, 24/ and (Fig. 6) a conversion of the myosin light chain pattern /12, 16, 23-27/. Long-term stimulation induces an almost complete replacement of fast by slow myosin light chains. A decrease in N-methylhistidine content points to additional changes in the myosin heavy chain composition /28/. The conversion of fast to slow myosin is evident from immunohistochemical studies and from histochemical staining for myofibrillar actomyosin ATPase which shows a complete transition of fast (type II) into slow (type I) fibres after prolonged stimulation /27/.

Changes in the protein composition of the contractile apparatus are not restricted to the thick filament. Studies on the subunit composition of tropomyosin, a main component of the thin filament, revealed changes indicating a fast to slow transition /29/. The transformation of the contractile apparatus is furthermore relevant from an increase in the thickness of the Z-disc /30/.

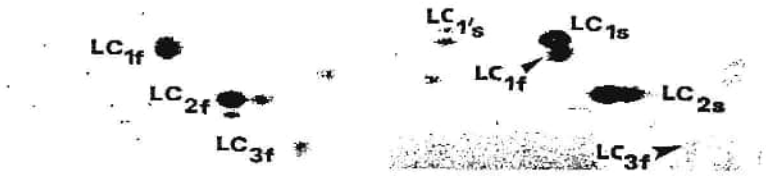


Fig. 6

Changes in the pattern of myosin light chains (LC) after prolonged (84 d, 24 h/d) indirect stimulation of rabbit tibialis anterior muscle. Myofibrillar proteins were separated by two-dimensional electrophoresis. Only the region of the LCs is shown. Control muscle left, stimulated muscle right. Note the replacement of the main fraction of the fast (f) myosin LCs by slow (s) myosin LCs. The stimulated muscle contains no LC2f and LC1f has been largely replaced by LC1's and LC1s. LC3f is markedly decreased.

Time course of transformation

Studies on the time course of the stimulation induced changes suggest a sequential transformation of the fibre. The decrease in parvalbumin content, the changes in composition and function of the sarcoplasmic reticulum, as well as transitions in the enzyme activity and isozyme patterns of energy metabolism precede by far the changes in tropomyosin and myosin /14, 26, 29/. These results indicate an ordered sequence in the transformation of the various functional systems of the muscle fibre which respond with different thresholds. Thus, the transformation of the sarcoplasmic reticulum and of the enzyme pattern of energy metabolism is complete before major changes are detectable in the myofibrillar proteins /14, 26/. These findings indicate that the conversion of the muscle results from a transformation of the pre-existing fibres and not from a replacement of fast-twitch by newly formed slow-twitch fibres.

The coexistence of different fibre type specific proteins within the same fibre /25, 27/ points to an altered program of gene expression. Recent studies of this laboratory /31/ have shown that chronic nerve stimulation elicits profound changes in transcriptional activity. The detection of mRNA species coding for proteins specific of slow-twitch fibres suggests that the transformation of fast-twitch muscle by chronic stimulation is caused by an altered gene expression, i.e. a switch from genes coding for fast muscle proteins to genes coding for slow muscle proteins.

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IV.

MODIFICATION OF COMPLEX MOVEMENTS BY ELECTRICAL STIMULATION [x]

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SUMMARY

Complex movements of an abnormal motor system may be modified by efferent, afferent or central stimulation. Clinical examples for each type of stimulation are given: a paraplegic for efferent and afferent stimulation, a hemiplegic for afferent stimulation and one M.S. patient and one head trauma patient for central stimulation.

Modification of abnormal motor control may be achieved by electrical stimulation in several ways. Regarding the neurophysiological mechanisms and structures which are activated by stimulation the following division is proposed:
- efferent stimulation
- afferent stimulation
- central stimulation.

In the following paragraphs each method will be briefly illustrated with examples of FES and therapeutic stimulation for treatment of spasticity.

Efferent stimulation

Direct stimulation of the efferent nerves produces muscle contraction which may generate useful, functional movements. The best known example of this technique is the electronic peroneal brace (1). In order to activate more than one muscle, multichannel stimulators have been introduced for upper and lower extremities. Each muscle group to be stimulated requires its own stimulator and at present stimulators with up to six-channels (2) have been applied in the clinical setting. They are used for gait improvement of hemiplegic patients, whereas two channels are already sufficient for standing of paraplegic patients (3). In multichannel stimulation of lower extremities the generation of control signals is not too difficult since gait is a cyclical process. In upper extremities however the control signals represent a real limitation. Except for minor "subroutines" not much can be programmed for movements of arms and hands. Therefore each individual paralyzed muscle has to be under voluntary control through one control site. For more than two or three sites the learning periods of the

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patient become exceedingly lengthy and may ultimately result in the rejection of the system. Thus at present very few multichannel stimulators are used for upper extremities (4) and advances in control strategies and technology will be required before further progress in this area is to be expected.

Afferent stimulation

Afferent functional stimulation is obtained by stimulating skin receptors, nerve endings of the skin and lowest threshold fibers in afferent nerves. Such stimulation triggers reflex patterns at various segments of the spinal cord and thus produces complex movements. A promising combination of efferent and afferent stimulation is the alternating stimulation of legs in paraplegic patients (3). In the swing phase efferent FES is applied to the quadriceps of one leg and afferent stimulation to one of the pure sensory or mixed nerves (e.g. n.saphenous) of the other leg where a flexion response is produced. After a double support phase when both knee extensors are stimulated, the stimulation pattern is reversed and simple walking is achieved (Fig. 1).

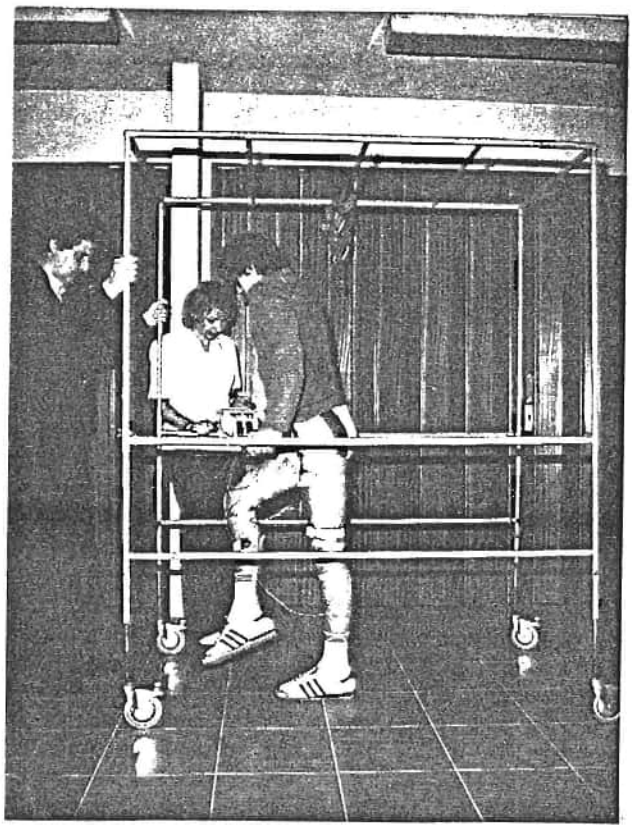


Fig. 1 Paraplegic patient walking with FES in a special walking frame. (With permission from A.Kralj and T.Bajd)

Afferent stimulation is also achieved during efferent stimulation since nerves always contain both types of fibers. Proof that afferent fibers are stimulated during efferent stimulation are sensation and therapeutic effects which outlast the duration of stimulation. It has been shown that efferent stimulation improves volitional control (4) (5)(6)(7) but it may also reduce spasticity (8)(9). Spasticity was measured with an electrohydraulic system with positional feedback control (Fig. 2). With position as input signal, the resistive torque

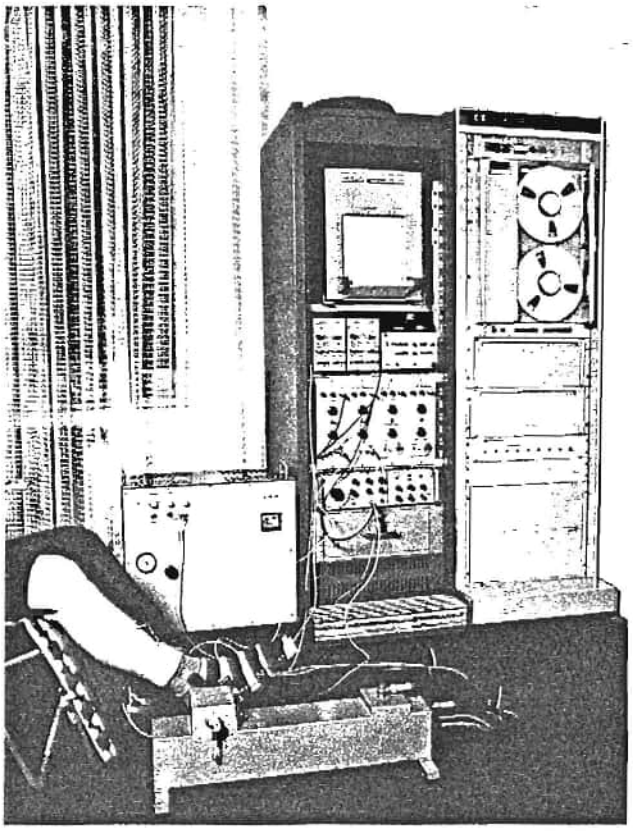


Fig. 2 Electrohydraulic system for measuring spasticity

of the ankle joint is measured as a quantitative parameter of spasticity.

A typical record of such measurements from a hemiplegic patient is shown in Fig. 3. The left side of the data shows tonic activity in both antagonists and a peak to peak resistive torque of about 8 Nm. After the application of reciprocal cyclic stimulation (1 sec on 1 sec off) to the triceps surae and tibialis anterior for 15 min with conventional stimulation parameters (40 Hz, 300 µs) the signals in Fig.3 right were recorded. The EMG practically disappeared and the resistive torque was reduced to 4 Nm. While not always such therapeutic effects were obtained it seems that about 50 % of the patient population with hemiplegia and spinal cord injury might benefit by therapeutic effects of electrical stimulation.

Central stimulation

If afferent stimulation produced functional movements of several muscles, central stimulation may enhance locomotor capabilities of the whole extremity. The best known technique of such stimulation is epidural spinal cord stimulation (10) but stimulation of cerebellum and cortex have been explored as well. All these methods seem to produce general facilitation of locomotor centers and thus enable improved execution of complex movements. From a series of measurements on spinal cord stimulated patients, let us present data on two patient who are using epidurally implanted electrodes at the thoracic level.

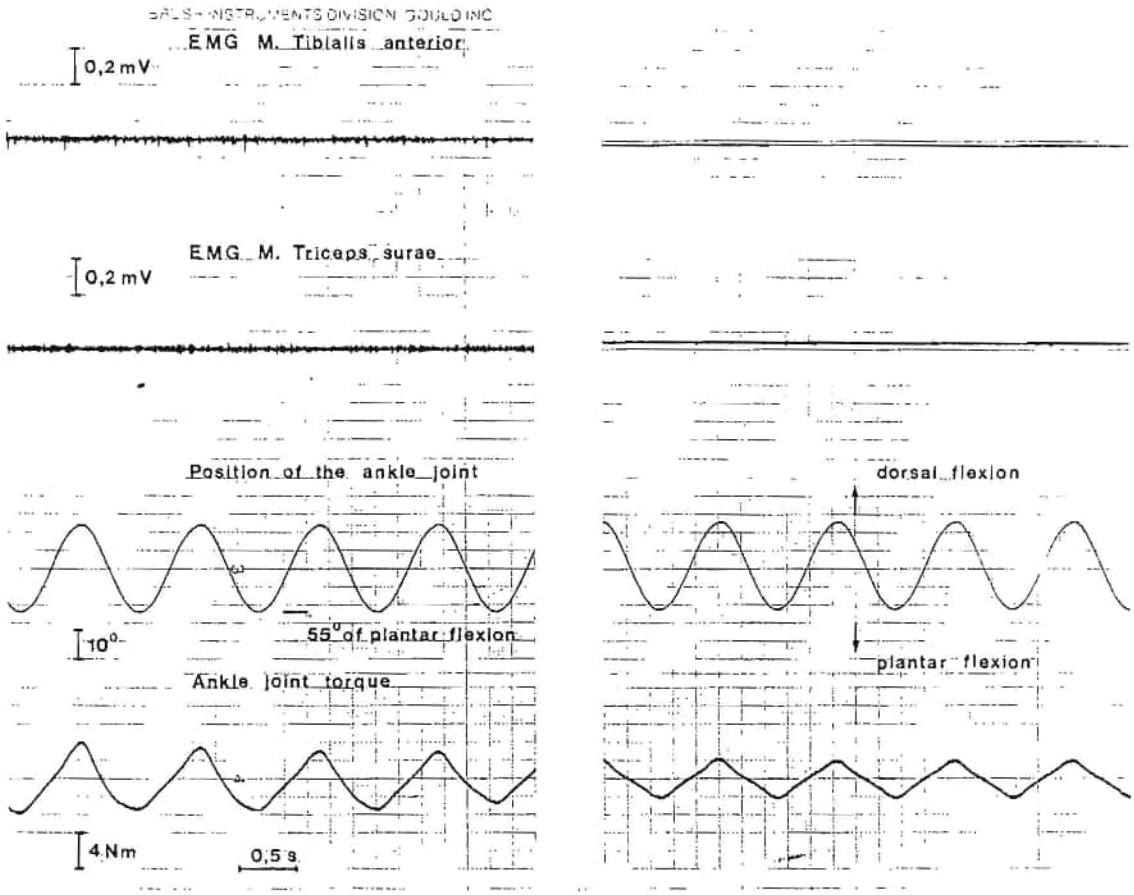


Fig. 3 Effect of electrical stimulation on spasticity

Fig. 4, left shows the record of a MS patient who is using continuous spinal cord stimulation for over three years. To this patient the stimulation was switched off for about 80 hours and then the measurement was taken again (Fig. 4, right). It is obvious that the lack of stimulation caused increased spasticity which may be observed from the torque records and to a smaller degree from the EMG. Another example is shown in Fig. 5.

A patient with extrapyramidal syndrome was using spinal cord stimulation for several years but then stimulation was interrupted for two months. At that time the upper record of Fig. 5 was taken. It is the goniogram of his knee when it was released from full extension and represents a quantification of the Wartenberg pendullum test for spasticity. It can be seen, that the knee only slowly and with minor oscillations approaches the resting position. The patient was then stimulated for 8 days and again the knee-goniogram was taken. The result is the lower record in Fig. 5. After the knee was released it returned to its initial position earlier and with greater speed which indicates a markedly reduced spasticity.

All the examples discussed indicate that electrical stimulation might be a useful method in improving abnormal movements or postures of the motor system. Further advances in technology and neurophysiology should contribute to the development of specific techniques for different patient cathegories as well as towards a better understanding of the physiological mechanisms involved in the therapeutic effects.

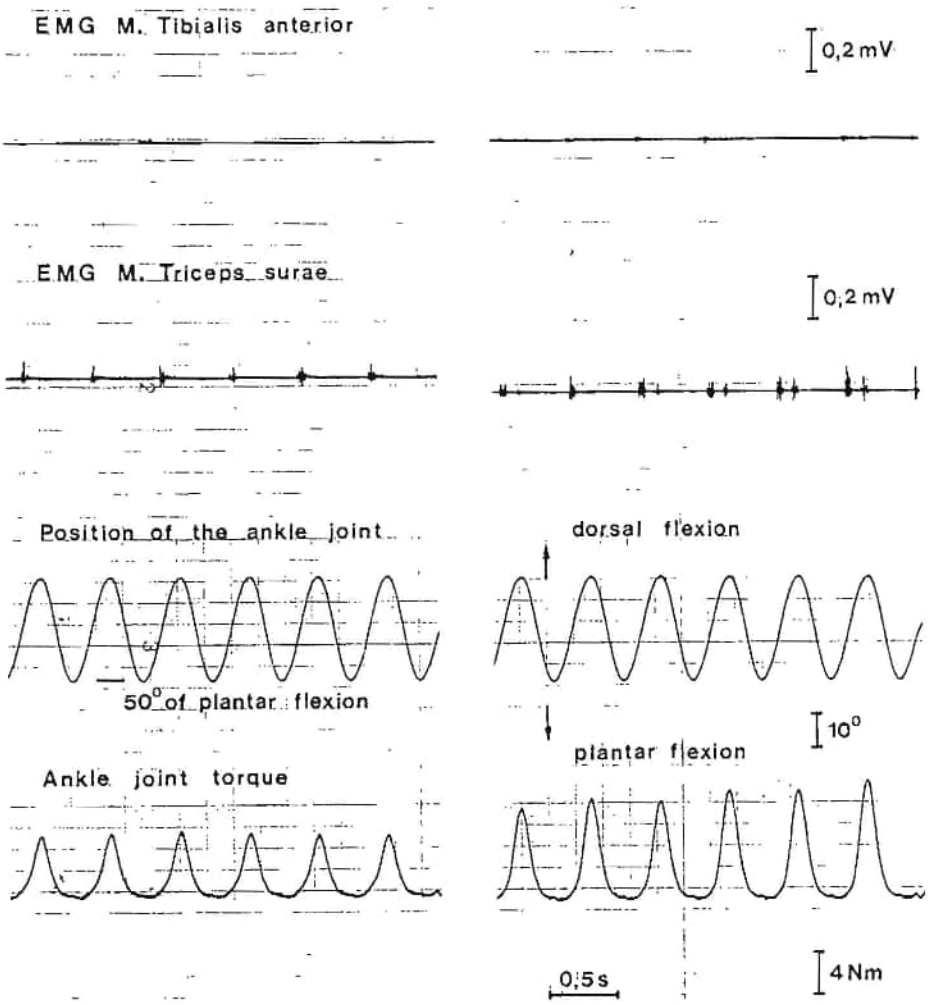


Fig. 4 Effects of spinal cord stimulation on spasticity in M.S. patient.

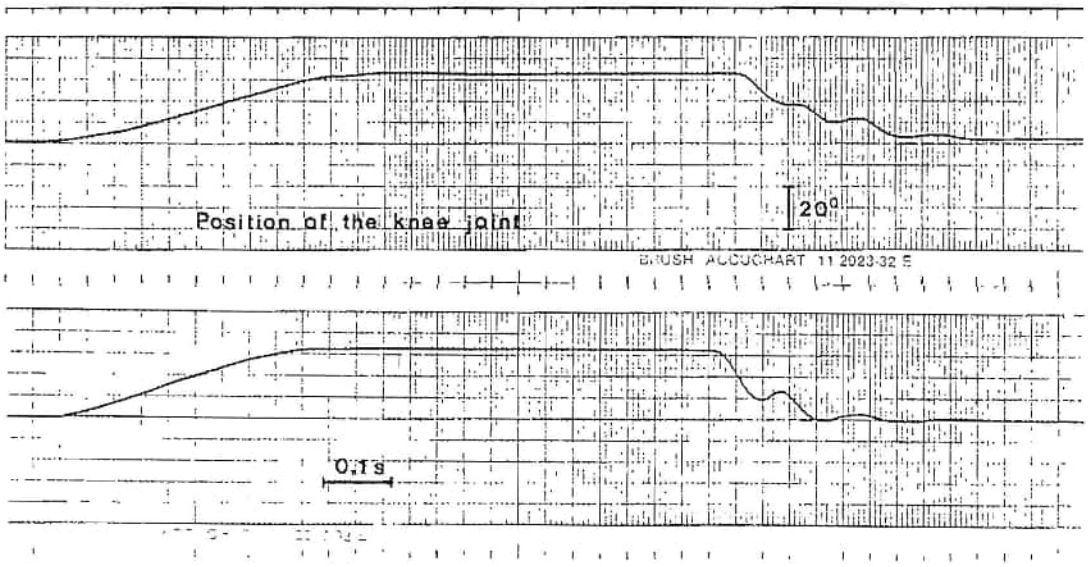


Fig. 5 Effect of spinal cord stimulation on spasticity in head trauma patient

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V.

THE APPLICATION OF FUNCTIONAL MUSCLE STIMULATION TO PARALYSED HANDICAPPED

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The area of Functional Stimulation (FS) was for 15 to 20 years an almost neclected field with research groups basically in Cleveland, Los Angelos and Ljubljana carrying the idea and developing the foundations of the field. During the recent years this situation has drastically changed as this conference and a respectable number of other conferences around the world prove. Therefore it might be assumed that the attendance of a specialized conference as this one is familiar with the basics of the field. This introductory talk will therefore concentrate more on an overall evaluation of where we stand now and what is still most prominently missing in FS of the extremities.

The present state of Functional Stimulation.

The body of knowledge we can foot on today are at first the stimulation parameters. It is possible to stimulate centrally paralyzed muscles with the motor neuron and the nerve connection still intact dependably. Even with electrodes implanted within the muscle the motor nerves are stimulated, because they have the lower threshold. Stimulation pulses of short duration need the least energy. The charge passed through the nerve membrane is the factor evoking the action potential. Therefore current controlled pulses of about 20 to 300 µsec duration for surface electrodes and 1 to 300 µsec duration for implanted electrodes are adequate stimulus parameters. To avoid a dangerous increase of the voltage when the impedance of the electrode rises, a voltage limitation might be provided. A more favorable solution is the measurement of the electrode impedance with a switching off circuit for too high impedances. This avoids the danger of too high current densities if the electrode contact is diminished. The use of bipolar pulses is necessary with implanted electrodes to reduce the electro-chemical reactions. But bipolar pulses are also advisable with surface electrodes for the same reason

to reduce skin irritation. For short pulses the positive component may reduce the stimulation effect of the negative one. This might be avoided by introducing a short delay, about 100 µsec, between the negative and the positive pulse component (For more details see i.e. Mortimer 1980). With these stimulus parameters centrally paralyzed muscles may be adequately stimulated and retrained to build up muscle force again. The training of the muscles improves also the total situation of the limb and the skin condition.

Through adequate positioning of surface electrodes different muscles or muscles groups may be stimulated and coordinated to achieve certain basic functions. The paper presented by Dr. Vodovnik will treat this point explicitly. A more specific stimulation of the muscles may be achieved by electrodes implanted within the muscles itself. This method was developed especially by Mortimer using thin coiled wire electrodes led through the skin. By this mode of application much less current is needed and the costimulation of the pain sense is avoided. The electrodes may also be positioned around or close to the nerve itself. But this results in a more global muscles stimulation and in addition the connective tissue of the nerve tends to react very strongly to the electrode and this may damage the nerve severely. In the practical application of FS to the handicapped all these methods allow to elicit very basic movements: A few modes of hand grip or single supported walking request great effort from the handicapped. In addition it is very difficult for the handicapped to control the functional stimulation procedure, especially for a quadriplegie, because he has only few motor functions left. But in general consciously only one to two degrees of freedom may be controlled continously and this is not sufficient for a more extended application of functional stimulation.The lack of an adequate control and a general aversion of the handicapped against the technical support system prevent the routine use of FS, although it might permit the handicapped i.e. a daily practice of his hands otherwise not achievable.

Future directions of development.

The considerations of improving and extending the stimulation procedure aim mainly in three directions:

a) Improving the (mechanical) handling of the system including the application of the stimulus
b) Extending the control procedures and the coordination of the muscle contraction

c) Incorporating the initiation and execution of the movement in a more natural way into the movement pattern of the handicapped.

Implantable stimulators.

a) In general it is hoped to make the stimulation apparatus more compatible with the patient by using implantable stimulators with wireless energy transmission. Simple stimulators are implanted already for quite a while. For instance the implantable stimulator developed by the Ljubljana group for perioneal stimulation fulfils its purpose principally well. To restore more complex movements multichannel stimulators are needed and a number of them are in the procedure of development. The stimulators have integrated circuits as a core with coded addresses for the individual channels. One principle consists of a central stimulator unit with leads to the stimulating points. The advantage is a good energy transmission with the central unit located beneath the skin. The disadvantages are the installation of the wires and the loss of the total stimulation unit in the case of a failure or an infection. Examples for this concept are a 16-channel stimulator developed by Thoma and an 8-channel stimulator by Peckham and his group. - Another principle is chosen for a distributed stimulator system by Hildebrandt and the author, consisting of a separate small stimulator for each channel, which is implanted independently. 8-channels may by addressed by one antenna. Aside of the development of these stimulators the stimulation units have to be made more patient compatible in such a way that the handicapped and his company may mount the system and care it themselves in order to ease the feeling of the dependency.

Control of the muscles contraction.

b) Up to now more complex movements induced by FS as walking or special modes of handgrip are executed in a preprogrammed manner. This requires a very stable electrode position - stimulus - muscle contraction relation and in addition tedious programming procedures. At least if muscle groups controlling larger joints are involved, as the knee, this condition is no longer fulfilled. In this case simple sensors as potentiometers are used to close the feedback loop and garantee the execution of the programmed movement pattern. In general as soon as the muscles of a limb are paralyzed more extendedly feedback is needed to control the movement. The first attempts undertaken to control muscle contraction proved what was to be expected: Muscle contraction is a multifold

nonlinear process in time and space , which can not be controlled by a simple controller with fixed or adaptive parameters. A control procedure applicable in this situation was developed by Nguyen and the author. The authors assumed a second order model of the muscles and the mass of the limb and identified the parameters of this model in every measurement cycle. To picture the procedure: The model parameters are moved along the surface of the nonlinear space always for a short distance. This gives a sufficient traking characteristic if the identification is executed fast enough (20 times per second). In addition the control procedure allows to separate the position and the force component of the movement and to identify the characteristic of an external object linked to or handeled by the limb.

The control of muscle contraction is only the lower stage of the control procedure needed to execute a limb movement. In addition the limb has to be guided along its movement trajectory. An appropriate way to achieve this might be by applying the Lagrange method of computing the momentum of forces in analogy to a technic used in roboties. According to the resulting momentum of forces the stimulation patterns of the different muscle groups involved in the movement have to be computed to obtain the coordinated movement.

In order to install the control the appropriate sensors are needed. This is so far not sufficiently covered. Because of the number and the construction of the joints numerous sensors are needed. On the other side the number of sensors tolerated by the handicapped might be very limited. Attempts with various principles to measure position and force are undertaken, good solutions are not yet in sight.

Control of the stimulation by the handicapped.

c) A number of methods are used to allow the handicapped himself to control the initiation and execution of FS. Moving a potentiometer with the shoulder, a joystick, a handvail, or the head, flipping switches or using electromagnetic coupling or a Hall generator, all these methods serve their purpose more or less sufficiently. As it seems to be right now for the specific situation of each handicapped a special system has to be fitted to match him best. The speech processor might turn out to be a more general control system especially suited for the working situa-

tion when the mouth is not occupied with other tasks. If the movement of a whole limb has to be controlled by the handicapped the trajectory of movement as the input to the following control stages has to be determined in advance for the initiation of the movement. The distance and angle in space of the object to be reached by the handicapped might be determined for instance by the use of an ultrasound beam. But the problem of the transposition of the coordinates relative to the base of limb has yet to be solved.

Considering the length of way which has been passed over so far to achieve what we can accomplish today in FS at least the same amount of effort has to be invested before the Functional Stimulation of the limbs might be used as routinely by the handicapped as we use today our motor cars.

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MODELLING NEURAL STIMULATION x)

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SUMMARY

The Frankenhaeuser-Huxley (FH) model of myelinated nerve is a system of five nonlinear differential equations which describe the space-clamped response of a neural membrane to current stimuli injected at a single node of Ranvier. The model equations are summarized in /1/ and will not be repeated here.

A modified version of the FH model, encompassing more factors of threshold significance in practical in-vivo stimulation scenarios, was used to predict threshold amplitude and charge functions for biphasic ramp and sinusoidal current stimuli. The model results have been found to compare favourably with experimentally determined threshold functions from guinea pig eighth auditory nerve, and from percutaneously and transcutaneously stimulated human median nerve. Threshold information derived from the model has been used to optimize stimulus waveform parameters with respect to a two component stimulation damage model. Such optimized stimuli are capable of eliciting active responses from neural elements while minimizing stimulus induced damage.

MATERIAL AND METHODS

All model computations were performed on a PDP 11/23, using a modified predictor corrector algorithm coded in Pascal, with a phase-based threshold detection algorithm /2/ Model parameters were selected to emulate each of the experimental stimulation scenarios described below.

Human Median Nerve.

Threshold data were collected for ramped stimuli both transcutaneously (TR) and percutaneously (PR) applied. In both cases, biphasic ramp stimuli were generated using two DISA 15E07 stimulators and a DISA 15G01 delay unit. In the case of TR stimuli, stimulation was through two saline moistened ring electrodes placed around the fourth finger. For PR stimulation, current was passed through two needle electrodes placed transverse to the median nerve at the wrist. Pulse widths ranged from 20 to 100 μs, and phase delays from 20 to 80 μs.

For both TR and PR stimulation, pulses were applied at a rate of 1 Hz. Responses were recorded using a near-nerve technique /3/ with electrodes inserted at the upper arm. Recorded responses were amplified by a DISA 15C01 amplifier, then passed to a DISA 15G01 signal averager where sixteen responses were averaged to reduce background noise.

The experimental threshold data were measured relative to an arbitrarily chosen set point - a

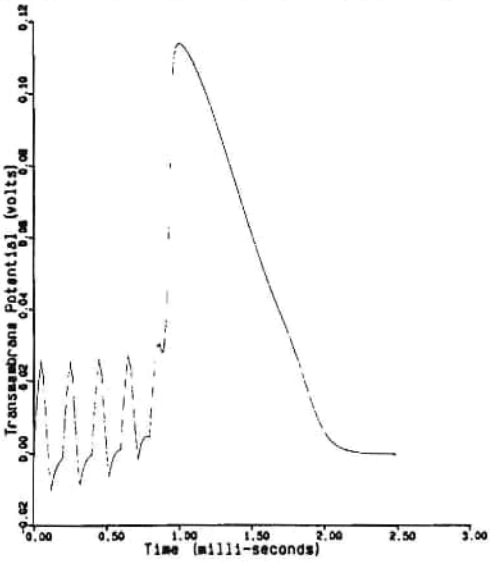


Fig. 1: Model threshold response to 5 pulse train of biphasic 1.46 mA/cm^2 square pulses, 50 μs duration, 20 μs phase delay, 80 μs between pulses.

stimulus with an amplitude somewhere between sensory threshold and maximal response, with a mid-range stimulus parameter set (pulse width 50 μs, phase separation 50 μs).

Guinea Pig Eighth Auditory Nerve.

Single cycles of sinusoids of frequency from 500 Hz to 16 kHz, were presented to stimulus electrode pairs through a constant current stimulator. The electrode pairs were separated by 1.5-2 mm along the scala tympani of anaesthetized pigmented guinea pigs. The brachial potential resulting from these transient stimuli was sampled at a rate of 25 kHz for 10.24 ms and averaged 50 times with a Nicolet MED-80 computer. The averaging was repeated while the intensity of the stimulating current was adjusted to estimate the threshold for an evoked response. The threshold was established as a minimally detectable evoked waveform on the cathode-ray computer display /4/.

RESULTS

Human Median Nerve - Percutaneous Stimulation.

The relative threshold amplitudes of model and experimental data are shown in Fig. 2. In general, the comparison is favourable with the same trends exhibited by both data sets. The greatest discrepancies occur at low pulse width and short phase delay where the model data consistently under-estimates the required threshold current.

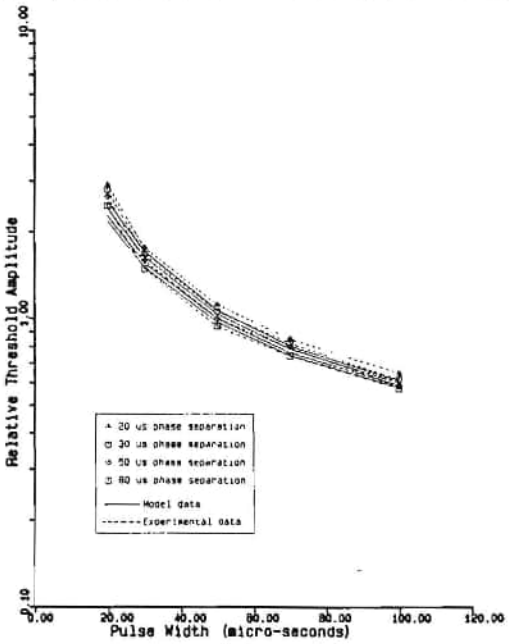


Fig. 2: Percutaneous median nerve and model data. Reference stimulus is 50 μs in duration with a 50 μs phase delay.

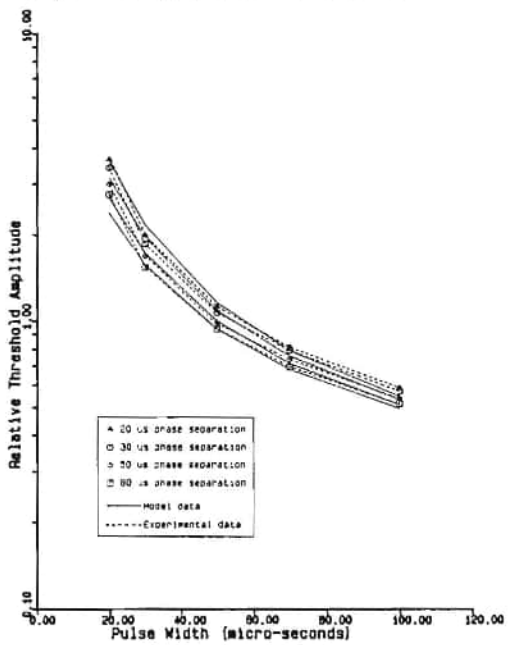


Fig. 3: Transcutaneous median nerve and model data. Reference stimulus is 50 μs in duration with a 50 μs phase delay.

Human Median Nerve - Transcutaneous Stimulation.

The relative threshold amplitudes of model and experimental data are shown in Fig. 3. The model data was generated assuming a fibre diameter of 15 μm for the largest fibres of the median nerve. As with the percutaneous case, correspondence of the two data sets is generally favourable. However, for all phase delay settings, the model data at long pulse durations is consistently lower than the measured threshold amplitudes. It is possible that nearby nodal membranes not accounted for in the model, may inflate the measured thresholds - especially in the case of longer duration stimuli /5/.

Guinea Pig Eighth Auditory Nerve.

The sinusoidal model threshold function appears similar to the cochlear threshold data with the exception of a higher 'best' frequency (Fig. 4). Stimulation through electrodes in the cochlea involves unknown combinations of multiple nodal, somatic and dendritic membranes, but in spite of these qualifications the threshold curves are similar.

Stimulus Optimization.

A minimum damage stimulus parameter set was derived using threshold results from the FH model, and assuming a parametrized two-component stimulus damage model. The damage model assumes charge, Q, and amplitude, H, damage components /6/, /7/. It expresses a damage measure, D, as a function of stimulus duration T, which is the sum of charge and amplitude dependent components. The function is parametrized by a factor, γ, which indicates the relative importance of the two damage mechanisms, with $0 \leq \gamma \leq 1$:

$$D(T) = \gamma H + (1-\gamma)Q$$

The minimum damage pulse widths for a biphasic pulse with 20 µs phase delay, and for a

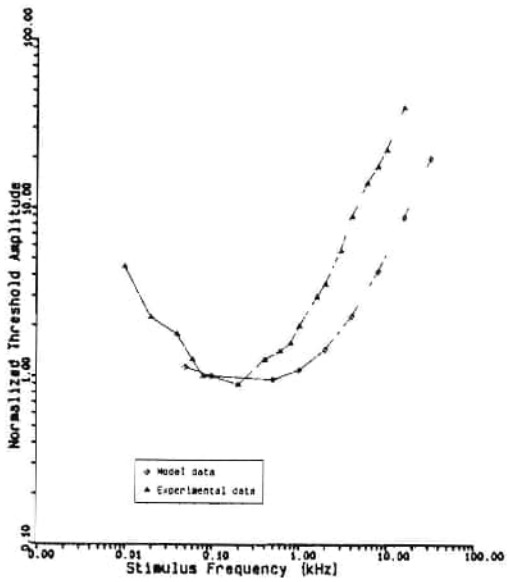


Fig. 4: Eighth auditory nerve and model data - threshold functions for single cycle sinusoidal stimuli.

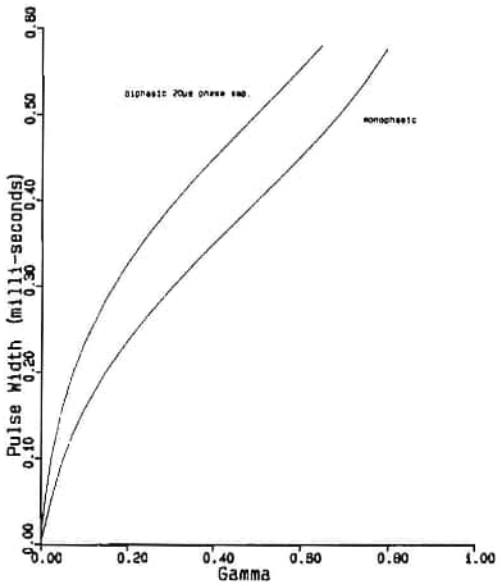


Fig. 5: Optimal pulse durations for biphasic 20 µs phase delay and monophasic stimuli.

monophasic pulse, are shown in Fig. 5 as functions of the parameter γ. If $\gamma=1$ (all amplitude related heat damage), a long duration low amplitude stimulus is best. If $\gamma=0$ (all charge related damage) then a short duration high amplitude pulse is optimal.

DISCUSSION

Changes made to the FH model greatly enhanced its ability to simulate the experimental situations under investigation. Most notably, the temperature correction coefficients, evaluated at 33°C, were extrapolated significantly beyond the 22.5°C limit of Frankenhaeuser's original data base. In addition, a passive chloride system was introduced to facilitate calculation of temperature influences upon threshold potential. Simulation of adjacent passive nodes of Ranvier - one on either side of the active FH node - further improved model predictions. In /5/ McNeal noted that five passive nodes on either side of the nodal site of stimulation, were required for accurate simulation.

Careful definition of experimental protocol in the median nerve case addressed two significant differences between model and experiment which could not be reconciled with simple model enhancements. These differences concern the simulation of a space-clamped fibre response compared to an in-vivo saltatory response; and in-vivo stimulation of many nerve fibres with subsequent measurement of a compound action potential (CAP) compared to simulation of a single fibre response. These two factors were addressed by assuming the CAP to be a linear superposition of single fibre responses; by assuming identical active populations of fibres with an identical recruitment order for stimuli with the same response level /8/; and by measuring stimulus threshold with respect to a fixed reference pulse.

The correspondence between experimental data and model predictions, while far from exact, is encouraging. The discrepancies reveal a need for closer examination of the modelling assumptions and the physiological conditions under which the data is collected. Although model derived data can never replace physiological observations, it can serve to indicate threshold trends and to assist in building a qualitative neural transduction data base.

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DYNAMIC CONTROL OF MUSCLE FORCE BY HIGH FREQUENCY ELECTROSTIMULATION

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SUMMARY

Physiological control of joint movement consists of interaction of four basic processes; rate of action potentials in individual motorunits, recruitment of motorunits of a muscle according to their size, proprioceptive/kinesthetic feedback and synergy of agonist/antagonist muscle pair.

When attempting to restore function to paralyzed extremity joint, application of variable pulse rate electrostimulation alone is not sufficient due to; 1) Jerky unfused force at rates below 25-30 pps, 2) regulation of only the upper 20% of maximal force for rates between 30 to 70 pps, and 3) rapid fatigue at rates above 50 pps. (1, 6)

Pulse width or amplitude variation is also deficient due to the low excitation threshold of large nerve axons which correspond to white, fast twitch and fast to fatigue muscle fibers with high innervation ratio which produce large initial force and force increments. True recruitment, i.e. small motor units first and larger units later could not be accomplished by direct stimulation. The results are large initial force, non-linear force response and rapid fatigue.

Our technique to induce true recruitment consists of dual electrode system on the muscle nerve. The proximal electrode delivers supramaximal stimulus at rates between 35-50 pps to induce smooth, fatigue resistant contraction in the muscle. The distal electrode delivers pulses at 600 pps with variable pulse amplitude or width. Our previous studies as well as others (2,3,4,5) show that high frequecny stimulation selectively blocks nerve action potential arrival to the muscle according to axon size. Therefore, when the high frequency stimulus amplitude is reduced from suprathreshold, the small axons with high threshold escape the block and induce weak muscular contraction first. Further reduction in block pulse amplitude allows larger fibers to become active and to gradually contribute to the force build-up such as in true recruitment.

Based on the high frequency induced recruitment technique we designed a Recruitment Based Synergistic Control System (RBSCS) incorporating Myoelectric Feedback (MEF) as artificial proprioceptive feedback as shown in Figure 1. In order to specify the various component transfer functions, as well as to demonstrate the capability of the system in dynamic control, we proceeded to develope the recruitment model of the muscle.

MATERIALS AND METHODS

The isometric Soleus/Gastroc muscle group of the cat was used as the experimental model. A proximal wrap-around bipolar electrode delivered the background suprathreshold stimulus at 35 pps from a Grass stimulator. The distal electrode delivered a sinusoidal envelope superimposed on DC voltage and modulate by 100 uS pulses at 600 pps stimulus derived from a custom designed and fabricated

stimulator.

The sinusoidal envelope frequency was varied from 0.1 H_z to 6 H_z and its amplitude was experimentally calibrated between subthreshold to suprathreshold of the sciatic nerve.

Recordings of muscle force and sinusoidal envelope were made simultaneously for frequency and time response analysis.

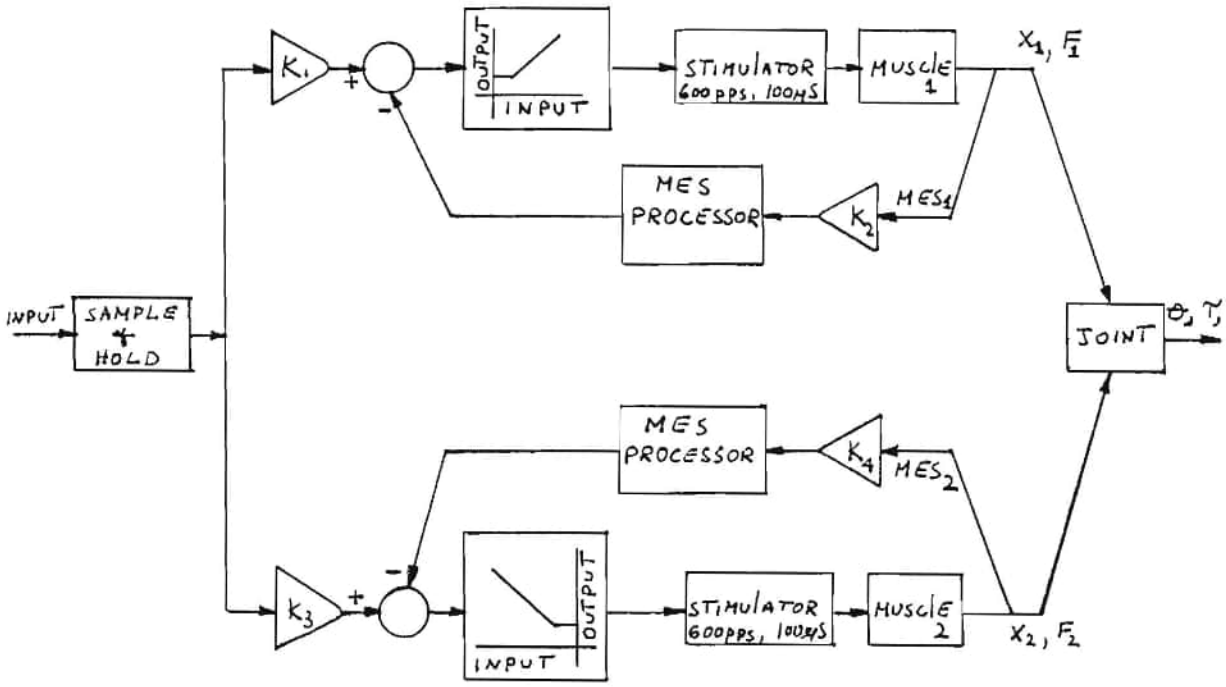


FIGURE 1

RESULTS

Analysis of the force frequency response for three cats is shown in Figure 2 as normalized gain as a function frequency. It is evident from the Figure that the general force response is consistant from animal to animal and follows the same pattern.

Figure 3 is a Bode plot of the frequency force response of one cat. Experimental curve fitting with a DEC-2020 computer generated the transfer function

$$G(jw) = \frac{K(1 + .026jw)}{(1 + .05jw)^2 (1 + .04jw)^2}$$

The value of K for this cat was 9.7, but was different for other animals probably due to variations in muscle tone, nutrition, age and other metabolic factors.

Superimposed on the experimental data is the actual curve generated directly from the derived transfer function. It is apparent that G(jw) is closely estimating the experimental data.

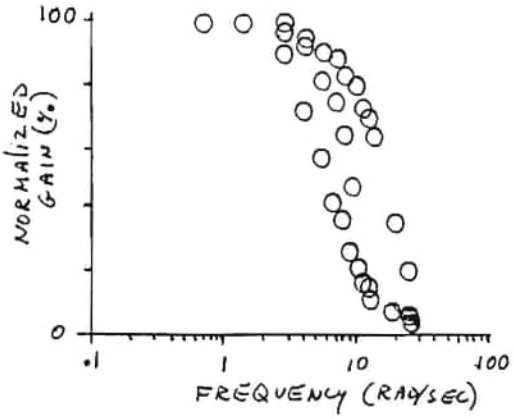


FIGURE 2

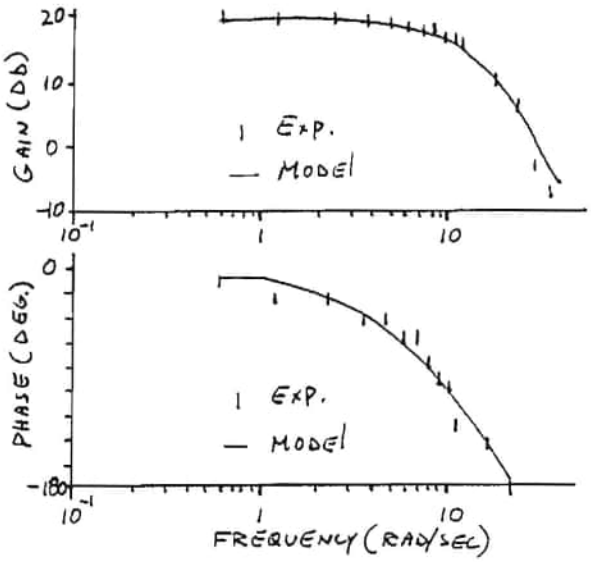


FIGURE 3

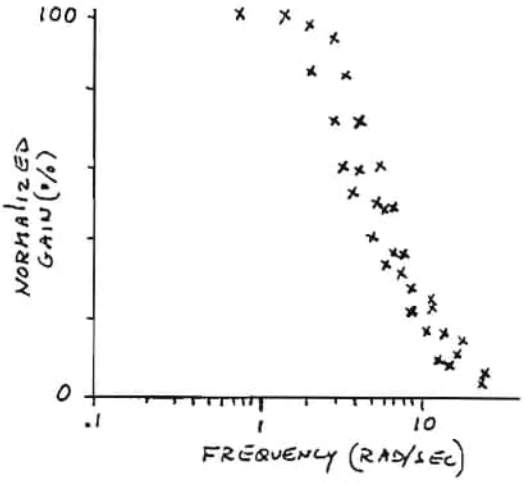


FIGURE 5

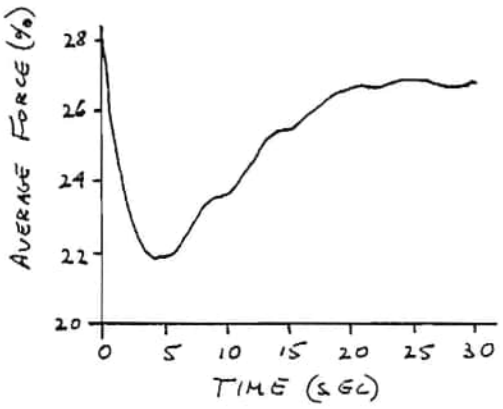


FIGURE 4

Time response analysis of peak to peak force is presented in Figure 4. It could be observed that muscle force has a practically instantaneous rise time followed by 18% undershoot peaking at 4 sec. The force then recovers to its original level in the following 15 sec.

Figure 5 is a plot showing normalized force as a function of frequency for perturbation levels of 20%, 40%, 60% and 80%. The close response pattern indicates the linearity of the transfer function with respect to perturbation levels.

CONCLUSIONS

Based on the data and its analysis, the following conclusions could be made:

1. The recruitment process induced by high frequency stimulation of motor

axons is linear and independent of force perturbation level.

2. The recruitment model describes a fourth order system with double poles at 20 Rad/Sec, double poles at 25 Rad/Sec, and a zero at 31.4 Rad/Sec.

3. The time response demonstrates an instantaneous rise time, 18% undershoot at 4 seconds and settling time of 20 seconds. No significant steady state error was observed.

For design purposes of a functional neurostimulation control system, the data indicates that the time response should be modified to yield better transient characteristics, primarily in reducing the moderate undershoot and the long settling time. A closed loop system incorporating artificial proprioception as shown in Figure 1 will provide such improvements when properly designed.

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FATIGUE OF ELECTRICALLY STIMULATED MUSCLE

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SUMMARY

The time dependent behaviour of the wrist joint moment is studied and modelled mathematically as forearm muscles, activated by surface electrical stimulation, become fatigued. Continuous stimulation and stimulation interspersed with periods of relaxation are applied. The joint moment is now held constant as the muscle fatigues by controlling the stimulation current. The stimulation current magnitude is modelled as a time dependent function.

INTRODUCTION

Functional electrical stimulation of the limbs using surface electrodes is characterized by a high rate of muscle fatigue. As part of the development of a computer controlled system for simple functional movements of the arm [1], the fatigue characteristics of the arm muscles were studied and modelled. The nature of this system requires slow movements only; limited by the speed with which control is possible using vocal commands. Muscle contraction will be isometric in essence, accompanied by slow movements and periods of relaxation. The stimulation current amplitude used in the system to control the strength of the contraction will thus need continuous adjustment to generate a given force in the decreasingly responsive fatigued muscle.

Three sets of measurements are carried out on the muscles of the forearm of one healthy subject: (a) The time dependent behaviour of the isometric joint moment generated by different stimulation current levels. (b) The fatigue response of the muscle to different periods of stimulation/relaxation. (c) The time dependent behaviour of the stimulation current in generating given levels of joint moment.

The three sets of response curves were modelled mathematically such that the fatigue properties of the muscle and the required correction to stimulation current could be included in the control equations for the FES system.

EXPERIMENTAL METHOD

Experimentation was mainly carried out on the extensor carpi ulnaris (ECU) and the flexor carpi ulnaris (FCU) muscles. Figure 1 shows the experimental arrangement. Square wave double pulses (0.3 ms duration, 0.7 ms interval, 40 Hz frequency) are generated by a stimulator designed and built in the university. The signal passes through the muscle via a pair of long slender surface electrodes (cathode 3.0 cm x 1.0 cm, anode 3.0 cm x 0.7 cm). The upper arm is clamped at 90° abuduction, the elbow at 90° flexion, and the wrist and radioulnar joints at mid-range. The forearm is tethered by strings just proximally to the wrist joint. The hand is inserted into a plaster glove which immobilizes the fingers and enables transfer of forces to a triaxial dynamometer [2] via a universal joint arrangement. The dynamometer both restrains and monitors the three orthogonal components of the moment generated at the wrist and radioulnar joints. The dynamometer output passes to a microcomputer* which calculates the resultant joint moment and plots it on a monitor as a function of time. Additionally, the computer sends a signal to the stimulator controlling the stimulation current level. In the closed loop experiment the stimulation current level was

*Apple 2 plus

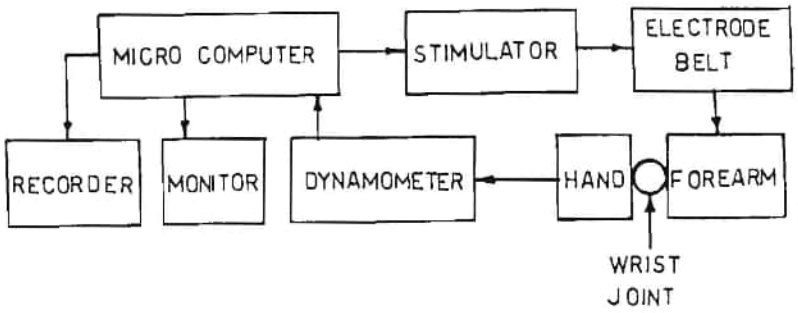


FIGURE 1.
DIAGRAM OF EXPERIMENTAL ARRANGEMENT.

continuously adjusted by an equation of the form:

$$I_{i+1} = I_i - K_1 e - K_2 \int e dt.$$

where I_i is the previous, and I_{i+1} the adjusted current level; K_1 and K_2 are constants, and e is the error in the magnitude of the generated joint moment.

RESULTS

Figure 2(i) shows the highly characteristic fatigue curves for isometric contractions of the ECU muscle. These curves are typical of all the muscles tested.

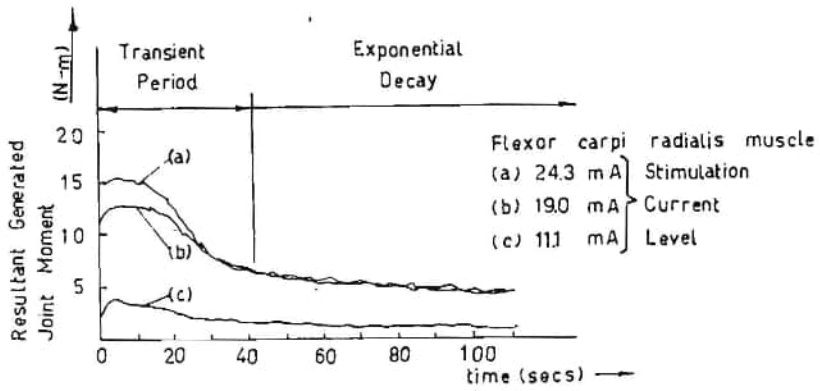


Figure 2(i).
The fatigue characteristics of muscle during continuous stimulation.

An initial transient period comprises a rise in the level of the generated moment, followed by a subsequent decline, falling to approximately one third to one half of the peak level after 30 to 40 seconds of stimulation. A slow exponential decay occurs thereafter. Measurements at different current levels show the magnitude of the transient peak to be more sensitive to the current level than that of the exponential decay. The duration of the transient period however seems unaffected by the current level.

Stimulation/relaxation cycles were carried out at three frequencies: 30 seconds stimulation, 30 seconds relaxation; 60 seconds stimulation, 60 seconds relaxation; and 120 seconds stimulation, 60 seconds relaxation. A typical result for the ECU muscle is shown in figure 3. The duration of the transient peak tends to shorten as the muscle fatigues, while the magnitudes both of the transient peaks and of the exponential decay region decline exponentially at approximately the same rate. Similar

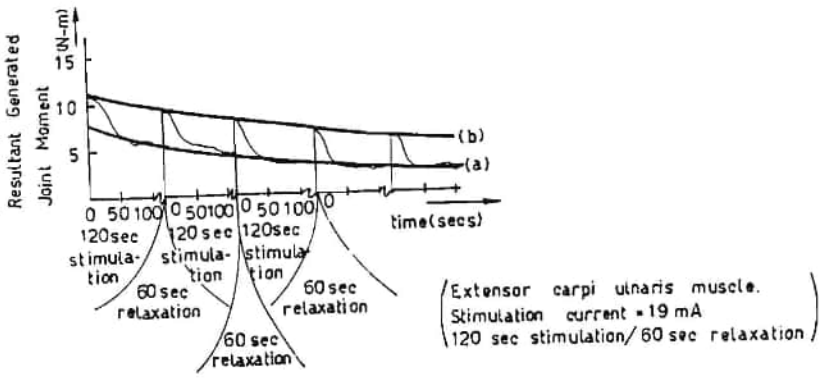


Figure 3.
The fatigue response of muscle during successive stimulation/relaxation cycles.

results were obtained for all muscles at the three stimulation/relaxation frequencies tested, the decrease in the duration of the transient peak and the rate of decay of the envelopes of the curves being greater as the stimulation period increases.

Figure 4 shows the average curves of the stimulation current level required to generate three constant magnitudes of the wrist joint moment as the muscle fatigues. The experimental results upon which curve (a) is based are shown. The curves show an

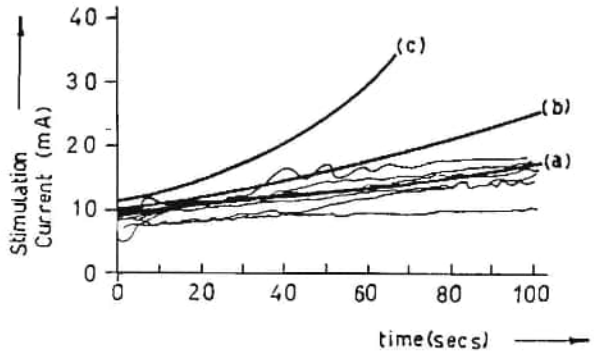


Figure 4

Time dependant behavior of the stimulation current in generating three constant magnitudes of wrist joint moment:
(a) 7.1 N-m (b) 10.6 N-m (c) 14.2 N-m

exponential rise in the current level during the duration of the tests. As the muscle fatigues, the curves fan out such that very high currents are required to generate the larger moments in the fatigued muscle.

MATHEMATICAL MODELS

Figure 2(ii) is a mathematical model of curve (a) in figure 2(i) using a Gaussian distribution function of the form:

$$M = K_o + K_1 e^{k_2 t^{k_3}}$$

where M is the generated moment, t is the elapsed time and K_o, K_1, K_2, and K_3 are constants. Adjustment of the values of these constants enables the function to be fitted to the experimental fatigue curve. This latter procedure was carried out on

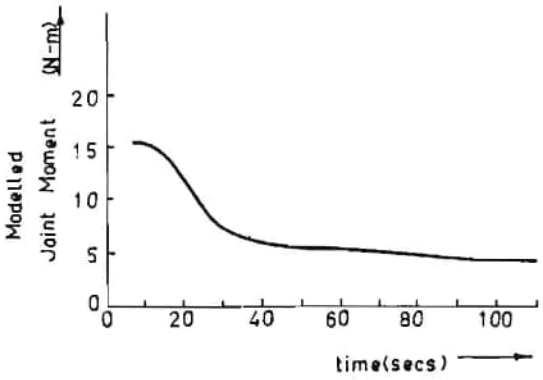


Figure 2(ii).
A mathematical model of the fatigue characteristics of muscle [Figure 2(i) graph (a)].

the microcomputer where the measured and synthesized curves could be compared directly.

The exponential moment decay seen in figure 3 was modelled using the same function, as was the exponential rise in the current in figure 4. As a numerical example of this function, we have for curve (a) in figure 4:

$$I = 1.91 + 7.69e^{0.0111t^{0.9}}$$

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CHANGES IN MIXED SKELETAL MUSCLE WITH LONG TERM INTERMITTENT STIMULATION

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SUMMARY

Recently there has been a lot of interest in the biochemical and physiological changes in muscle that has been subjected to periods of electrical stimulation. Our interest arose from our use of implanted stimulators for the treatment of scoliosis in children (1,2). Our initial studies suggested that the changes were similar to those reported for muscle subjected to exercise training programs (1,3,4). Our investigations have used long term intermittent studies on a mixed fibre type muscle (5). Both histochemical and physiological studies have been included.

MATERIALS AND METHODS

Animal Model: Twenty Crossbred pigs (6-8 wks; 13-16 kg.) were used for this study. Pigs are good models because the paraspinal muscles are composed of a mix of fibre types. The pig is also large enough that a totally implantable stimulator can be used, since there are serious technical challenges in trying to use any sort of external stimulator. Growth is rapid in the pig and the muscle bulk at all times is adequate to provide reasonable biopsies, without excising a significant part of the stimulated area.

Stimulators: The stimulators were designed and assembled by the senior author. The units consisted of two different types. The first was magnetically switched on/off using an external magnet. The output consisted of a train of AC coupled pulses running at 30 pulses per second, switched on and off by an envelope timer. The pulses were 1 ms. wide and 8 volts in output. The envelope timing was set at 1 sec. on, and either 1, or 4 sec. off for these experiments. The stimulators were cast in a filled polyester potting compound with a room temperature cure. They were coated with silicone rubber to enhance the tissue compatibility. The electrodes were platinum corkscrews, either straight (Medtronic Inc, model 3160) or at right angle to the leads (Medtronic, Inc. model 6917).

The second stimulator model was an automatic switching type (6). Pulse counting from a clock circuit was used to control timing parameters. It was set to cycle on for 15 hours per day, and off for 9 hrs. The other output parameters were the same. For both units, all timing parameters were set at the time of assembly by the selection of the timing components.

Strain Gauge: We designed a small strain gauge unit to allow us to measure the intramuscular tension developed by the paraspinal muscles in a non-destructive manner. Four SR-4 type strain gauge elements

were mounted in full bridge arrangement on the top and bottom of a thin (0.02 in) copper strip (3.5 cm long x 1.5 cm wide). Legs (1 cm high) were mounted on the ends of the strip, forming a "U" shape. Small surgical needles were inserted into the bottom edge of the legs, with the points exposed. The needles were placed into the muscle to be measured, so that the strip was parallel to the muscle surface. When the muscle contracted, the legs moved towards each other, causing the copper strip to flex. The bridge was excited by the signal from a Hewlett-Packard prressure module (T 3205A). The output was amplified and connected to a chart recorder. Deflection on the chart was proportional to the force on the legs of the unit, with a linearity of 10%.

Fatigue Tests: Muscle fatigue testing was carried out under general anesthetic after exposure of the paraspinal muscles. The strain bridge unit was hooked into the muscle, two temporary stimulating electrodes were connected, and a test sequence of parameters initiated. Eleven different sets of parameters were tested to show up the response with varying frequencies of pulses, varying duty cycles, and different absolute on times (at constant duty cycle). The temporary electrodes were placed in the midthoracic and upper lumbar regions of the longissimus muscle, 2 cm. lateral to the spine. They were then connected to a Grass S88 stimulator for the tests. The strain gauge unit was placed midway between the electrodes. At the end of the tests, the electrodes, and strain unit were removed.

Muscle Biopsies: Muscle biopsies were taken as a cube approximately 1 cm to the side. They were snap frozen in iso-pentane in liquid nitrogen. Thin sections were cut and stained with H _E, ATPase, SDH, NADH, acid and alkaline phosphatase. Fibre typing was carried out using the ATPase and NADH, or SDH stains (7).

Protocol: Under general anesthetic, a midline skin incision was made to expose the paraspinal muscles. A muscle biopsy was taken from the left paraspinal muscle opposite the level T12. The strain gauge was inserted in the left paraspinal muscle and a series of 11 sets of test parameters run. Each test was 10 min. with a 10 min rest period between. At the end of the testing, a stimulator was implanted under the skin in the right paravertebral area. The electrodes were placed into the paraspinal muscles on the right side, about 10cm apart, 2 cm lateral to the midline. The skin was closed, and the unit turned on.

After 8 weeks, the animal was returned to the operating room, and under general anesthetic, the skin was opened. The stimulator was removed. Biopsies were taken at corresponding locations on the two sides, and perielectrode biopsies taken at the site of the stimulator electrodes on the right side. The strain gauge tests were repeated bilaterally, alternating sides. The incision was closed and the animal returned to the facility for an 8 week period with no stimulation.

At 16 weeks, the animal was returned to the operating room. Under general anesthetic, the paraspinal muscles were exposed, biopsies taken bilaterally and the strain gauge tests repeated on both sides.

RESULTS

Gross Findings: The animals accepted the stimulation extremely well. They ate and gained weight at a normal 3 kg. (approx.) per week.

Histology: On visual examination of the sections, significant muscle fibre hypertrophy of the stimulated side was evident after 8 weeks of stimulation. At 16 weeks, these changes were not as obvious. Increases in the thickness of the intramuscular septa were also evident at that time. Perielectrode biopsies showed significant areas of fibrosis around the electrode. This finding seemed to be independent of the polarity of the electrode, and was also present in the non-stimulated control animals. Some muscle fibre degeneration, regeneration, and fibre splitting was evident in this area. This was not observed in the biopsies taken between electrodes.

Histochemistry: No difference was seen between the non-stimulated (left) and sham stimulated (right - a non-functioning stimulator was used) in the control animals either at 8 or 16 weeks.

Fig. 1 shows the changes recorded for the three fibre types after 8 weeks of stimulation and then a further 8 weeks of rest (16 wks. total). Note that the data points occur only at 8 and 16 weeks. In all cases there is a drop in the proportion of fast white (FTW), an increase in the fast red (FTR) population, and for the 75 cps group, a statistically significant increase in the slow red (STR) group. The 10 cps. group also shows changes in the STR fibres that just verge on significance. After 8 weeks of non-stimulation, the changes are partially reversed with none of the data showing significant differences.

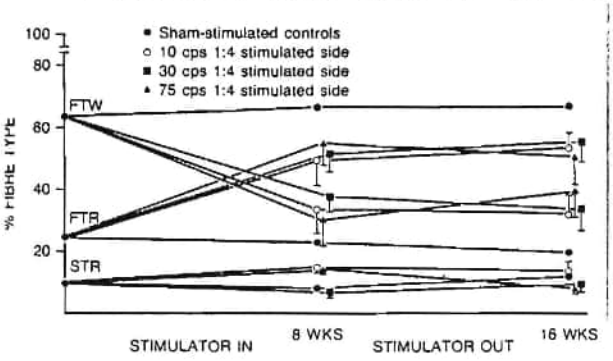


FIG 1: FIBRE TYPE CHANGES IN EXPERIMENTAL 1:4 AT 10, 30, 75 cps VS CONTROLS (PIGS)

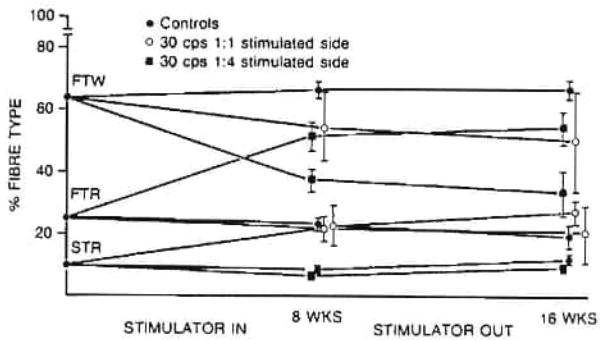


FIG 2: FIBRE TYPE CHANGES IN EXPERIMENTAL 30 cps ANIMALS VS CONTROLS (PIGS)

Fig. 2 compares the results of muscle stimulated at 30 cps. but with different duty cycles. In the case of the 1:4 (1sec on, 4 sec off; 20% on time), the conversion is mainly to the FTR fibres, with STR showing no significant change. However, the results of stimulating at 1:1 (1 sec on, 1 sec off; 50% on) shows a conversion to STR, but no significant change to FTR. By 16 weeks, the changes are again showing signs of reversal.

Fatigue Tests: The results of the fatigue testing were harder to interpret. Non-parametric statistics were used to analyze the results of the tests. After 10 minutes of test, there was statistically significant less decrease in the strength of the contraction on the stim-

ulated sides (at 8 weeks). Individual tests showed more dramatic differences in the two sides when the strength of the contraction was tested with parameter sets that had higher duty cycles.

DISCUSSION

The preliminary results of the experiments looking at the long term effects of intermittent electrical stimulation show that there is a conversion from the more rapidly fatiguing fibre types to the more resistant after an 8 week period of stimulation. As the stimulation imposed becomes more 'severe', the change is forced to the slow red type. There is no obvious difference at this stage between the firing rates of fast and slow motoneurons in the conversion of muscle fibres. After 8 weeks of non-stimulation, the changes are at least partially reversed.

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THE EFFECT OF IMMOBILIZATION ON THE ELECTROPHYSIOLOGICAL PROPERTIES OF THE NEUROMUSCULAR JUNCTION OF SKELETAL MUSCLE

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SUMMARY

The effect of immobilization, using a plaster cast, for 5, 10 and 15 days on the electrophysiological properties of the neuromuscular junction of gracillus anterior and posterior muscles of mice were studied using microelectrode technique. Immobilization decreased significantly the resting membrane potential. There was a progressive increase in the amplitude of the miniature end plate potential. MEPP duration increased gradually up to 10 days and then started to normalize. The frequency of MEPP was decreased significantly after 10 days and thereafter returned to normal. These findings suggested that immobilization affects not only the skeletal muscle but also the motor neurone endings supplying that muscle.

INTRODUCTION

Structural, mechanical and electophysiological changes have been observed in the muscle fibres after prolonged immobilization. We investigated the effect of immobilizations on the electrophysiolgical properties of the neuromuscular junction by studying the miniature end plate potential (MEPP).

MATERIAL AND METHODS

In vivo electrophysiological recordings were made on the neuromuscular junction of the gracillus anterior and posterior muscles of the hind limb of mice (JCI-ICR). The animals were selected withen the three months of age. Both hind limbs were held with the plaster of Paris bandage which was extended arround the abdomen. A small metalic strip was sandwitched in between the plaster to prevent the animal from eating the cast (1). The animals were kept in a seperate cages for 5, 10 or 15 days with daily routine care.

After the period of immobilization the animal was anaesthesized using Urethanium (B.P.) in a dose of 0.3 mg/kg. The cast was removed and the legs were washed adequately with a concentrated solution of EDTA and then with saline to remove all residual calcium attached to the hair of the animal. A small opening was made at the anterior medial side of the upper half of the thigh and the superficial muscles were exposed and covered with a drop of Kreb's solution at 37 C and pH - 7.4. The main area of interest was around the blood vessels supplying the gracillus anterior and posterior muscles.

A freshly prepared glass microelectrode filled with 3 M KCl was used for recording. The microelectrode was connected to the Grass model P16 microelectrode amplifier via a non-polarizable silver-silver chloride electrode. The amplifier output was fed to the dual trace differential amplifier of a Tektronix R56473 storage oscilloscope. One trace was selected on D.C. level with the sensitivity setting of 20 mV/division to provide continous surveillance of resting membrane potential. The other trace was set on A C level with the sensitivity of 0.5-1 mV/division to monitor MEPP.

All MEPP signals were fed to the 15 G07 Averager of a Disa-1500 digital electromyograph (a 50 K ohm potentiometer was inserted between the Grass P16 amplifier and The Disa-1500) and 16-64 MEPP signals were averaged. The averaged

signals were used to measure the MEPP amplitude and duration. The MEPP signals were also recorded on a magnetic tape for 5-10 min. The frequency of MEPP was analysed by inputting the recorded signals to the Tektronix differential preamplfier type 3A9 and to the signal conditioning unit of the Grass polygraph integrator model 7P 10B to reduce the noise. The noise-free signals were then fed to two integrators: the Grass 7P 3D which organizes the signals so that it could be fed to a digital pulse counter, and to the Grass D-C pen driver amplifier 7D AF to record the signals on paper. The second integrator was a Grass 7P10B which provided a continous add on integration of signals.

All data were analysed by an 1130 IBM computer, using Student's t test and F value for the analysis of variance.

RESULTS

Fifty-five mice were included in this study, seven died during the immobilization period for various reasons. The remaining 48 mice were included in this study of which 18 were studied without immobilization (control group). The remaining thirty animals were divided into three batteries (10 each) and were immobilized for 5, 10 or 15 days. 376 muscle fibres and 239 neuromuscular junctions were studied in this work.

1. Resting membrane potential: (fig. 1) The resting membrane potential of the control group was 91±0.99 mV (mean± S.E.M). There was a significant decrease ($p<0.005$) after 5 days (81±1.25 mV), 10 days (83±1.25 mV) and 15 days (85±1.17 mV) of immobilization. Greater variation was observed in the resting membrane potential between different fibres with 10 and 15 days immobilization (coefficient of variation (14%) in comparsion to 9% in the control group).

2. MEPP Amplitude: (fig. 2) The mean value of MEPP amplitude in the control group was 216±15.9 uV. There was a progressive increase in the amplitude after 5 days (238.4±16.2 uV N.S.), 10 days (300.3± 19.1 uV $P<0.005$) and 15 days (365± 14.7 uV $p<0.001$) of immobilization.

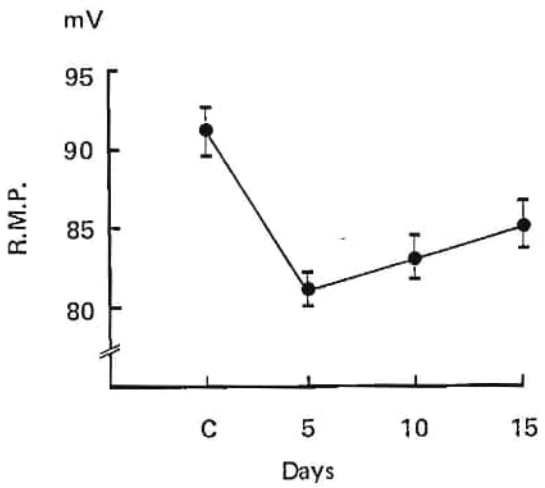


Fig. 1
Changes in the resting membrane potential (R.M.P.)
C = Control group

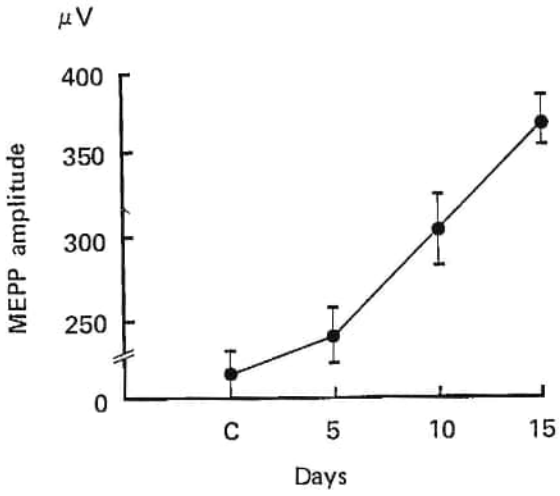


Fig. 2
Changes in the MEPP amplitude

3. MEPP Duration: (fig. 3) MEPP duration was measured between the rising time and half decay. The duration in the control group was 4±0.1 msec and it increased significantly ($p<0.005$) to 5.6±1.1 and 5.5±1.1 msec after 5 and 10 days of immobilization respectively. The MEPP started to decrease after 15 days of immobilization (5±0.7 msec).

4. MEPP Frequency: (fig. 4) There was 387.7±28.8 MEPP/min in the control group. The frequency decreased significantly after 5 days (296.9±17.8, $p<0.005$) and 10 days of immobilization (227±13.1 $p<0.001$). The frequency returned to its control level after 15 days immobilization (360± 179.2). A 100% increase in the physiological solution osmotic pressure around the neuromuscular junction increased the frequency of MEPP to 2.8 times the basic frequency in both the control and immobilized groups.

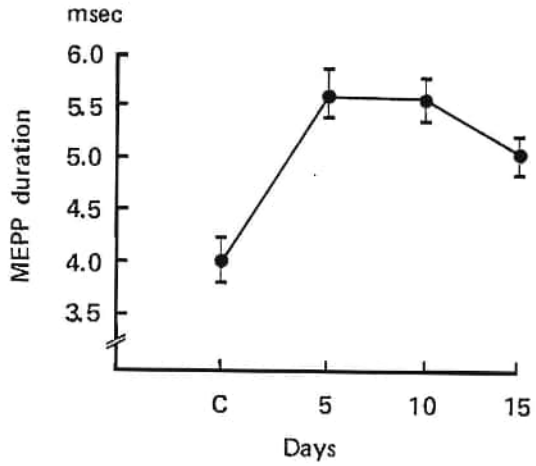


Fig. 3
Changes in the MEPP duration

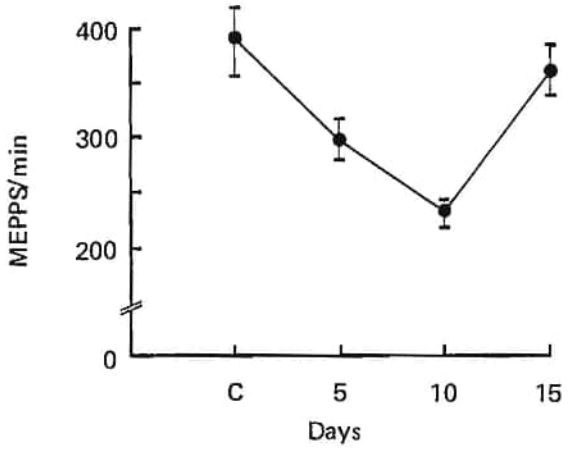


Fig. 4
Changes in the MEPP frequency

DISCUSSION

The changes in the parameters of MEPP represent the effect of immobilization on the neuromuscular junction. The progressive increase in the MEPP with immobilization could not correspond with the decrease in resting membrane potential. There were little evidence to suggest an increase in the ACh senstivity in the neuromuscular junction associated with disuse atrophy (2,3) inspite of an increase in the ACh sensitivity in the extra-junctional portions of the muscle fibres (2,4). Input membrane resistance increases with the decrease in the muscle fibre diameter seen in disuse atrophy. It has already been observed that MEPP amplitude is proportional to the input membrane resistance (3,5). This may explain the increase in the MEPP amplitude after immobilization.

The increase in the MEPP duration after immobilization may be due to a prolonged binding time of ACh to post-junctional receptors. This probably because changes in the geometry of the post-junctional membrane which are seen in disuse atrophy (6) cause widening of the junction which seperate the receptors and hence reduce the repetitive rate of ACh binding. The decrease in the cholinesterase after long immobilization (7) may be anather possible explanation for the increase in the MEPP duration.

The decrease in the MEPP frequency after immobilization indicates a possible changes in the pre-junctional membrane. It is difficult to speculate the nature of these changes. The similar effect of osmotic pressure increase on the frequency of MEPP in the immobilized and control groups may suggest that the cause of the decrease in the MEPP frequency after immobilization is probably due to a decrease in trophic substances from the muscle to the nerve (8). The normalization of the MEPP frequency after 15 days immobilization may suggest a kind of compensatory mechanism. The increase in the frequency of MEPP might contribute to the slight decrease of MEPP duration after 15 days of immobilization, probably by increasing the repetitive rate of AC binding as explained above.

In conclusion, prolonged immobilization may affect the physiological properties of both pre and post-junctional membrane. The nature of these changes needs further study.

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QUANTIFICATION OF MUSCULAR WEAKNESS BY SIMULTANEOUS EVALUATION OF MECHANICAL AND MYOELECTRIC EVOKED RESPONSES x)

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SUMMARY

Measurement of evoked responses has become the method of choice to quantify alterations in neuromuscular (nm) transmission eg. induced by neuromuscular blocking drugs (relaxants). In order to compare the evoked summated electromyogram and the isometric mechanical force a microprocessor controlled instrument was developed and tested both in animals and in patients. Even very slight alterations in nm transmission caused by relaxants can be detected by both methods using special stimulation patterns. The technique therefore might also be of distinct value for paraplegic patients as a test method to prove therapeutic effects following physical exercises and/or functional electrostimulation.

INTRODUCTION

Monitoring of nm function during anaesthesia has gained increasing importance during recent years. One reason to be mentioned is that monitoring equipment satisfying the special requirements of routine clinical work has become available; secondly, new short acting non-depolarizing muscle relaxants have been developed. Two techniques for the estimation of muscle paralysis are in common use based on the measurement of isometric muscle contraction (MMG) and/or of electrical muscle activity (EMG), signals being evoked by supramaximal stimulation of a peripheral motor nerve. In order to evaluate both the quality and the degree of nm depression induced by nm blocking drugs, traumatic lesions, systemic diseases etc. special stimulation patterns have been deviced. EMG and MMG recordings obtained during voluntary exercising (1,4,6) and also in case of decreased nm transmission (eg. induced by relaxants; 2,5) seem to agree in a quantitative manner. Up to now only few reports exist on investigations applying both methods simultaneously. Therefore we have developed a nm transmission analyser capable of processing the evoked mechanical and electrical response (3) such especially facilitating clinical measurements of nm transmission.

Design criteria of the analyser:

The following features were considered essential: Complete electrical isolation of the signal pick-up circuits and nerve stimulator in order to guarantee patient safety, generation of various stimulus patterns, constant current stimulation and current limitation, visualisation of the signals measured (compound action potential, isometric force), documentation of the processed signal, instantaneous display of the

x) Supported in part by Hochschuljubiläumsfonds der Stadt Wien

evoked responses in absolute units (Newton, mVoltsec) or as a percentage of control, calculation of pharmacodynamic parameters characterizing the nm blocking drug used.

System configuration:

a) Hardware: A microprocessor (µP) including keyboard and LED-display (Rockwell AIM 65) was selected as a controller of the instrument. Additional analog and digital circuits (optically isolated preamplifiers, voltage-frequeny convertors, sample-hold stages, integrators etc.) were developed for preprocessing the evoked response. A second µP acquires the amplified EMG after A/D conversion, storing and displaying it on a liquid crystal matrix array; an additional output of the time-expanded EMG is also provided. Two thermal strip chart printers are used for documentation; for convenient application and easy clinical use all the electronic is fitted within a tool-box.
b) Software: Program subroutines are written in machine language, both to save memory space and to enhance processing speed. Computing algorithms and input routines are written in BASIC.

RESULTS

Upon power up the analyser (fig. 1) automatically locks into default operating conditions: Only the mode of data acquisition (EMG or MMG or both signals at the same time) has to be selected. Any further changes from preset conditions (single twitch stimulation at 0.1 Hz) have to be entered via the keyboard by pressing predefined keys: eg. the time interval between succeeding stimuli can be decreased or increased and a different stimulation pattern (train-of-four: 2 Hz, 2 sec; tetanus: 50 Hz, 5 sec; short tetanus: 50 Hz, 100 msec) chosen. Twitch height is calculated by the computer from preload and peak force measured, the EMG integrated during a period of 18 msec following the stimulation. Measurements are plotted graphically on the strip chart printer; when determining the EMG any drift in preload is also indicated. Evoked EMG and isometric twitch tension were recorded simultaneously under a variety of experimental conditions both in animals and in patients. As an example the time course of nm depression following the injection of 2 single bolus doses of a nm blocking drug is shown in fig. 2.

DISCUSSION AND CONCLUSIONS

Various twitch recording devices commonly used are capable to process different stimulus patterns like single twitch or train-of-four; usually no additional evaluation is performed. EMG monitoring systems rely on various techniques for delayed time-expanded signal output or store the evoked action potential on an oscilloscope screen, by such means offering interactive signal processing. Measurements are, nevertheless, quasi-continuous at best. On the other hand very sophisticated and expensive large computer-based systems for processing evoked potentials have become available commercially.
The EMG-MMG analyser discussed facilitates continuous recording and on-line evaluation of nm transmission in any application in case control values have been obtained. Documentation of both peak force or torque (depending on the transducer used) and the integrated compound action potential is automatically performed immediately; data are output in a calibrated manner. Therefore, troublesome and time-consuming off-line calculations as usually employed in investigations

of nm blocking drugs are avoided. The amount of nm depression and its time course are readily available. Algorithms developed to determine onset time, duration etc. are based on the assumption of continuity and the steady increase of the evoked response during recovery from nm depression; indices calculated by these algorithms are as accurate as if processed the conventional way.
The features of the analyser also suggest the use of the instrument in patients suffering from spinal injury, in cases with traumatic nerve lesions after reconstructive surgery, myasthenia etc. So far this device has been used mainly in clinical anaesthesia. Due to its versatility however, it easily can be modified by changing certain program subroutines.

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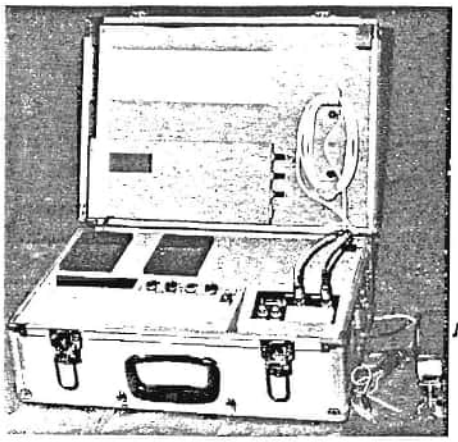


Fig. 1

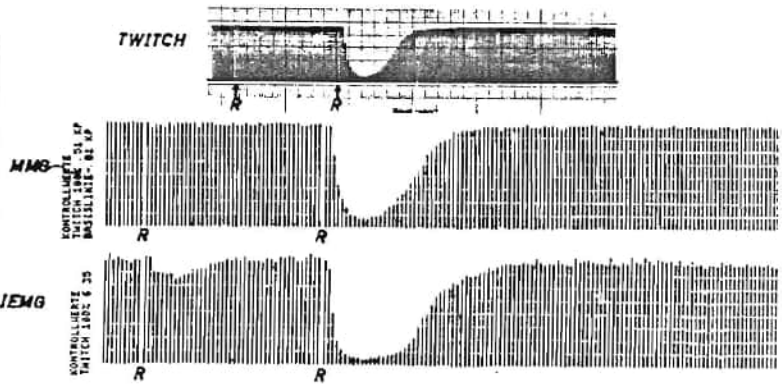


Fig. 2

Fig. 1: Portable µP-controlled nm transmission analyser. The system is operated via the keyboard, 2 strip chart printers are used for graphic documentation of the processed MMG and EMG respectively. Evoked action potentials can be stored on a liquid crystal display. The isometric force transducer and the EMG-amplifier used are also shown.

Fig. 2: Monitoring of nm transmission by simultaneous measurement of evoked EMG and MMG. The first panel depicts an analog recording of isometric force, in the second and third panel resp. the computer processed MMG and EMG (scaled to 100%) are displayed. Note slight discrepancy between the evoked responses following the administration of Vecuronium (75 µg/kg). Nm depression is not detected by the MMG technique, yet clearly visible on the EMG recording. Injection of a bolus of Vecuronium (225 µg/kg) causes the typical time course of nm blockade. Time interval between stimuli is 10 seconds, application of the drug is marked by R.

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COMPARISON BETWEEN ELECTRODIAGNOSTIC FINDINGS OF PATIENTS WITH FACIAL PARALYSIS

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SUMMARY

Sixty patients with peripheral facial paralysis were included in this study and examined with galvanic and faradic currents.The aim of this investigation was to predict the out-come of the peripheral facial paralysis by a simple electrodiagnostic test.
Eighty per cent of the patients examined in the first seventy two hours of their disease showed an exagerated response to faradic and galvanic impulses.After a period of five to twelve days generally this increased response changed to partial reaction of degeneration. Two third of these patients had complete nerve regeneration after two to six weeks.(1)(2)(5)(8)
In patients examined after three or more weeks after the beginning of the paralysis a partial or total reaction of degeneration was observed in fifty patients.After medical and physical therapy ninety per cent of these patients had also some improvement but this partial or complete recovery took much more time in patients with total reaction of degeneration.(3)(4)(6)

MATERIAL AND METHODS

During the last eight years patients complaining of unilateral paralysis of facial muscles were examined and cases of specific disorders such as injury to the facial nerve following an operation or fracture of the skull,acustic neurinoma,geniculate herpes zoster basilar meningitis and supranuclear corticobulbar lesions were excluded from sixty patients with "Bell's palsy".In these patients the correlation between the course of the disease and the results of electrodiagnosis were studied.For electrodiagnosis a simple galvano-faradic test was used and facial nerve and muscles of the face especially Frontalis,Corrugator Supercilii,Orbicularis Oculi,Zygomaticus,Orbicularis Oris,Quadratus Labii Superioris and inferioris were stimulated from their motor lines or points with faradic and brief galvanic(direct current) impulses every two to three weeks.

RESULTS

Eight patients out ten who had their electrodiagnosis within three days after onset of the disease showed an increased response to galvanic and faradic impulses.A partial "Reaction of Degeneration" was later observed in half of patients of this group within twelve days.Six of these eight patients had complete facial nerve regeneration after a period of two to six weeks. Table:1.
Fifty patients were referred to us after three or more weeks after the beginning of their disease for electrodiagnosis and medical and physical therapy.A partial reaction of degeneration was found in thirty four patients and total reaction of degeneration in sixteen patients.Some of the patients of this second group showed also an increased response but only to galvanic impulses.The upper branch of the facial nerve in thirty eight patients and middle and lower

branches in twelve patients were more severely affected.Ninety per cent of these patients were also completely or partially recovered but the time required for axonal regrowth was longer and more often incomplete especially in patients with total reaction of degeneration Table:2.

Time of electrodiagnosis		Within three days	After two weeks	After four weeks
Normal response		2	4	7
Increased response	faradic	8		
	galvanic	8		
Partial R.D.			5	3
Total R.D.			1	

Table:1.Electrodiagnostic findings of ten patients who showed an increased response to galvanic and faradic impulses at the third days of their disease.(R.D.-Reaction of degeneration)

	Patients	Partial Recovery	Complete Recovery
Partial R.D.	34	10(% 30)	24(% 70)
Total R.D.	16	8(% 50)	10(% 50)
Total(patients)	50	18	34

Table:2.The results of medical and physical therapy of fifty patients at the third month of their disease who gave signs of partial or total R.D. at their first visit.

DISCUSSION

Unilateral paralysis of the facial muscles appears when facial nerve is affected without a demonstrable cause and the disease takes the name of "Bell's Palsy".Study of this pathologic condition showed gross swelling of facial nerve in the narrow facial canal.In Bell's Palsy it is commonly accepted that exposure to cold may cause a focal edema which damages the seventh cranial nerve by compression. In patients ~~patients~~ with Bell's palsy who show an increased response to galvanic and faradic impulses there is possibility of an irritation of the facial nerve with a edema of minor importance.Some of these patients may completely be cured in a few weeks.But in other patients this slight edema later may also increase its compression which partially or completely damages the facial nerve.At this state of the Bell's palsy,increased response to electrical impulses changes to a partial or total reaction of degeneration during electro diagnosis.Recovery of partially and especially completely damaged facial nerve,as it may be expected takes much more time and often many motor units never regain its function and some weakness of facial muscles persists.(1)(5)(7)(8)(9)(10)

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ISOMYOSIN CHANGES IN DIRECT ELECTRICAL STIMULATION OF DENERVATED RAT EDL

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SUMMARY

Adult fast and slow skeletal muscles are composed of a large number of fibers with different physiological and biochemical properties that under neuronal control can respond in a plastic manner to a variety of stimuli. Although the differences are mainly quantitative in nature, some are qualitative, implicating a switch in the control of gene expression in single fibers. Indeed, in skeletal muscles almost every myofibrillar protein exists in polymorphic form. The myosin isoforms are widely used as markers of heterogeneity and plasticity of the muscle fibers and motorunits. Although muscle cells synthesize contractile proteins in the absence of motoneurons, after innervation the neuron controls (that is, induces and maintains) the particular isozymes subsequently synthesized. However an agreement has not been reached on the mechanism (either chemotrophic or impulse-mediated) by which the nerve influences gene expression in the muscle. The effect of direct, low-frequency electrical stimulation (at 10 Hz continuously 24 h daily) of the muscle on myosin light chain pattern of a permanently denervated fast muscle has been observed in EDL of adult rats. After three weeks, unlike the sham-stimulated muscles, the stimulated EDL showed a dramatic increase in the content of the slow type myosin light chains. Taking into account the large body of evidence demonstrating the absolute dependence of slow myosin on specific innervation, the present results strongly support the hypothesis that the slow motoneuron influences the myosin light chain expression through the activity it imposes on muscle.

MATERIALS AND METHODS

Adult male Wistar rats (body weight between 300 and 350 g) were anesthetized with thiopental and ether. The right posterior limb was denervated by removing a section of and reflecting the sciatic nerve near the trochanter. Stimulating electrodes from an external stimulator (Grass Model S 8) were implanted along the denervated EDL on one side. The naked ends of the electrodes (15x1 mm platinum wires) were sutured to the surrounding muscles. The insulated electrode leads were led subcutaneously to the back of the animal and attached to a teflon patch placed on the skin between the scapulae. The animals were housed singly and maintained on ad libitum chow and water. For one week the animals were administrated tetracyclin in drinking water to avoid infections. After three days of healing, animals were gradually conditioned by direct unilateral stimulation of the EDL. Three days later the animals commenced the direct low-frequency stimulation program, continuously 24 h a day for three weeks. Stimulus duration was 4 ms at a frequency of 10 Hz. The intensity was adjusted every day by palpating the contracting muscles. Stimulus polarity was reversed between each stimulus to reduce po

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larization of the electrodes. Isolation and purification of myosin and two-dimensional analysis of myosin light chains were as described in Carraro et al. /1/. Myosin was prepared also from EDL and soleus muscles of adult intact or denervated animals, diaphragm of adult or 1-day-old animals, EDL 15-day-regenerating in absence of the nerve and from sham-stimulated (implanted electrodes without electrical stimulation) denervated EDL.

RESULTS

In adult rats the EDL muscle (predominantly fast type fibers) was stimulated for 24 h a day at 10 Hz for three weeks. The 10 Hz stimulation frequency was selected because of its known effects on the metabolic and contractile properties of muscle /2/. The pattern of myosin light chains of control and stimulated muscles was then analyzed by two dimensional gel electrophoresis. Myosin light chains of normal, denervated or sham stimulated EDL were also analyzed. The high resolution of the two-dimensional gel electrophoresis permits the analysis of the muscle myosin light chains in complex mixtures of myosins. The three light chains of fast muscles (LC1F, LC2F, LC3F) and the three of mammalian /3/ slow muscles (LC1'S, LC1S, LC2S) can be separated and distinguished without ambiguity in a single gel analysis from other proteins and from the light chain (LCemb) that characterizes the myosin of embryonic /4/ and regenerating /5/ muscles (Fig. 1,c). The myosin of EDL of adult rats is dominated by the three fast light chains, the slow type light chains are present as faint spots (Fig. 1,a). They are due to the small percentage (3-5%) of slow fibers in this muscle. No consistent increase of these faint spots could be detected in EDL muscles either after denervation (Fig. 1,d and g) nor after implantation of electrodes without electrical stimulation (Fig. 1,h and k). Furthermore, as previously described /5/, the EDL regenerating in absence of the nerve accumulates fast not slow myosin light chains after a transient expression of the embryonic myosin. Figure 1,i and l shows the electrophoretic analysis of the myosin light chains in EDL muscles which were stimulated continuously at 10 Hz for three weeks. It is evident that in these muscles high concentration of the slow type light chains are present. Indeed the pattern resembles that of the diaphragm (Fig. 1f) a muscle with a mixed population of fast and slow fibres /1,6/.

DISCUSSION

Skeletal muscles may be classified broadly into two types according to their function. Those involved in maintaining posture are called slow because they contract relatively slowly with a sustained pattern of activity, while fast muscles shorten more rapidly and are used for intermittent bursts of more vigorous movement. Differences between these two types have been demonstrated by a variety of physiological, histochemical, biochemical and immunological techniques. They have different frequencies of activation by their motor neurones and contain different isoforms of myofibrillar proteins. It is well known that the nerve reaching a muscle determines its characteristic response. Thus cross-reinnervation produces a reciprocal transformation of muscles' properties, including the type of myosin isoenzymes synthesized. However what factors regulate the genes that are expressed in a particular motorunit? The evidences suggest that the differentiative influence of the nerve on muscle is mediated in part by the impulse activity of the efferent nerves and in part by mechanisms independent of the impulses /2/. To account for impulse activity-independent influences the existence of trophic substances, delivered to the muscle by axonal transport has been suggested; however the hypothetical trophic substance have not yet been identified or exactly defined. On the other hand experiments using chronic stimulation showed that the pattern

of nerve impulse activity is the major factor that determines the differentiation of skeletal muscles into fast or slow types. However in these experiments innervated muscles are used and it is difficult to distinguish between transformation in the muscle caused by changes in muscle activity per se or by changes in flow of trophic substances resulting from altered nerve activity. To overcome this inherent difficulty denervated muscles have been stimulated with different patterns of stimuli. It has been shown that a slow type artificial stimulation pattern at 10 Hz maintains the isometric contractile characteristics of denervated slow muscles, while phasic type stimulation changes the isometric characteristics and histochemical profile toward the characteristics of an innervated fast muscle /7/. Furthermore four weeks after electrode implantation and high-frequency phasic stimulation, the denervated slow muscle contained almost exclusively fast myosin. However, electrode implantation without any stimulation resulted also in an almost complete replacement of the original slow fibres by

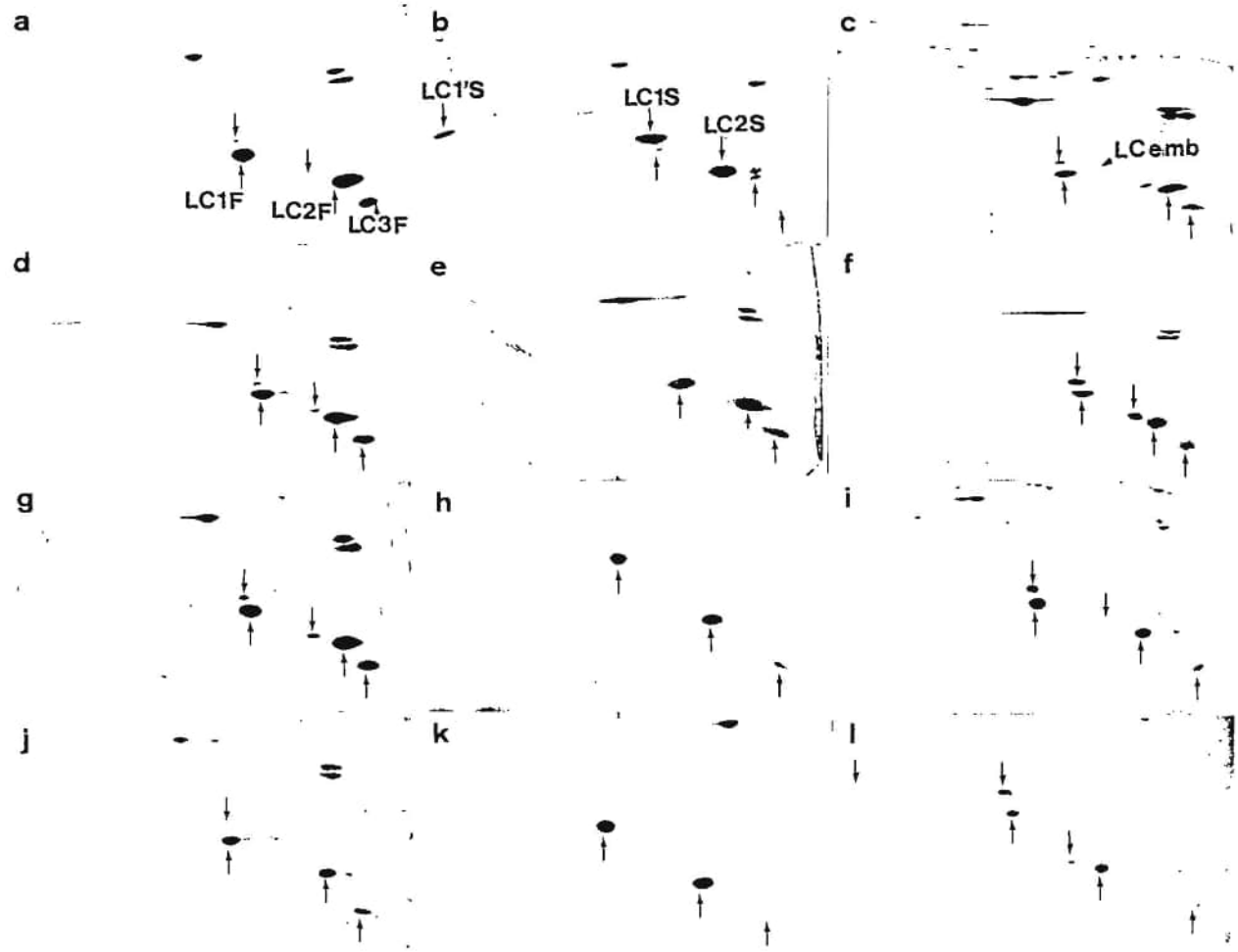


Figure 1. Two-dimensional gel electrophoresis of myosin light chains of a normal EDL; b normal soleus; c 1-day-old diaphragm; d 15-day-denervated EDL; e EDL 15-day-regenerating in absence of the nerve; f normal diaphragm; g 30-day-denervated EDL; h denervated EDL 3-week-sham-stimulation; i denervated EDL 3-week-stimulation; j control EDL; k denervated EDL 3-week-sham-stimulation; l denervated EDL 3-week-stimulation. The position of the light chains (LC1'S, LC1S, LC2S, slow type, downward arrows; LC1F, LC2F, LC3F, fast type, upward arrows; LCemb, embryonic type) is indicated. The denervated EDL after three weeks of continuous, direct electrical stimulation at 10 Hz shows a high concentration of slow type myosin light chains.

fast ones /2/. Therefore these findings have been explained by regeneration events rather than by transformation of preexisting fibers for small fibers with centrally located nuclei were present in experimental muscles. Indeed newly formed fibers in regenerating muscle synthesize fast type myosin after a transient expression of embryonic myosin even in the absence of the nerve /5/. Since aneurogenic regeneration /5/ or the lack of innervation itself (both during development and adulthood) can lead to the accumulation of fast myosin, but prevents the expression of slow myosin /2,4-6/, we have unambiguously tested the activity hypothesis by investigating the possibility to switch the synthesis of myosin light chains from fast to slow forms in the fibers (either preexisting or regenerated after electrode implantation) of the rat EDL by low-frequency electrostimulation of the denervated muscle. After three weeks of direct stimulation at 10 Hz, 24 h daily (a protocol that mimics the slow motoneuron discharge pattern), slow myosin light chains accumulate in the denervated EDL. The findings are comparable with the pronounced alterations induced by long-term stimulation of adult muscles through the nerve /2/. Taking into account the large body of evidence demonstrating the absolute dependence of slow myosin on specific innervation /1,5,6/, the preliminary results we have presented strongly support the hypothesis that the slow motoneuron influences the myosin light chain expression through the activity it imposes on muscle fibers.

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HISTOLOGIC EXAMINATIONS OF NERVES AFTER APPLICATION OF LOW D.C. BY ELECTRODES x)

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SUMMARY

During different periods of time electrodes of stainless steel were sutured to the right Nervi ischiadici of 62 rats and supplied permanently with D.C. of less than 1 µA. After 6 to 65 weeks functionally proper movements could be elicited by external stimulation in 80 % of the animals. The histologic examinations showed in 90% of the animals microscopically visible alterations of nerve structure. The results of the physiological-bioclinical and the histological examinations are compared. The tissue changes observed, seem to be caused rather by mechanical than electrolytical factors.

MATERIAL AND METHODS

The place of contact between electrodes and nerves is a very critical point in functional electrostimulation. There are fundamental problems of conductivity from metallic conducting materials to tissue leading to a possible trauma caused by biochemical and/or mechanical reasons, respectively. The present examination aims to show the stability of electrodes over a long period of time and to demonstrate the consequences of low D.C. on tissues and electrodes.
The electrodes used were developed by Thoma et al. of the Biotechnical Laboratory of the II. Surg. Clinic of the Univ. Vienna and are protected by patent. One electrode consists of 17 stranded wires of stainless steel with a diameter of 0,05 mm each, twisted and covered by silicone rubber. The electrode was formed as a loop with 1 mm diameter in order to prevent a concentration of the electric field. In all, 62 male white laboratory rats of 200 to 300 g were operated on by three surgeons alternating. Each animal received two electrodes, which were sutured to the Nervus ischiadicus in the region of the right thigh. A constant D.C. of less than 1 µA was continously applied, which did not depolarize the nerve. However, in the electrolytical point of view this D.C. simulated the worst circumstances possible, when an impulse train is applied to the electrode. Insulated D.C.-generators, powered by mercury cells, sereved as source of current and were implanted in the neck region. Five animals received only electrodes but no D.C.-generators.
During a period of time from 6 to 65 weeks after implantation the animals were re-examined. The rats were divided into five experimental groups depending on the lapse of time between implantation and the follow-up examinations:

Group 1	6 to 8 weeks	11 animals
group 2	13 to 22 weeks	22 animals
group 3	28 to 32 weeks	6 animals
group 4	37 to 42 weeks	9 animals
group 5	52 to 65 weeks	14 animals

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During follow-up examinations the D.C.-generator was disected free under anaesthesia and the cable splice to the electrodes was connected to an external stimulation unit. Following parameters were examined:

a) the stimulation current necessary to elicit a movement of the limb;
b) the smoothness and strength of movement;
c) the condition of electrodes and D.C.-generators;
d) the position of the electrodes in relation to the nerve;
e) the reaction of connective tissue at the site of the implanted electrodes.

Subsequently,the animals were killed and the Nervi ischiadici were examined histologically. After fixation in formalin-calcium (Baker) the nerves were embedded in Celloidin. 10 µm thick cross sections proximal and distal to the pairs of electrodes were stained with hemalaun-eosin (routine staining), iron hematoxyline and toluidine-blue (staining of nerve fibres), and aniline-blue-orange G (connective tissue) and compared microscopically.

RESULTS

During the follow-up examination the nerves of seven animals could not be stimulated by the external stimultion unit, because the electrodes had been lost, or were displaced subcutaneously, or the leads to the electrodes were interrupted, respectively. The intensity of current necessary to induce a functional movement at the follow-up examination alternated between 0,3 and 3,0 mA. Remarkablely, all animals of the first experimental group needed between 1,2 and 2,0 mA, whereas in the fourth experimental group for all rats, except one, less than 1,0 mA sufficed to induce a functional stimulation. In the other three experimental groups the intensity of current necessary for stimulation varied rather more. It should be stressed, that an exceptional high proportion (3 animals out of 14) of the fifth experimental group required a stimulation current of more than 2,0 mA. A functionally proper stimulation (powerful in strength according to the body weight) was obtained in 43 of 55 experimental animals. At the end of experiments, no signs of electrode corrosion were detected. During the follow-up examination the anatomical electrode-nerve relation of the 55 rats, that were effectively stimulated, was determined. 27 rats showed optimal positions of both electrodes, 15 rats that of only one (the distal electrodes being four times more frequently dislocated) and 13 animals none of all. All rats of the first group exhibited a strong connective tissue reaction at the implantation site.

The nerves of 59 rats were examined histologically. Three main deviations from the normal nerve structure were detected and qualitatively evaluated:

a) increase in cell number;
b) loss or alteration of nerve fibres;
c) increase in interstitial connective tissue within nerve fibre bundles.

The most striking result was the numerical increase in the cells proximal and distal to the implantation site. It was shown by about 30 % more rats than the other alterations. Only six animals showed no increase. In general, qualitative tissue changes were more frequently distal to the location of electrodes than proximal by about 25 %.
19 nerves demonstrated no changes in nerve fibre and interstitial connective tissue composition. On both sites of the electrode implantation an increase in cell number was demonstrated by 2/3 of the animals, a loss and alteration of nerve fibres by 1/3, and an increase in interstitial connective tissue by 1/4 of the animals. Mostly, a larger proportion of the cross sectional area of nerve fibre bundles exhibited

the increase in cell number than the other tissue changes, especially situated close to the perineurium. There, the tissue alterations used to be more prominent, in general. In 2/3 of all cases, the area covered by alterations amounted to less than 30% of the total area.
The increase in cell number seems to be caused by an addition of Schwann cells, fibroblasts and/or fibrocytes, as well as some histiocytes and mast cells. The numerical relation of the cell species varied depending on the tissue reaction as well as the cell density. A complete loss of nerve fibres was usually restricted to rather small areas of nerve fibre bundles. In cross sectional areas of nerves with a diminished number of nerve fibres, there, numerous fibres were surrounded by thin myelin sheaths, their axons being concomitantly enlarged or attenuated in diameter. These changes were most prominent close to areas of normal nerve structure.
Alterations of the perineurium were observed in 22 nerves consisting of its thickening caused by an increase in cell number (mainly fibroblasts). Sometimes the perineurium was totally destructed within segments of its perimeter. The area of altered nerve fibres was always located adjacent to perineural defects, but no functional and quantitative correlation could be detected between both.

DISCUSSION

The intensity of stimulation current necessary to induce a functional movement depended partly on the extent of the connective tissue reaction at the site of electrode implantation, because all animals with an extensive connective tissue reaction needed between 1 and 1,8 mA. Only a minimal influence of electrode position (optimal, partly optimal or non optimal, as mentioned above) could be detected on the intensity of the stimulating current necessary, since the average intensities needed for the three groups differed only by 0,18 mA. However, a tendency to higher intensities was caused by displaced electrodes, as well as by a more extensive loss in nerve fibre number.
In twelve rats the external stimulation did not result in functionally proper limb movements. However, the individual experimental results were too inhomogenous to permit a clear cut linking with causing factors although nerve fibre diminuation might be of influence. Comparing the histologic results in the three groups with differently positioned electrodes, and, disregarding the increase in interstitial connective tissue, there was no significant difference in number and extent of other nerve structure alterations when both electrodes or none were properly located. But there was a marked difference of 20 % to 30 % comparing these nerves with those having only one electrode properly positioned, when the increase in cell number and the loss/alteration of nerve fibres were evaluated.
The present report is based on serial cross sections taken from the neighbourhood of implantation sites, so that a decisive opinion concerning the longitudinal extension of the structural changes is not yet permissible. There are indications, however, that perineural alterations and cell number changes are restricted to a small area. It was not possible to connect the perineural alterations with the bioclinical results. The former seem to be prevented by an optimal loction of both electrodes.
The individual skill of the three surgeons placing the electrodes did not influence the bioclinical and histological results substantially. There was no essential and uniform difference in nature, number, and quality of structural changes to be detected.
Only 10% of the nerves investigated were histologically unchanged, but 90 % of all rats could be electrically stimulated to perform proper functional limb movements. This apparent discrepancy may be explained

by the fact, that the increase in cell number should not impair the nerve function essentially. Moreover, even in areas of nerves, with loss and/or alterations of nerve fibres, there was always a certain number of normal or almost unchanged fibres left, permitting a conduction of nervous stimuli. In particular, the histologic findings after 6 to 8 weeks of experimental treatment, demonstrated no perineural alterations, no interstitial connective tissue increase proximal to the implantation site and there were less tissue changes in number than in the other experimental groups except the third (28 to 32 weeks), in which they were similar. This could indicate an attempted nerve regeneration after the surgical stress of electrode placement up to the 37th week that showed as a limited tissue reaction.

Mechanical factors are certainly of importance to explain the tissue reactions. However, electrolytical factors may also be of influence as indicated by those rats with two properly located electrodes. In this group the number of tissue alterations was higher than in the animal group with only one well placed electrode, where the density of the electric field within the nerve should be less than in the former. The number of tissue changes in the animal group with no well placed electrode was similar to that in the group with two properly placed electrodes. In the former the higher number may be explained by more severe mechanical stresses such as the complete disruption of the nerve-electrode-suture, which might have been caused by growth and/or excessive animal movements.

Mechanical factors alone suffice to elicit the tissue alteration as proven by the 5 rats, that did not receive D.C.-generators. All of these demonstrated tissue alterations after 52 to 65 weeks, not strikingly different from animals which had been permanently supplied with D.C. during this period of time. To summarize, the alterations seem to be caused rather by mechanical than electrolytical factors.

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MORPHOLOGICAL EFFECTS OF CHRONICAL INDIRECT STIMULATION OF PSOAS MUSCLE

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SUMMARY

Samples of stimulated (15 cps for 6-9 weeks) and unstimulated contralateral muscles were examined histologically by HE-stain. Stimulation effects were a slight increase of connective tissue and fat tissue.
After stimulation the diameter of type 1 muscle fibres decreased for about 20% and that of type 2 increased slightly.
In stimulated nerves some axons degenerated but the mean of fibre sizes shifted towards larger diameters.
Histologically the chronically stimulated muscles showed increased NADH-diaphorase activity and transformation of type 2 into type 1 fibres, as revealed by Actomyosin ATPase.
The observations well correspond to the physiological and biochemical results, indicating that the muscles were transformed to slowly contracting, fatigue-resistant muscles.

MATERIALS AND METHODS

In 5 adult sheep compact battery adjustable stimulators were implanted under the abdominal skin and the electrodes were adjusted to the motor branches of the lumbar plexus supplying the psoas muscle. The periods of stimulation were 6 and 9 weeks respectively, at a frequency of 15 cps at intervals of 1:2 . At the final experiments the contraction force and -speed were examined by mechanography.
Samples of the stimulated and contralateral unstimulated muscles were stained histochemically for NADH-diaphorase and Actomyosin ATPase.
ATPase stained sections were evaluated by planimetry and histograms of the fibre size distribution were plotted.
The muscle nerves were embedded in epon and thick sections were also evaluated by planimetry.

RESULTS

Normal psoas muscle is characterized by few soft connective tissue and an unimodal distribution of muscle fibre diameters. Actomyosin ATPase stained sections show two fibre types: type 1 fibres (light stain) comprising about 25%, and type 2 fibres (dark stain) forming about 75% of the muscle fibres. Type 1 muscle fibres stain dark for NADH diaphorase, whereas type 2 fibres stain either dark (smaller fibres) or light (larger fibres) for NADH diaphorase (Fig. 1), (Tab. 1).

Cronical electrostimulation at 15 cps transforms the muscle thoroughly. Connective tissue and fat tissue are slightly augmented. The histochemical fibre types are changed: Type 1 fibres increase

in quantity. This effect is less pronounced in sheep with 6 weeks than with 9 weeks of stimulation. In histochemically stained sections it is obvious that many type 2 muscle fibres have been transformed into type 1 muscle fibres. Another characteristic effect of stimulation is the marked increase of staining intensity for NADH diaphorase. The mean diameter of type 1 fibres decreased for about 20%, whereas the diameter of type 2 fibres showed a slight increase (Tab. 2).

The muscle nerves showed a certain reduction of the number of axons. It was not possible to get reliable absolute numbers of the motor nerve fibres because the size and number of the motor branches to the psoas muscle varies to a large extent. The density of axons is reduced in most of the chronically stimulated nerves. The large diameter group in nerve fibres is enhanced in relation to the group of small axons. The mean of the fibre diameters of stimulated nerves increased for 20 to 46 per cent. In stimulated as well as in unstimulated nerves the distribution was bimodal.

DISCUSSION

In preparative surgery not only transposition of tendons and muscle transplantation but also artificial indirect stimulation of muscle is gaining importance (1). It is well documented by physiological and morphological studies that the impulse pattern of the supplying nerve is of crucial importance for the contraction speed and metabolic parameters of muscle fibres (2, 3, 4). The aim of the present experimental series was to find a model of a strong fatigue-resistant muscle suitable for long term electrostimulation. In order to get results which may be useful also for human dimensions we chose the psoas major muscle of sheep. The stimulation frequency was that of a slow fatigue resistant motor unit.

As was expected, the physiological characteristics of the psoas musle, normally consisting of 75% fast muscle fibres, changed to slow contraction times and low fusion frequency for a tetanus. The massive transformation of the histochemical staining properties regarding Actomyosin ATPase and NADH diaphorase well corresponds with the physiological data: The increase of the number of type 1 fibres reflects the transformation towards a slow muscle, whereas the massive increse of NADH diaphorase reflects the shift of fibres towards oxidative aerobic metabolism which is also in good correspondence to our biochemical observations (5). Obviously a skeletal muscle is capable to adapt to chronical low frequency stimulation.
Most of the nerve fibres to the psoas muscle adapt to chronical stimulation. The mean diameter of stimulated muscle nerve fibres was larger than the axons of unstimulated muscle. Some fibres were found degenerated. Obviously they have been overstrained by stimulation.

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tab.1		unstimulated	stimulated
SHEEP L3	type I	25,7 %	37,o %
	type 2	74,3 %	63,0 %
SHEEP K7	type I	23,6 %	36,6 %
	type 2	76,4 %	63,4 %
SHEEP K2	type I	---	92,8 %
	type 2	---	7,2 %

tab.2		UNSTIMULATED	STIMULATED
SHEEP L3	TYPE 1	48,07 ±0,23	41,49 ±0,39
	TYPE 2	39,40 ±0,13	40,97 ±0,30
SHEEP K7	TYPE 1	46,33 ±0,12	38,79 ±0,31
	TYPE 2	36,62 ±0,06	37,65 ±0,22
SHEEP K2	TYPE 1	---	38,79 ±0,07
	TYPE 2	---	39,08 ±0,30

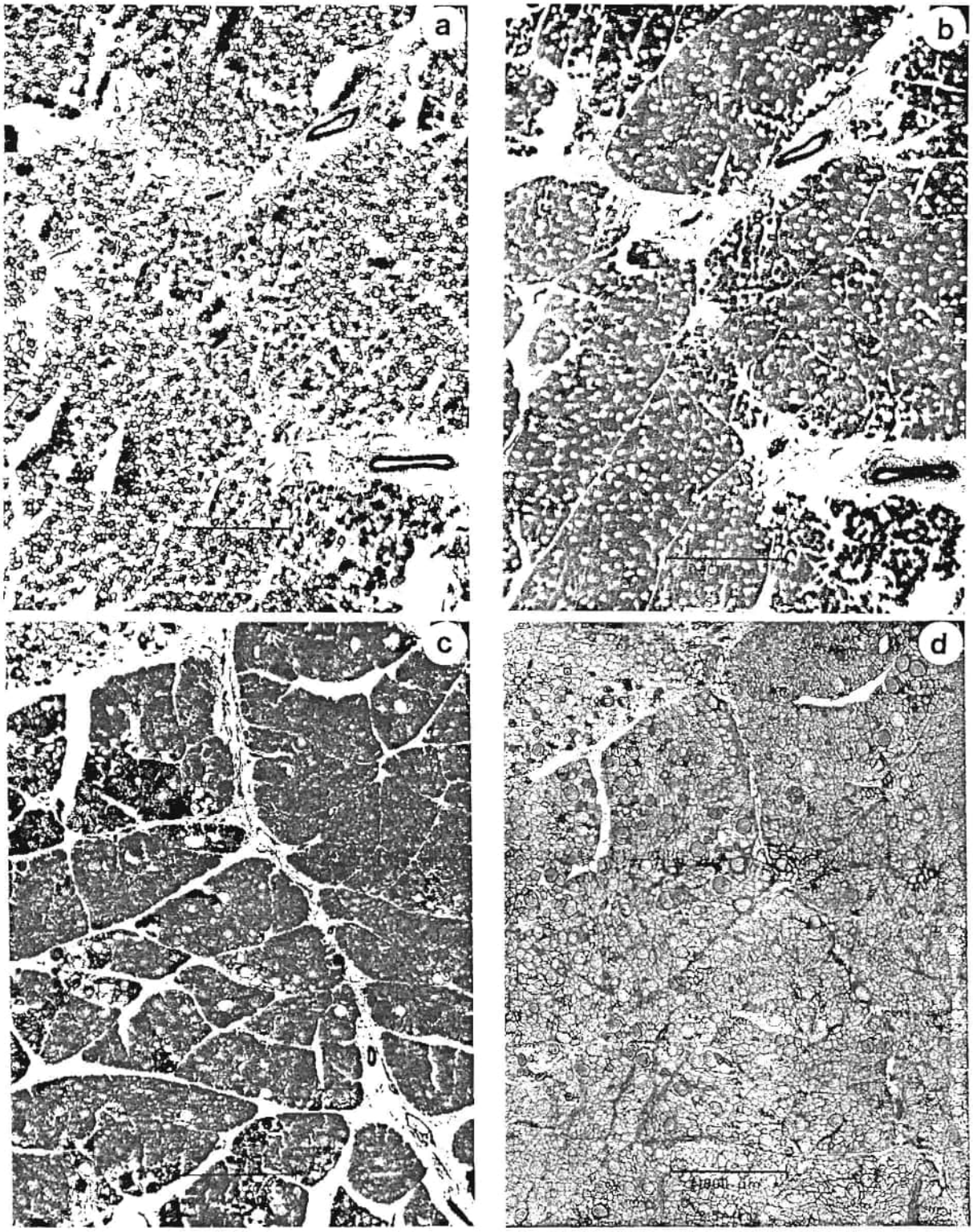


Fig 1: CROSS SECTIONS OF NORMAL(a,b) AND STIMULATED(c,d)PSOAS MUSCLE(15cps for 9 weeks).COMPARE INTENSIVE HOMOGENEOUS STAIN IN c FOR NADH AND NEARLY UNIFORM LIGHT STAIN FOR ATPase in d.

BIOCHEMICAL EFFECTS OF CHRONICAL INDIRECT STIMULATION OF PSOAS MUSCLE

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SUMMARY

The aim of the present study was to find an experimental model for biological energy supply by means of chronically stimulated striated muscle.The sheep psoas muscle was chosen for its size, anatomical position and homogenous fibre composition.From the energetical point of view it seemed necessary to use a low frequency for the chronical continuous stimulation.The irritation of the animal was minimal due to implantation of a small portable stimulator.Also the contractions of the psoas muscle obviously did not pertubate the normal life of the animals.Activity levels of Lactat Dehydrogenase (EC 1.1.1.27),Malat Dehydrogenase (EC 1.1.1.37),Creatin Kinase (EC 2.7.3.2.) and Hexokinase (EC 2.7.1.1)have been determined in the stimulated psoas muscle.In two animals the biopsies were used also to determine the content of ATP and ADP by means of luciferase. Cryostat sections were homogenized for the radiochemical assay for Cholin-Acetyl-Transferase (CAT).The untreated side was used as normal control.Chronic electrostimulation with low frequency (15 cps) induces a transformation of the enzyme-pattern.The activity of Hexokinase was approximately three times higher than in normal contralateral muscles,Creatinkinase was reduced to about 70 %,Malat Dehydrogenase to 50 % and Lactat Dehydrogenase to 30 %.The radiochemical assay of CAT activity,the enzyme which synthesizes the transmitter Acetylcholin at the motor nerve endings, showed no differences between the stimulated and unstimulated psoas muscle.Chronical electrostimulation caused a decrease of ATP and an increase of ADP.

MATERIAL AND METHODS

Electrostimulation

At 5 adult sheeps the left psoas major muscle was exposed under halothane anesthesia and 2 electrodes were adjusted to the branches of the lumbar plexus to the psoas muscle.The compact portable stimulator containing batteries was implanted beneath the abdominal skin.Stimulation was 24 h per day with a frequency of 15 cps and intervals of 1 : 2.The periods of stimulation were 6 and 9 weeks, respectively.

PREPARATION OF EXTRACTS AND HOMOGENATES

After the period of stimulation the animals were anestesized again and immediately small biopsies from the surface of the psoas muscle were taken and frozen in liquid nitrogen for biochemical analysis.The tissue was homogenized in a pre-cooled homogenator.The muscle specimen were homogenized in EDTA buffer 5.0mM,ph7.5.The disintegration was performed in 4 periods of 20 sec each,with intervals of 30 sec in between.During this time the homogenate was kept cool by ice.50 mg psoas muscle free from fat and connective tissue per ml EDTA buffer was used.After disintegration the homogenate was centrifuged 20 min with 2000rpm The supernatant was decanted and kept in an ice bath.For the determination of Lactat Dehydrogenase it was necessary to dilute the supernatant with EDTA buffer(5mM ph7.5) 1:100,also it was necessary to performe a dilution for the determination of Malat Dehydrogenase with EDTA buffer(1 : 10) and Creatinkinase (1 : 1000).
Cryostat sections were homogenized for the radiochemical assay for cholin Acetyl Transferase as has been described in detail(1). The preparation for the determination of ATP and ADP has been described previously(2).

ENZYME ACTIVITY DETERMINATIONS

LDH,CK,MDH were measured at 334 nm with an Eppendorf photometer. For the determination of thes enzymes commercially available kits were used.For the determination of Hexokinase the following assay mixture was used:0.3 ml TRA-buffer,0.25 ml glucose,0.02ml NADP

0.01 $MgSO_4$,o.o5 ml extract,0.002 ml G-6-PDH,0.02 ml ATP.Hexokinase was measured at 334 nm.

ATP AND ADP DETERMINATIONS

In two animals the biopsies were used also to determine the content of ATP and ADP by means of Luciferase as has been described in detail(2).A Lumac Biocounter tm M 2000 was used.

CAT ACTIVITY DETERMINATIONS

Cryostat sections were homogenized for the radiochemical assay for Cholin Acetyl Transferase(after FONNUM)(1).A liquid szintillation counter was used.

RESULTS

We compared the LDH,CK,MDH and Hexokinase activities of the stimulated left psoas muscle with the enzyme activities of the unstimulated right psoas muscle.Results are shown in Tab.1.There is an increase of Hexokinase and a decrease of LDH,CK and MDH.

Sheep NO.	LDH ST U/GWW	LDH UNST U/GWW	CK ST U/GWW	CK UNST U/GWW	MDH ST U/GWW	MDH UNST U/GWW
E 5	59	143	841	1010	53	95
L 3	76	126	1262	1515	79	105
E 2	92	135	1094	1430	36	42
K 7	109	151	1514	926	47	50
K 2	76	219	926	1515	42	84

Sheep No	Hexokinase St U/GWW	Hexokinase Unst. U/GWW
E 5	9	4
L 3	11	7
E 2	20	11
K 7	26	9
K 2	17	9

TAB . 1

Chronical electrostimulation caused a decrease of ATP and an increasa of ADP(TAB.2).ATP and ADP activities in nm/mg protein.

Sheep	ATP St	ATP Unst.	ADP St	ADP Unst.
E 5	15.2	53.9	4.2	0.55
L 3	11.9	47.5	2.3	3.40

TAB . 2

CAT activities showed no characteristic differences between stimulated and unstimulated control muscles(TAB . 3).

Sheep No	CAT Unst. %	CAT St. %
E 2	100	104
E 5	100	104
K 7	100	105
L 3	100	124

TAB . 3

DISCUSSION

In the present study a countinous stimulation for 24 h a day was used. The periods of stimulation were 6 and 9 weeks respectively at a frequency of 15 cps at intervals of 1:2.The results of this stimulation pattern were similar to that of other authors,who stimulated with a discontinuous stimulation pattern(3).In agreement with Pette (3) we think that stimulation with low frequency leads to a transformation to a slow contracting,fatique resistant,aerobic muscle.We cannot explain the lower levels of MDH and ATP in the stimulated muscle.MDH and ATP correlate well with the resistant to fatigue by other authors (4,5).

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DIFFERENT METHODS OF FUNCTIONAL ELECTRICAL STIMULATION IN HEMIPLEGIA (x)

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SUMMARY

After stroke or head injury one channel or multichannel functional electrical stimulation (FES) is applied as a routine therapeutic method at an early or late stage with respect to the begining of the illnes and certain stimulators are prescribed as orthosis. Different muscles or muscle groups of upper and lower exstremity can be stimulate to exert an influence upon the pathologic synergy especially during the gait. Research programs include the clinical evaluation of implantable sistems and methodology of the evaluation of immediate or long-term therapeutic effects.

MATERIAL AND METHODS



Fig. 1: FES of m. quadriceps (H. S.)

One-channel electrical stimulation of the peroneal nerve is used in everyday psysiotherapeutic practice (1) in order to achieve dorsiflexion and eversion of the foot during the swing phase. The therapy is started in the sitting position and, later on, in the course of the function itself, that the patient should practice gait in a corrected position (2). In this way any muscle or muscle group can be stimulated, therefore, stimulation of m. quadriceps is often combined with a mechanical peroneal brace in order to invigorate the function of knee extensors at a simultaneous correction of equinovarus(Fig. 1). Where an improved function of the hand is aimed at by stimulating the extensors of the wrist and the fingers so that the hand is being opened at a partial existing active flexion of fingers and at fairly good activity of proximal musculature, we can facilitate the dropping of an object which the patient has actively taken hold of (3) (Fig. 2)

(x) Supported by the Research Communities of Slovenia and the National Institute for Handicapped Research, Washington, D. C. USA



Fig. 2: FES of extensors of the wrist and fingers (H.D.)

Multichannel surface electrical stimulation is of a therapeutic nature, applied for the purposes of correction the pathologic pattern of gait in the swing and the stance phase. In the course of gait maximally up to six muscle groups are stimulated (m. glut. max., m. glut. med., knee flexors, knee extensors, pretibial m. group, m. triceps surae or m. gastrocnemicus and m. soleus, respectively) in corresponding programmed sequences and after a preliminary kinesiological analysis of gait (4). One has to determine typical stimulation sites, to provoke a suitable selective functional movement, and then decide upon the stimulation program. Research programs include also implantable systems (5) with implanted electrodes along the peroneal nerve. This procedure is chosen in cases where a permanent orthosis is indicated and no active control, i. e. restitution of motor activity can be expected. Before deciding upon the implantation the following should be attended to: analysis of gait, EMG of the adequate nuscles and measuring analysis of the load on the affected exstremity. This procedure has to be repeated every six to eight months.

RESULTS

The present findings show that in everyday extensive routine use the most suitable devices are surface one-channel electrical stimulators used in the stimulation of pretibial m. group, m. quadriceps, extensors of the wrist and fingers. About 80 % of our patients are applied FES in the so-called gait school facilitating of agonists and inhibiting spastic antagonists (6). The correction of equinovarus can be noticed in 100 % during the stimulation itself and by lower number of patients long-term effect is observed resulting in better volitional, active control of lower and upper exstremity (7). In the course of fifteen years one channel devices have been tested on about 3.000 patients. Using multichannel stimulators a certain correction of various anomalies is established by a subsequent clinical analysis of gait. For instance: equinovarus in the swing phase can be corrected by 100 %, circumduction by more than 50 %, external rotation by more than 50 %, and unappropriate knee flexion likewise by more than 50 %; a fairly positive influence exterted upon the hip position in the heel-on and less so upon the stability

of the knee. If we have decided upon electrical stimulation of m. triceps brachii, the gait is satisfactorily accompanied also by the affected hand (8). In order to objectify the results and substantiate them with biomechanical data, electrogoniograms and measurements of reaction forces by means of special measuring shoes are added (Fig. 3, 4) to the clinical kinesiological analysis of gait. The data obtained and computerized result in the movement control of the hip, the knee, the ankle joint, and taht in the sagital plain. Then there is established the transfer of weight onto the affected side, the heel-on, and the load force onto the affected extremity itself and the crutch (9). There is a good possibility of comparing the symmetry with respect to the affected side, determining the velocity of gait and the manner of heel-on. Implantable peroneal stimulator has been implanted in 17 patients. After a year and a half to two years we can state that the surgical intervention implies no complications, the postoperative course involves no problems, correction is satisfactory, no noxius effects are exerted upon n. peroneus.

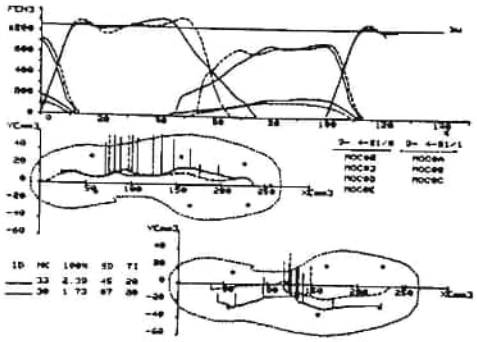


Fig. 3: Measurement of ground reaction forces (H. D.)(___ without FES, ___ with FES)

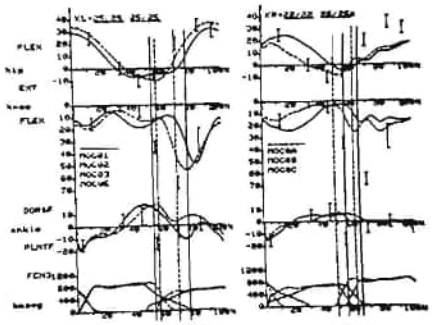


Fig. 4: Electrogoniograms (H. D.) (___ without FES, ___ with FES)

DISCUSSION

The main purpose of the application is to correct the position and function, the initial position for the beginning of gait, and to bring the patient to step onto the heel and not onto lateral border of the foot, therby simultaneously transferring his weight onto the affected side. Concerning the function of upper extremity we try to perform different activities which make part of programs of occupational therapy. The program of multichannel electrical stimulation in part still belongs to our research area as it is our intention to study long-term therapeutic effects and to determine the lowest possible number of stimulation channels which would enable a satisfactory correction of the anomalies during gait (10). However, problems result from the apparatus as such, which is quite complicated, implying the presence of a skilled therapist or a bioengineer; the adjustment of this apparatus is rather time-consuming, and together with the corresponding measuring system it represents encumberment for the patient. Incorporating a microprocessor for a simultaneous data recordal will undoubtedly offer better possibilities. The problems connected with the positioning of surface electrodes could be eliminated by an implantable multichannel system (11).

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RESTORATION OF MOVEMENTS OF THE UPPER EXTREMITIES USING SURFACE ELECTRODES x)

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SUMMARY

This is a preliminary report about our medical and technical initial experiments. We stimulate the grasp movement by tetraplegic patients by the help of skin electrodes. The minimal medical conditions are : paralysis must be a flabby one, musculature must not have atrophied too much, there must not be any contractures at the joints, there must be no hypersensibility in the stimulation area. The technical realization : the electrical impulse sequence is generated by a battery-operated device which supplies oblong impulses of various breadth and frequency. The conditions for constant-current work are fulfilled. The intensity of the current (peak value 0 - 150 mA) corresponding to the power of the grasp can be adjusted by the patient himself.

PREREQUISITES FOR PATIENTS

Not every patient suffering from traumatic tetraplegia is fit for being cared for with FES. In the course of our investigations we have found out that five requirements must be fulfilled if the care of the patient is to be successful.

(1) The paralyzed musculature that is to be stimulated must be flabby. If, on the other hand, the patient is suffering from spastic paralysis, either spastic, i.e. uncontrollable contractions are elicited or a state of spastic motoricity has existed already. In this case there is no longer any possibility to obtain an intended movement by superimposition of an artificial impulse sequence.

(2) The musculature must not have atrophied too much, i.e. the paralysis must not have happened a long time before. If a longer period of time between accident and care with the device has to be bridged, a special therapy with the physiotherapeutic stimulation current is indicated.

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x) Supported by research project "Artificial Organs and Biomaterials"

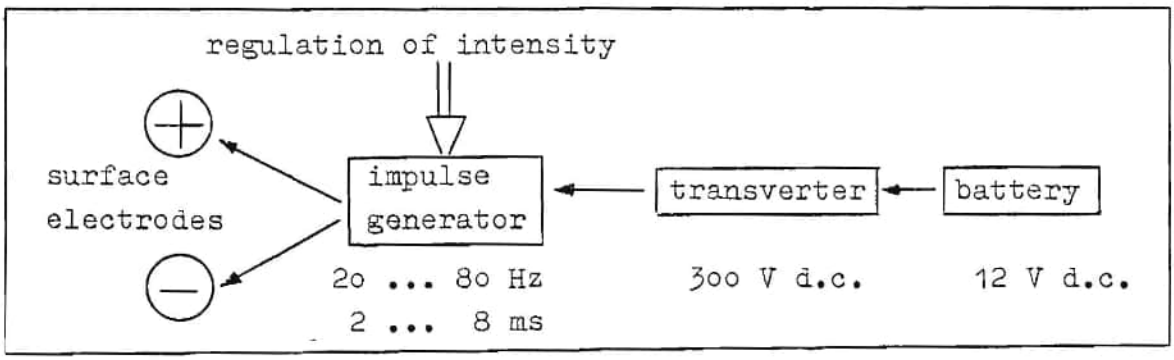
(3) There must be no contractures at the joints that are to be stimulated. A grasp movement through stimulation will, therefore, only be possible if the wrists and finger joints have total passive flexibility.

(4) There must be no hypersensibility in the skin area where the surface electrodes are fixed. It is even to be considered an advantage if the sensibility in the respective area is reduced, so that the necessarily high strengths of current can be conducted.

(5) The last pre-condition concerns the mental ability of the patient. That is why care with FES also presupposes that the patient by using surface electrodes will guarantee the strict and unexceptional observance of all safety measures. The safety precautions that have been taken into account electronically and in the whole design will, no doubt, exclude any danger of accident, provided that suitable application is ensured.

TECHNICAL REALIZATION OF THE DEVICE

We have built a stimulation device that is handed to the patient for permanent use. The following figure shows the schematic diagram:



Current supply: This is achieved with batteries, which has two advantages. On the one hand, the device is independent of any connection to the mains and can, therefore, be operated everywhere. On the other hand, the patient is entirely separated galvanically from the mains, so that dangerous earth circuits are excluded.

Transverter: This element transforms the 12 V d.c. of the battery to 300 V d.c. This very high voltage is necessary on the side of the patient, because the skin-tissue resistance lies in the range of 1 kΩ and the peak value of the impulses must amount up to 150 mA, if the contraction of the muscles is to have the desired intensity that is strong enough for carrying out the movement of the hand.

It is, however, much more essential to point out that comprehensive safety precautions have been considered in our design, so that it is practically impossible for the current to increase beyond 150 mA.

Impulse generator: Here the impulse image is generated according to the constant-current system, which means that the current is independent of the strength of the load resistance, which is the resistance of the patient. The pulse recurrence frequency is between 2o and 8oHz and the pulse rectangular width is between 2 and 8 ms. It must be mentioned that the shape of the pulse fronts does not have any marked influence on the range of movement.

Intensity control: While another person is needed for regulation of pulse recurrence frequency and the pulse width, the patient himself can regulate the pulse amplitude. It is, therefore, possible for him to select the strength of motion all by himself, which in the present case concerns the intended speed and strength in clenching the fist. This especially large-size intensity regulator the tetraplegic can move with his other hand, i.e, the one that is not stimulated.

ORTHOSIS

In our first experiments concerning the stimulation of the grasp movement of tetraplegics a clear drawback became visible, which consisted in the patient's inability to carry out the desired grasp with the finger tips, because the hand clenched uncontrollably. Besides this, there was another problem. As it is not the extensors that are stimulated when the hand is being unclenched, this unclenching of the hand must happen in a passive way. Both requirements are met with the orthosis.



Figure 1
Orthosis and electrodes

Figure 1 shows an orthosis with the surface electrodes. Both the orthosis and the mounts for fixing the electrodes are made from a plastic material ("Piacryl") which shapes easily when being heated.

PRACTICAL USE

Figure 2 shows the finished device with the patient's wheel-chair. It rests on a supporting plate between the wheels. This base plate



Figure 2
Caring for a patient suffering from tetraplegia

can be taken out without difficulty, so that the complete device can be put in every place. Thus the advantage of the supply by battery takes full effect.

With the left hand the intensity regulator is operated, in his right hand the patient is holding a bottle. This example has been selected on purpose, because it shows that as a consequence of FES the patient is for the first time again able to drink without the help of another person.

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OUR EXPERIENCES WITH FUNCTIONAL ELECTROSTIMULATION BY SPASTIC PES EQUINUS

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SUMMARY

We report in this paper on our objective experiences with functional electrostimulation of spastic pes equinus.
At the same time the patients' attitude toward peroneal stimulators and the actual use they make of such device at home have been examinated.

MATERIAL

Since January 1982 2o patients with upper motor neuron lesions due to cerebral palsy and to injuries of central nervous system with consequential hemiparesis have been treated with a peroneal stimulator (M i c r o f e s - Gorenje) (Table 1).
All the patients, respectively their pare_nts have been trained during hospitalization time before becoming the stimulator. At the same time physiotherapy on a neuro-physiological basis war carried out. The patients have been regularly controled at intervals of 2-3 months.

METHODS

By the objective clinical interpretation the effect concerning gait and spasticity was considered. At the same time we asked the patients as final users of the stimulator about their subjective opinion using the brace. The questionnaire was organised partially according to M e r l e t t i /1/. Two groups of questions were asked. The first concerned the use of the brace, that is the number of hours/day of use, the use out door, problems and difficulties of application. The second group concerned the subjective results obtained through the stimulator.

OBJECTIVE RESULTS

By 5 of 2o patients (=25%) we had to interrupt the treatment with the stimulator within 3 months because of difficulties with use

(2 cases of hemiplegia after stroke, 1 case of hemiplegia after trauma), poor results (1 case of hemiplegia after stroke) and wrong indication (1 case of hemiplegia by cerebral palsy with a partial contracted spastic pes equinus).
The remaining 15 patients are still using the stimulator. We noticed in all of them an improvement of non assisted gait and a decreasing of spasticity. An exact measurement of the improved dorsal flexion of spastic pes equinus during gait is only possible by a gait analysis. This test was not performed in our follow-up.

SUBJECTIVE RESULTS

All the 15 patients, who are still using the stimulator complained about the high rate of technical failures, especially concerning the switch in shoe insole and the electrodes. That is probably the main reason why the stimulator was used only indoor (Table 2). In spite of these onerous technical problems all the 15 patients noticed AN AN IMPROVEMENT OF THE GAIT quality combined with an active dorsal flexion of the spastic pes equinus (Table 2).

CONCLUSIONS

Although our follow-up study was performed without a biomechanical gait analysis, the results we obtained are satisfactory, as demonstrated in this case.

Case 1: S.P., 15 years old boy, spastic Diplegia by CP. Notice improvement of gate and control of spastic pes equinus especially left by treatment with stimulator (Fig.1).

We also are of opinion that, by critical selection of the patients, the functional peroneal stimulator represents an ideal rehabilitation aid by patients with spastic pes equinus.
The high rate of technical failures, which we unfortunately had to complaine in this type of stimulator, hindered its larger application.

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TABLE I

20 Patients

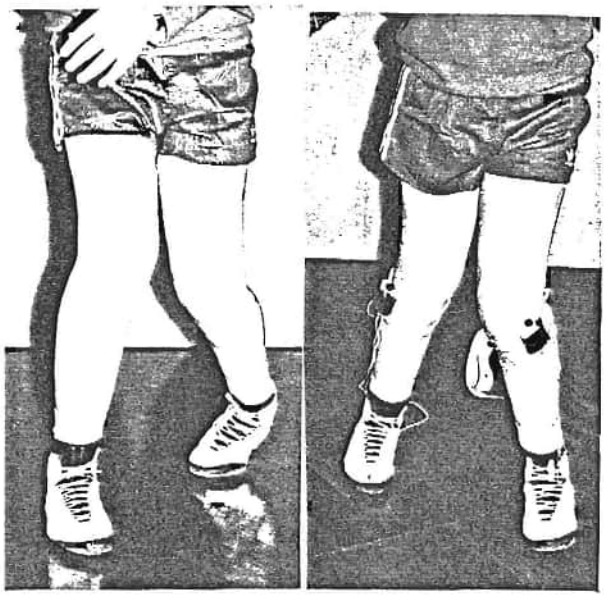
7 children with CP (6-15 years)	13 adults with hemiplegia (18-67 years)
5 hemiplegia	9 after stroke
2 diplegia	4 after trauma

TABLE 2 (Subjective Results)

n = 15

		average h/day
Stimulator used only indoor	15	2,0
Stimulator used also outdoor	0	
Non assisted gait improved	15	
Spasticity decreased	15	

Fig. 1



FUNCTIONAL ELECTROSTIMULATION IN CERVICAL SPINAL CORD PARALYSIS

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INTRODUCTION

Injuries to the spinal cord in the cervical segment lead to one of the most serious disabilities - the paralysis of the lower and upper extremities.Advancement in the treatment of spinal injured patients has resulted in the survival of those patients,but very rarely noticeable neurologic improvement can be obtained.Such patients are entirely dependent on others for help.Therefore we consider it our duty not only to treat the patients but to find a way to make life easier for the severely handicapped,to find a method of securing them some independence and enabling them to perform some simple daily activities,as well.

At the Rehabilitation Clinic of the Medical Academy in Konstancin/Warsaw for over 10 years we have been carrying investigations into the stimulation of peripheral nerves and spinal cord of those patients in order to improve the conditions of regeneration of the injured nervous structures and to stop the process of deterioration of the mass and abilities of the paralyzed muscles.To activate the paralyzed nervous structures,implanted stimulators have been used with the electrodes located at the site of the injury or the nerves,and the receiver /starter/ placed directly under the skin.

TECHNIQUE OF IMPLANTING THE STIMULATORS

The investigations of stimulation of nerves by means of implanted stimulators in humans were preceded by experiments on animals.The experiments on dogs with paralyzed bladder have been successful./3/ Stimulators were implanted on peripheral nerves under local anaesthesia.This kind of anaesthesia makes it possible to maintain verbal contact with the patient and to assess the effect of stimulation at operation,and, what is more important,to state precisely where to place the electrodes to obtain the most effective stimulation without reaching the threshold of pain.

Stimulators were initially implanted on the median nerve,and recently on the median and radial nerves.

At operation skin incision of 10 cm is made in the triangle of the elbow,passing from the lateral to the medial-palmar surface of the forearm,rendering the preparation of the radial and median nerves possible. When the nerves are exposed along a short distance,test stimulations are performed using an external stimulator and the best location for the electrodes is found.Sterile and electrically checked stimulators are placed in the subcutaneous tissue below and above the wound.Electrodes of both stimulators are placed at the sites chosen during the test stimulation,and are fixed to the epineural sheaths by means of single silk sutures.Before the wound is closed,the operation of the

implanted stimulators is checked,supplying the stimulators from an external device.

Test stimulations and then systematic stimulation training are begun a few days after implantation /from 6 to 10 days depending on the rate of healing of the wound and general condition of the aptient/.

The stimulators were implanted in the cervical segment during decompression of the spinal cord from anterior approach with partial or complete resection of the vertebral body.After removing the fragments of the vertebral body compressing the meninx and forming the bed in the adjacent vertebral bodies,the electrodes of the stimulators were placed under the vertebral bodies adjacent to the damaged vertebra,one below and one above the damaged one,and then autogenic bone graft was inserted over them.The starter was placed in the front upper part of the chest in a canal formed in the subcutaneous tissue.Laminal suture ended the surgery.

Electrodes were implanted in the thoracic segment either during spring alloplasty,when the electrodes were inserted beneath the vertebral arches below and above the site of injury,or during decompression of the spinal cord from latero-anterior approach.In this case one electrode was inserted under the meninx sac anteriorly,the other one was inserted under the vertebral arch dorsally.

There were only 4 cases of electrodes implanted under the dura mater, on the arachnoidea.This kind of operation was avoided,as a rule,for the fear of mechanical irritation of the injured spine segment by the electrodes,and because of prolonged time of the surgery.The starter was placed in the subcutaneous tissue toward the lateral surface of the chest.

THE RESULTS OF CLINICAL INVESTIGATIONS OF THE PERIPHERAL NERVES STIMULATION

The first clinical experiments have demonstrated that stimulators are well tolerated by human tissues,and systematic stimulation training helps to cease the atrophy of the muscles supplied by the stimulated nerve.Distinct increase of force produced by paralyzed muscles,as an effect of stimulation , was noted.

Subsequent experiments showed not only multiple increase of muscle strength /Fig.1./,and prolonged maintenance of maximum moment produced

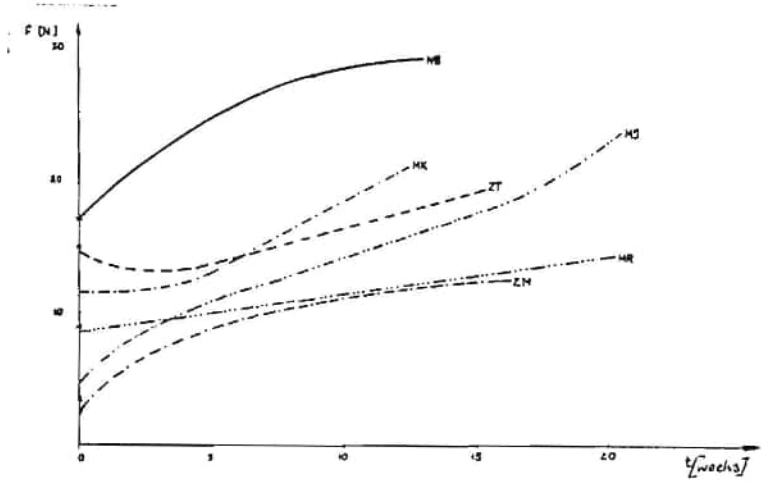


Fig.1. Increase of force exerted during stimulation by muscles of thumb in function of time of application of stimulation programme.

by the muscles in consequence of stimulation training,but in numerous cases the patients were capable of active magnification of the force developed by muscles after stimulation./3/.

The obtained results encouraged the authors to make attempts to construct an electronic-orthotic device which would make good use of the paralyzed muscles of the hand to perform simple functions of the hand by means of stimulating the uninjured nerves.

The principle of operation of the device /Fig.2./ consists in the activation of the flexor and extensor muscles of the fingers by means of electric stimulation of the radial and median nerves by implanted stimulators.



Fig.2. View of all the parts of the device for controlling grasping function of the paralyzed tetraplegic's hand.

Properly programmed joint action of a pair of stimulators and application of a set of feed-backs and of external control system create good conditions for functional movements/Fig.3././3,4/



Fig.3. Photograph of a patient wearing orthosis,control system and glove with transducers during grasping movement.

STIMULATION OF SPINAL CORD

Beneficial effects of electrostimulation of peripheral nerves resulting in some functionality and force of paralyzed neuro-muscular structures and good effects of stimulation on the injured segment of the spinal cord encouraged us to apply electrostimulation to the spinal cord directly.So far,56 patients with symptoms of complete or incomplete injury of the spinal cord /with complete paralysis in each case/ have had stimulators implanted in the cervical or thoracic spine segments.Our investigations show a distinct influence of local stimulation on injured spinal cord.A markedly quicker regulation of excretion automatism and fuller neurologic and functional recovery were recorded,compared to the group of patients treated in analogous way,but without stimulation. Bladder automatism in stimulated patients appeared after 6 weeks,on average,whereas in cases of other treatment methods it usually appeared 3 months after injury./1, /

Attempts have been made to apply stimulation in three cases of sclerosis multiplex.In one case only a temporary neurologic improvement was observed /better movement coordination,attempts to walk/.

STIMULATION OF PHRENIC NERVES

Attempts were made to stimulate the phrenic nerves in 2 patients with spinal cord injury above the 5th cervical segment.They had 2 stimulators implanted.Alternating action of the stimulators forced the action of the diaphragm in accordance with the respiratory cycle and restored the patient's ability to breathe unaided.

CONCLUSIONS

It has been observed that application of stimulation in the treatment of patients with cervical spinal cord injuries makes it possible to :
- cease the process of atrophy of the paralyzed muscles and to increase their functionality,
-accelerate the regeneration of injured nervous structures and to create the connection of the spinal cord to higher central nervous system,
-force the grasping function of the paralyzed hand,
-markedly quicken the regulation of the excretion automatism /by half/,
-achieve more distinct and fuller neurologic and functional recovery compared to unstimulated patients.

Thus,the results of investigations point out to significant advantages of the electrostimulation method applied to spinal injured patients and they seem to be worth applying in clinical practice.

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ON ONE SYSTEM APPLIED TO SUPPORT THE LOST FUNCTIONS OF PREHENSION MOVEMENT x)

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SUMMARY

The problem of prehension in patients with spinal cord injuries is discussed. Orthotic device forming the hand is combined with the stimulators for supporting lost functions of opening and closing of the palm and fingers.
Based on the results obtained in 1971 to 1980 a new system included the possibility of stimulation of pain and bone coalesce was design.

MATERIAL AND METHODS

Motor dysfunction can be caused either by trauma, or past as well as current sicknees (e.g., poliomyelitis, apoplexy, polineuropathia and myopathia). Another reason, which practically eliminates the use of technical means for resorting the motor functions, is muscular spasticity. The latter occurs as a result of high-level damage to the motor control system, or, in other words, damage to the central nervous system.
Damage to the spinal cord, regardless of the lesion level, results in vast changes in motor activity of the organism. The lesion site becomes a temporary or permanent breaking point of ascending and descending signal pathways.
In such a case, the brain cannot receive information being sent from parts of the body served by the spinal cord and nerves below the level of the lesion. This lack of informations makes it impossible for the brain to form an adequate answer to what is really happening in the peripheral zone. On the other hand, the commands sent by the brain do not reach the peripheral zone because the descending pathways of informations are blocked by the lesion.
In such a situation, that which happens in the peripheral zone cannot be controlled by the brain, and may be created by the part of the spinal cord which extends below the lesion. Such activity can be manifested by uncontrolled spasticity, or by aimless and undirected muscular response to various stimuli coming from the peripheral zone. The patients with such damage are indifferent to such environmental stimuli as high and low temperatures, pain, and touch. They are also unable to perform a purposeful motion since the flow of necessary brain impulses through the spinal cord and peripheral nerves to the muscles is blocked.
Spinal centers above and below the place of trauma - analogically to the peripheral nerves - are not damaged; both the nerve and the muscle preserve their properties of reacting to various kinds of stimuli, which means that they retain their excitability.
In this solution a special method for forcing the grasping function was proposed.
In this method, the links of the extremity are driven by the retained muscles powered from their own biochemical sources of energy. Low-energy external sources of electrical energy used in this method only play a role of control for the system.

RESULTS

During investigations carried out in the years 1971 to 1976, the influence of electrical stimulation of peripheral nerves on functional improvement of the paralyzed hand of tetraplegic patients, in cases of spinal cord injuries at the C5 to C7 level, was

x) Supported by the key-problem no. 0.6.5 coordinated by the Research Center for Medical Technology.

verified under clinical conditions.[2]
Based on the results obtained during the preliminary investigations, an hybrid system for program control of paralyzed muscles in order to obtain useful movements of the paralyzed extremity of the tetraplegic patient was designed, and suitable experiments were carried out from 1976 to 1980.[1]
This system can be achived by simultaneous cooperation between a patient and a system of stimulators implanted on the nerves, and external apparatus.
A position-measuring transducer-precision potentiometer assures the possibility of controlling the position of the fingers during opening and closing of the hand. The force transducer, by maintaining contact with the object, makes it possible to develop the force necessary for picking up or shifting the given object.
This system insures direct control of the duration of the stimulating signal so as to secure a firm grip. In turn, the programming system controls the work of an individual subsystem in such a manner that after a patient starts a movement, all the remaining operation occur automatically at suitable time sequences.
Stimulators, implanted on the radial and medial nerve of the paralyzed extremity, have been used to stimulate selected muscle groups. Suitable programmed cooperation of such pairs of stimulators creates favorable conditions for performing functionally useful motion.

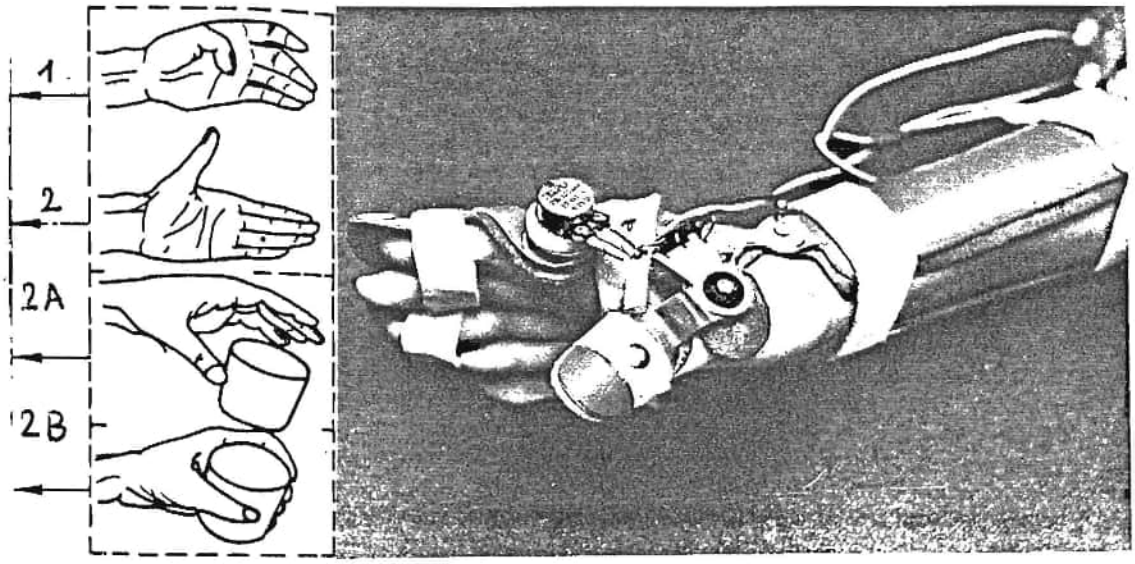


Figure 1. The sequence of activities in the grasping movement and an example of technical solution.

The whole process consists of three phases and activities A and B. In phase 1, the device is turned on and is ready for operation. The flexors and extensors are not stimulated. In phase 2, the hand is extended (the fingers are straightened). The stimulation of the flexors is turned off. The stimulation of the extensors is turned on and the third phase consists of a sequence of two activities:
1. Activity A: After turning the stimulation on and increasing with time the stimuli sent to the flexors, the hand grasps an object. The system of velocity control is turned on to coordinate the finger flexion.
2. Activity B: The object is lifted. As a result of the stimulation of the flexors by means of the force reflecting transducer, the grasping force is adjusted to the weight of the lifted object.
The device is controlled by means of one signal source. Switching on successive phases of motion is accomplished through application of impulses evoked by the patient's head movement.

DISCUSSION

Tests were carried out on four patients with spinal cord injury at the C6 level by implanting two stimulators on the median and radial nerves. An orthotic with the position transducer installed in the metacarpophalangeal joint was mounted on the right extremity.
Many investigations and improvements were conducted.[3, 4]. In one of applied method of finger flexion control the impulse time, associated with the state of muscular excitation, was used to control flexion of the fingers. The amplitude of voltage was set so that 50 μs impulses caused no motion. The impulse time could be stretched to 220 μs (the control performed by a change in applied voltage). Using this method in an open control system, a record of finger closing angle versus time was made. It was evident in this case that the deviations of the graph of actual motion from the theoretical relationship represented by a straight line are less then ± 10%.
Figure 2 shows the record of the angle of closing of the hand versus time for the system fitted with a feedback loop. In this case, the performed motion is fairly smooth.

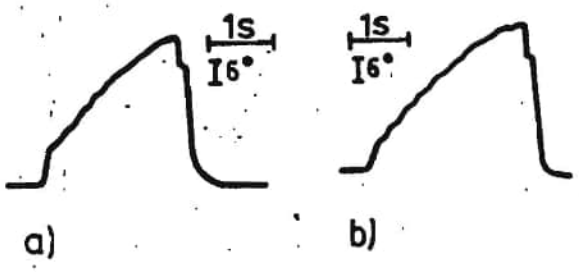


Figure 2. Angle of finger closing time with feedback loop control.

CONCLUSION

Based on the results obtained in the years 1971 to 1980, a new system for program control of the paralyzed hand of tetraplegic patients combain with the possibility of pain and bone stimulation too, was designed.[5]. This whole system is composed of the following subsystems:
- Amplifier,
- Program unit - digitimeter,
- Unit for stimulation of the motor system included pain,
- Unit for stimulation of bone coolesce,
- Implanted stimulators placed on the nerves, bone or surface electrodes placed on the skin.

A set of technical conditions and a program of investigation in clinical conditions was elaborated in cooperation with two Clinics.

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PREVENTIVE MEASURES IN MAINTAINING MAN'S PHYSICAL FITNESS AND ORTHOSTATIC CAPACITY UNDER HYPOKINESIA

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SUMMARY

The objective of this report was to sum-up the results of a set of rehabilitation measures and recources that were applied in preserving man's physical fitness and orthostatic stability under the influence of 100 days of hypokinesia (HK), that is, a rigorous bed rest regime. The use of physical exercise (PE), electric stimulation (ES), lower body negative pressure (LBNP), controlled intake of fluid and salt (CIFS), pharmacological agents (PA),combined preventive measures, was evaluated. The efficacy of these measures was assessed on the basis of excitability and liability of the musculus rectus femoris by the method of ES. The function of cardiovascular and respiratory systems was examined using a graded physical exercise test (GPE). PE is the principal mean of preventing the development of hypokinetic disorders of the neuromuscular system and preserving physical fitness and muscular strength, LBNP combined with leg exercises at the hight of rarefraction increased orthostatic stability, CIFS increased intravascular blood volume, as well as the effect of sodium chloride on vascular tonus, PA influenced favorable man's fitness and cardiovascular function, ES improved general condition and elevated physical fitness, and combinetion of these agents facilitated endurance to hypokinesia. All these effects, however, were of moderate value and inconsistent in nature. It was concluded that none of the applied preventive measures can be used to retain completely man's physical fitness and orthostatic stability under the influence of diminished muscular activity conditions.

ITRODUCTION

From the very beginning of development of modern science and technology, it became apparent that the application of computation and automation to different sections of life is linked with drastic reduction of muscular activity of man as well as knew and rather complex problems, unknown or little-known to medical science (1, 2).

The problem of preparing man to penetrate into a complete automated society made it necessary to investigate the efficiency of preventive measures to counteract the effects of a number of physical factors, including some that have been very little-studied and difficult to reproduce under laboratory conditions but which have an adverse effect on man under limited motor activity.

Some of the measures that developed and used under hypokinetic conditions are the following: physical exercises, electric stimulation, lower body negative pressure, controlled fluid and salt intake and pharmacological agents. Thus, the aim of this study was to evaluate the efficacy of these measures in preventing the manifestation of deleterious effects of diminished muscular activity on physical fitness and orthostatic stability of man by examining the available data (3).

ANALYTICAL PRESENTATION OF PREVENTIVE MEASURES

Physical Exercise (PE)

Physical fitness and orthostatic stability problems were evaluated on 12 essentially healthy men using a set of physical exercises (combination of athletic exersizing) under 100-days of HK. Their energy expenditure was not more than 450 kcal/h and they involved the main muscle groups (4). The work-out was scheduled as follows: three days of PE with loads in different directions and one day of rest (cycle based exercises of 3-days training 1-day rest; cycle 3+1).

The obtained data revealed that the use of PE preserved the strength of flexor and extensor muscles (10-groups of muscles were examined), as well as physical fitness of the men, according to the results of a physical load test performed on a bicycle ergometer. Orthostatic stability was, however, less than the initial level. A biopsy of the soleus muscle demonstrated that the sarcoplasmic and contractile protein levels did not changed, nor their enzymatic activity. Thus, PE aided in preserving the main physical qualities of man, as well as physical fitness, but it did not have a beneficial effect on his orthostatic stability and general well-being.

Electric Stimulation (ES)

Experiments were conducted on 12 healthy men ranging in age from 18 to 22 years (in previous as well as in the subsequent studies men's age was the same) under 100-days of HK. The 1st and 2d group of men were subjected to stimulation of anterior and posterior muscles of the legs and thights, as well as back and abdomen, using a Tonus-2 instrument. The 3d group of men served as control. In the 1st group of men, ES was delivered using 20 electrodes, stimulating each of the previously mentioned group of muscles with a separate pair of electrodes. In the 2d group of men, 12 electrodes were used to stimulate the same muscle groups. In addition there were performed functional tests with physical exercise loads on a bicycle ergometer.

General condition and endurance to HK were much better among the men whose muscles were submitted to electrostimulation. As a rule, the sessions gave the men satisfaction and were perceived as a pleasent treatment, which elevated their confinement to strict bed rest. The sensations following ES resebled those experienced after a mild PE or massage of the muscles.

There were indications that the delivery of ES of muscles has some preventive effect on certain parameters of the neuromuscular system and physical efficiency of man under HK. The most substantial protective effect of ES was observed in the 1st group of men; and it was less distinct in the 2d group of men; however, the differences between these two groups were found to be insignificant, according to the examination of a number of parameters (perimeter of lower leg, muscular tonus, ichnography, static endurance, tested with measured and stepped-up load on a bicycle ergometer). Thus, it can be said that ES of muscles may be an effective ancillary method for preventing neuromuscular disorders under limited motor activity conditions.

Lower Body Negative Pressure (LBNP)

Experiments performed on 12 healthy men (6 control and 6 experimental) under 100-days of HK and LBNP training, on the 56th-60th and 94th-98th days, at the rate of 4-5 times of 1-hour, were demonstrated mild effects on physical fitness and orthostatic stability and only in three

of the experimental group of men. With maximum rarefraction (up to -75 mm Hg) and mandatory leg movements simulating walking at the rate of 10-20 steps per min, the men continued to feel well, even those who exhibited a prefainting state during the functional tests with LBNP at "static" rarefractions of -40 or -50 mm Hg. There was a reliable decrease in excretion of fluid and sodium during the LBNP training, and a significant effect was demonstrated on the 2d day of conditioning. It was concluded that combined LBNP with leg movements at the height of rarefraction was more effective than pure LBNP in maintaining man's orthostatic stability and physical fitness under bed rest.

Controlled Intake of Fluid and Salt (CIFS)

For inproving man's capacity to orthostasis (75°-- 0 min) and LBNP tests (-25, -35, -40 and -50 mm Hg for 2, 3, 4, and 5 min, respectively) by artificially increasing hydration of the organism, with additional intake of fluid and salt, 90 tests were performed, lasting 1-3 days and involving 10 men who were kept on a strict measured diet. The most reliable preventive effect, without any unpleasent subjective sensations, was demonstrated when the men ingested dry tablet salt (0.18-0.20 g/kg body weight per day) in divided doses together with food. It was revealed that endurance of man to orthostatic and LBNP tests improved considerably after the additional fluid and salt intake. Even 8-10 hours after the final doses of water and salt, was observed a substantial positive balance of fluid and sodium in the examined men. It was possible to obtain comparative data on the use of different variants of fluid and salt supplements, and to select the most reliable program of intake thereof under hypokinetic conditions.

Pharmacological Agents (PA)

The effect of a mixture of ephedrine and strychnine was measured under 100-days of HK on 26 men (20 control and 6 experimental). The effective dosage tolerated without any side-effect, against the background of changed reactivity,constituted 20-40 mg ephedrine and 1 mg strychnine. The drugs were given for 12 to 14 days, beginning on the 70th day of HK. Physical fitness, as was determined by PWC-170 test, reduced by 45% in the control group of men on the 98th day of HK and by 34% in the experimental group, as compared to the initial level. It was possible to correct only to certain extent the disturbances referable to man's physical fitness and orthostatic stability under HK.

Combined Preventive Measures (CPM)

The efficacy of combined LBNP, on the 82d day of HK, for 1-hour, with CIFS, against the background of PE, was estimated. These measures were found to be compatible, did not elicit unpleasent subjective sensations and led to significant retention of water and sodium in the body. On the 96th-98th day of HK, in this and the following test, the men were trained in the protective pressure suit in the morning hours, alternating simulated walking and jumping (1-2 min each) at the initial levels of rarefraction, without consideration of fluctuations thereof. After LBNP conditioning the men received a fluid and salt supplement, and the last portion of dry salt was given to them about 2-hours prior to orthostatic tests. This study maked it possible to provide experimental substantiation for the CPM. It was revealed that combined CIFS with LBNP could increased orthostatic stability and have a favorable effect on man's physical fitness at the final stages of hypokinesia.

Evaluation of Efficacy of Preventive Measures

In order to assess the efficacy of these measures, excitability and

liability of the musculus rectus femoris was measured on 54 men (18 experimental and 36 control) under 100 days of HK using ES method. A comparative analysis of changes in excitability and liability of the neuromuscular system of both groups of men demonstrated significant differences between the men who were physical conditioned and those who served as control. An evaluation of parameters characterizing excitability and liability of the neuromuscular system of the men who were exercised only with a combination of athletic exercizing unit (3 days training 1-day active rest), as well as those who followed the sets of preventive measures, revealed that these parameters underwent essentially insignificant changes under HK. Retention of excitability and liability of the neuromuscular system, which was demonstrated in these experiments, along with retention of force of flexor and extensor muscles (10-groups were tested), made it possible to conclude that PE is the principal means of preventing the developmenent of hypokinetic disorders of the neuromuscular system under diminished muscular activity.

Graded Physical Exercise (GPE)

The cardiorespiratory system was studied before and after HK, using GPE on 12 men (6 experimental and 6 control) and CPM on 12 men. The heart rate at the end of GPE on the bicycle ergometer, performed after HK, exhibited virtually no difference from the heart rate in the control group of men.The volume of exercise performed, maximum oxygen uptake and the amount of oxygen utilized by the body with a maximum load per systolic volume decreased reliably in the control group of men ($P < 0.05$), whereas in men who subjected to CPM these parameters were not differ statistically from the initial values and showed a tendency toward increasing.

DISCUSSION

The obtained data made it possible to demonstrate that these measures were not able to inhibit deterioration in physical fitness, orthostatic stability, cardiovascular and neuromuscular systems of man under HK. The most pronounced changes thereof were determined by the end of the 60th day. The impaired regulation of the examined parameters was related primarily to deconditioning and significant reduction of desirability of man to perform any kind of activities so that PE is reverted to an additional stress stimulus that intensifys the adaptive mechanisms of organism, when they already functioning intensively under diminished muscular activity conditions (5). With the use of these preventive measures it was not possible to guarantee to any significant extent preservation of physical fitness and orthostatic stability of man under HK. Thus, the problems and objectives formulated have not yet been definitively resolved.

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MAINTENANCE, TRAINING AND FUNCTIONAL USE OF DENERVATED MUSCLES

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The impressive results of electro-therapy and functional stimulation are achieved in the field of central paralyses. In peripheral or flaccid paralyses however, it is already considered a success if atrophy can only be retarded. The explanation for this situation is given by the completely different symptoms.

Central paralyses are often incomplete as there is mostly only one tract affected, either the extra-pyramidal system, the pyramidal tract or the cerebellospinal system. The damage appears as spastic paralysis, muscular weakness or a disturbance of the muscular coordination.
Peripheral paralyses are caused by a disturbance of the motor neurone which starts a degenerative atrophy in the affected muscle. Excitation will gradually be reduced until at last only sluggish twitches are produced, the so-called reactions of degeneration. Any reflex activities as well as any tonus are missing. In addition to this secondary damages are appearing due to reduced metabolism, reduced circulation of blood and lack of active movement. Such damages are for example infections, bad condition of skin, decubiti, injuries to a joint and restricted growth of the bones.

Table 1 shows a comparison between central and peripheral paralyses with regard to electrostimulation./1/ The parameters chosen for the indirect muscle stimulation are identical to those applied for functional electrostimulation - a pulse duration between o,1 and 2 ms and current intensities up to 5 mA.
All current intensities are valid for a transcutaneous supply of currents.
Concerning the direct muscle stimulation we have indicated for comparison the values valid for the conventional treatment by exponential currents. (Fig. 1) This type of stimulation enables the selective stimulation of a solitary, paralysed muscle by means of accomodation to its intact environment. /2/
The main obstacle to a restoration of muscles, thus exceeding a mere retardation of atrophy, is the fact that only few single twitches can be produced. This fatigue however, can be eliminated to a most extended degree by the hereby applied bidirectional currents.

In contrast to the single-point stimulation of normal muscle or nerve membranes, stimulation is now effected via the electrical field between the electrodes as the muscle membrane is no more capable to generate or to spread excitations. If polarity changes different areas of the muscle are stimulated, similar to the alternating acting of motor units in natural movements. As the charge is balanced the ionic density in the membrane area is not changed on the average. The necessary pulse duration of several 100 ms in the case of most severe degeneration can be shortened down to about 20 ms by daily training. Initial single twitches will then turn over to considerably more powerful contractions.
The necessary current intensity depends above all on the time gap between denervation and the beginning of therapy and will thus only little be changed by the daily training.
Moreover, in sensitive patients current pains may arise which can however be reduced to a tolerable degree by suitable pause duration. But training will then become less efficient and will require more time per day.

The changed kind of excitation implies a different application of the electrodes. Bipolar electrodes are attached to the skin at both ends of the muscle belly so that we get a current flow all over the whole muscle. The size of the electrodes must be adapted to the cross-section of the muscle. We are using electrodes of a diameter of 3 or 7 cm^2.

Large or multicipital muscles may require the application of several electrodes and multi-channel stimulators.
We are convinced that the necessary current density all over the whole volume of the muscle can be obtained by transcutaneous electrodes only.

The targets for the therapy of flaccid, denervated paralyses are ranging below those set up for central paralyses. As the latter deal with maintenance, re-achievement or substitution of function, we are concerned in the maintenance of the muscles or extremities and prevention of secondary damages.
This can only be achieved in daily training with a minimum stimulation of one minute per muscle.
Considering costs and time this kind of training should be executed by instructed laymen at home, using home stimulators. On the premises of a continual training, the muscle tissue, the condition of skin and the growth of the affected extremities can considerably be improved within few months./1/

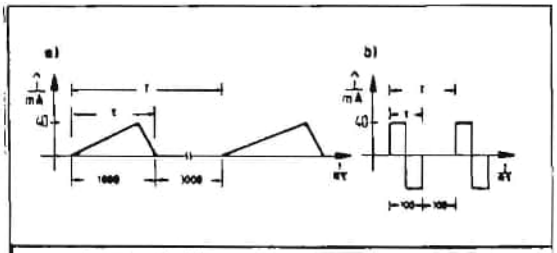


Figure 1 Stimulation currents
a) triangular b) bidirectional

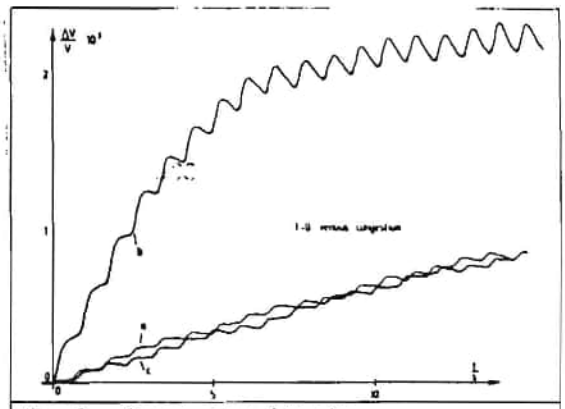
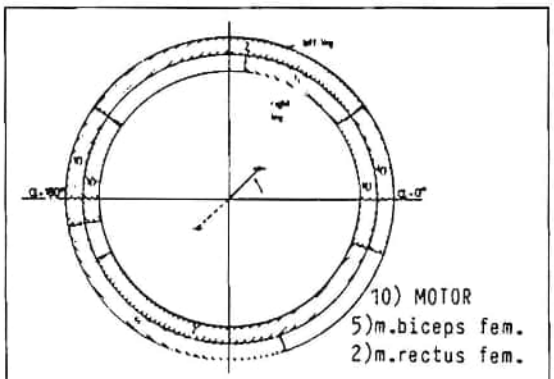


Figure 2 Blood circulation of lower leg



Driving diagram

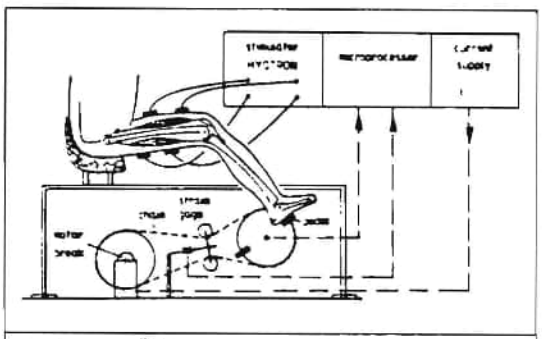


Figure 3 Four channel microprocessor controlled stimulator

PARALYSES	CENTRAL (SPASTIC)	PERIPHERAL, FLACCID
stimulation (muscle)	indirect	direct
electrical stimulus,pulse duration	0,1 - 2 ms [1]	(800-1000 ms) [2] 10- 100 ms [3]
current intensity (transcutaneous)	5 mA	(80 mA) 2-40 mA
pulse duration (pulse/period duration	1 : 20	(1 : 5) 1: 1
fusion frequency	40 - 150 Hz	(---) 15 Hz
stimulus conductivity	nerv 70 m/s muscle 5 m/s	(---) ---
excitation process	single pointed by current density depolarisation of nerve membrane	spatial by current field direct release of calcium ions
electrodes	transcutaneous or implanted	transcutaneous only
arrangement	monopolar on motor point	bipolar at both ends of the muscle belly
target	maintenance or substitution of function	maintenance of muscle or extremity

1) monodirectional 2) exponential (monodirectional) 3) bidirectional currents

Table 1: Comparison between central and peripheral paralyses concerning electrostimulation.

Fig. 2 shows the blood circulation of a trained lower leg measured before and after stimulation by means of pletismography. At first blood circulation rises steadily during a two-minutes-stimulation, it remains stable on the higher lever for about half an hour and then slowly fades away. We also stimulated with medium-frequency currents for comparison, as those are often said to have a special effect in the case of flaccid paralyses. /4/ We did not get any contraction by this kind of stimulation, nor could we measure any improvement of blood circulation.

With the kind support of Fa. Siemens - Unternehmensbereich Medizinische Technik - Erlangen we were able to measure the phosphorus metabolism by means of N M R (Nuclear Magnetic Resonance).
Adenosin Tri-Phosphate and Creatine Phosphate are the direct carriers of energy in the muscle.
The absolute amplitudes in the paralysed leg were distinctly lower compared to those measured in the non-paralysed arm. After a short period of stimulation we noted at first a decrease of the amplitudes, but after a few minutes they were steadily increasing until they reached the value measured in the arm.
Considering these results we are convinced that home stimulators are indispensable in the case of flaccid paralyses. /3/ We have developped a special home stimulator and its industrial production has started recently.
As these stimulators are applied by laymen, we paid special attention to security equipment to get the utmost protection from defective device and operation errors. A further important aspect was a comfortable handling.

By means of multi-channel, processor-controlled stimulators the time for stimulation can be shortened, treatment will be intensified and will become more efficient. Besides this stimulation can be executed almost autonomously by the disabled patient himself.

Fig. 3 shows the scheme of a laboratory arrangement especially adapted to the patient.
The child, suffering from a transverse lesion of the cord, is sitting on a home trainer which can be pushed on or stopped by a motor, if necessary. The paralysed muscles -here extensors and flexors of the upper legs - are stimulated according to the pedal angle by transcutaneous electrodes. In addition to the pedal angle the processor controls the straining of the chain which depends on the produced torques. During a first turn for measuring purposes the system finds out step by step any possible forces and their corresponding parameters. After this the active training can start.

Table 4 shows the diagram of motion.
Above the pedal position - forward motion, left leg - there are indicated the operation areas for muscle and motor. We can see that without integration of the joints only horizontal force components can be transferred to the chain. In the areas of 0° and 180° motor force must be joined. The diagram thus illustrates the task to replace motor and braces by using the activity of further muscles.
Ankle-, knee- and hip joint can be controlled by stimulating the corresponding agonists and antagonists and can then be used for more complex motion chains.
The up to now attained strengthening of the muscles offers the chance to exceed functional training towards a functional use of denervated muscles.

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CLINICAL USEFULNESS OF A SOFTWARE CONTROLLED DDD, MO PULSE GENERATOR WITH TELEMETRY AND EVENT RECORDS

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INTRODUCTION

Over the past 25 years, artificial pacemaker systems have become the treatment of choice for slow ventricular rhythms resulting from sinoatrial disease or varying degrees of heart block. The available technology once limited these devices to a fixed rate, asynchronous mode of operation; subsequent technological advances have made possible more sophisticated units with sensing, programming, and telemetry capabilities. There are, at this time, commercially released devices for the treatment of bradyarrhythmias which sense in both the atrium and the ventricle, and which can pace both chambers sequentially as needed. These DDD pacemakers were thought to be state-of-the-art, "universal" systems, which could be safely implanted in any patient for whom artificial pacing was indicated. However, it soon became apparent that the limited programming and telemetry available in these devices were less than ideal for the management of the pacemaker patient. Indeed, in a significant number of patients with intact retrograde conduction, the pacemaker induced a reciprocating tachycardia. This pacemaker-mediated tachycardia, or (PMT) resulted in, or had the potential to result in, negative physiologic consequences such as angina or tachycardia induced congestive failure. The limits imposed by the pacemaker and/or programmer hardware often meant that the clinician had to sacrifice or compromise on the mode of therapy otherwise best suited to the patient's needs. The therapeutic responses to the PMT are either increasing the atrial refractory period or otherwise blocking one limb of the loop.

Our experience with a new pulse generator which, with the incorporation of computer-like "memory", provides a previously unavailable degree of programming flexibility and expanded telemetry capabilities, is reported herein. We believe that the gap between those devices now commercially available and a truly universal pacemaker is being narrowed.

DEVICE DESCRIPTION

The pulse generator, Cosmos^{TM} Model 283-01 (Intermedics, Inc., Freeport, TX), is a lithium powered, titanium encapsulated, dual unipolar device weighing 65 grams. It contains 64 bytes of random access memory (RAM), which, in essence, makes the unit an implantable computer. The "intelligence" imparted by the RAM allows the pacemaker to monitor itself and its environment, and adapt accordingly. Moreover, the operating instructions contained in RAM can be erased or altered, via the programmer, permitting a certain amount of "redesign" even after the pulse generator is implanted. These factors provided the capability for implementation of:

1) Virtually limitless programming flexibility of, and resolution over, a wide range of parameters.
2) Event counters which record selected pacemaker and physiologic events, and which can be accessed via telemetry.

3) Algorithms which detect potential problems and prevent or protect against such problems.
4) Temporary programming of selected parameters.
5) Telemetered sense event markers, measured data (such as battery voltage, lead impedence, etc.) and stored data (programming information, pacer model/ serial number identification, event counters).

CLINICAL IMPLICATIONS

The clinical utility of many of these features may be demonstrated by considering the problem of pacemaker-mediated tachycardia in patients with intact retrograde (ventriculo-atrial or V-A) conduction.

The heart has an intrinsic system of impulse formation and propagation. The pacemaker system has the impulse generator for formation and the lead for impulse propagation. The superimposition of one system on the other revealed previously unsuspected problems.

Prior to the superimposition of DDD pacemakers onto the heart's intrinsic conduction system, it was widely believed that retrograde V-A conduction was present in only 5-10% of all patients, and was precluded by complete A-V block. Both suppositions have recently been proven wrong. Current data[1] indicates that approximately 50% of the patient population is capable of V-A conduction, including a significant proportion of patients with complete A-V block.

If V-A conduction exists, a reciprocating tachycardia similar to that found in patients with Wolff-Parkinson-White Syndrome may occur, with the pacing system acting as the antegrade limb of the "loop" and the intrinsic conduction system serving as the retrograde limb. When an event (such as a PVC) occurs which results in A-V desynchronization, retrograde conduction may be manifested. If the resultant atrial depolarization occurs late enough to fall outside the pacemaker's atrial refractory period (ARP), the P-wave will be sensed by the pacemaker and, following the programmed A-V delay, ventricular pacing will ensue. Published data has indicated that V-A conduction times range from 110-380mS, with a mean of about 235 + 50mS.[1,2] Once this circuit has been established, it may be self-propagating, resulting in protracted, non-physiologic high rates.

The commercially available DDD's have not been totally effective in dealing with this problem.[2,3,4] Athough many have programmable ARP's, the selections are extremely limited. Additionally, prolongation of the ARP results in a decreased upper rate limit which, while of little practical consequence in sedentary patients, may compromise the effectiveness of the pacing therapy in an otherwise healthy, active individual. When the ARP is not programmable, patients have often been programmed out of the DDD mode.[2] One available unit (Versatrax II, Medtronic, Inc., Minneapolis, MN) prolongs the ARP following a PVC, but this feature is of no value if the PMT is not initiated by a PVC, and no commercially available device can stop a PMT once induced.

The software-controlled device (Cosmos™) approaches the problem of PMT in three ways. The ARP is programmable in 5mS increments over a wide range, providing maximum flexibility. It incorporates a programmable post-PVC ARP extension, allowing the normal ARP to be short (and the upper rate limit high) while still preventing PVC-induced PMT. Finally, the available RAM permits the implementation of an algorithm which can recognize many (but not all) PMT's as non-physiologic, and terminate them on the 16th cycle.

A study was undertaken, at two institutions serving as investigational centers for Cosmos™, using the pulse generator's capabilities to assess V-A conduction, and evaluating the unit's ability to prevent and/or terminate PMT. A sequential unselected group of 24 patients (7 male, 17 female) who were candidates for DDD pacing therapy had this device implanted. Prior to discharge and at monthly intervals, the pacemaker was evaluated and the three types of telemetry data (programmed values, measured data, and event counters) were obtained.

V-A conduction was assessed in the following manner: The pulse generator was programmed to a rate greater than the patient's intrinsic rate, and the A-V delay was shortened. Using the temporary programming features, the atrial output was reduced to subthreshold levels for four cycles, resulting in atrial non-capture and A-V desynchronization. Simultaneously, atrial sense event markers were activated, thus allowing observation and measurement of atrial depolarization resulting from V-A conduction following the desynchronized ventricular paced beats. Our data is presented below.

Indication for Pacing	# of Patients	# (%) with V-A Conduction	# Using Algorithm to Terminate PMT
A. Heart Block	7	4 (57)	4
B. Sick Sinus Syndrome	13	5 (38)	3 +
C. Pacemaker Syndrome	4	1 (25)	-- *
Total	24	10 (42)	7

+ Other 2 patients had self-limiting PMT.
* V-A conduction time short-retrograde P-wave fell within refractory period, no PMT induced.

A total of four patients in Groups A and B received these implants as replacements for generators which had reached end of service. The four patients in Group C had single-chambered units replaced due to cerebral hypoperfusion and/or congestive heart failure. In all cases in which V-A conduction was present, PMT was prevented or controlled by programming to some combination of ARP, post-PVC ARP extension, and A-V delay, or was self limiting. No patients were programmed out of the DDD mode as a result of PMT.

Several other features proved clinically useful as well. The wide range of programmability allowed independent reduction of atrial and/or ventricular output to the minimum safe level, reducing current drain and prolonging battery life. The event counters were used to guide reprogramming to maximize the device's effectiveness in meeting a particular patient's physiologic needs. Other algorithms in RAM prevented "crosstalk" (the inappropriate interference of an atrial output pulse with the ventricular sense amplifier) or ventricular output inhibition as a result of crosstalk.

CONCLUSION

The addition of RAM to the microprocessor-controlled pacemaker has enlarged the functional capabilities of the system. Its interaction with a software-based programmer has broadened the available clinical capabilities, and will enable introduction of instructional systems yet to be implemented.

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CENTRAL VENOUS BLOOD TEMPERATURE (CVT) AS A GUIDE FOR RATE CONTROL IN PACE-MAKER-THERAPY

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In patients with Sick Sinus Syndrome or Atrial fibrillation physiological pacing by conventional means is not feasable. Therefor biological sensors are worldwide under investigation.

After pilotstudies in dogs with encouraging results a specially manufactured PM-lead with an integrated thermistor was implanted in the RV of one of the authors as well as in volunteers via puncture of the subclavian vein. Treadmilltests were done with 3, 6 and 1o kmh. external pacing was done with 15o bpm. In 24 experiments CVT and heart rate were continously measured.

CVT correlates with work load and differs up to 1.35 oC in our studies. CVT increases independent from rate increase. CVTdifferences in rest due to respiration and metabolism up to o.24 oC were registered. External pacing has no influence on CVT.

CVT can be picked up easily by PM-circuits. Programmable features will be necessary to determine the borderline frequencies as well as the correlation between temperature and rate increase.

20 YEARS OF INTRACARDIAC PACING WITH THE SAME LEAD BUT DIFFERENT ELECTRODES

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SUMMARY

An endocardial pacemaker lead (EM 588) made out of four thin bands of stainless steel wound around a core of therylene and isolated with polyethylene has been used since 1962. The electrode transmitting the electrical impulses from the lead to the endocardium, however, has been modified. This and a change in surgical technique has reduced the early complication rate from over 15% towards 1%. Late lead related complications do still occur.

MATERIAL AND METHODS

Permanent intracardiac pacing was introduced over 20 years ago in order to meet an urgent clinical need. The desirable background knowledge of what should be required of the electrode directing the impulses to the heart was at that time practically non-existing and had to be collected at a later date.

The predominant problem of the first 15 years of intracardiac pacing was the limited power supply of the impulse generators which necessitated frequent replacements. However, when the cardiac pacemakers were provided with long lasting lithium batteries the question arose whether the electrode instead would become the time-limiting factor of the system. In order to elucidate the situation a follow up was made during 1978 of all the patients that were given an intracardiac electrode up until the end of 1967 /1/.

Out of the 306 patients treated 121 were found to have lived for 10 years or more. An uneventful history with regard to their electrodes was found in 75 patients among the ten year survivors. They were paced throughout the period with their original intravenous electrode which required no adjustment or exchange. In 39 of these patients, the stimulation threshold was measured with 3.3 uF capacitor discharge of 1 msec duration at both 5 and 10 years and was found to be 2.3 ± 0.6 and 2.2 ± 0.8 volts respectively. Thus, a continuous slow rise in the stimulation threshold does generally not occur.

Complications with the electrode were found in 46 patients (38%) among the 10-year survivors. In 13 patients (11%) electrode problems occurred during the first year. Late electrode problems were common with 28 patients (23%) having their electrodes corrected between 1-10 years and in 5 patients (4%) after 10 years of pacing.

The high incidence of complications with the intravenous electrode in the 10-year survivors could be ascribed to several factors. The first electrodes were made of stainless steel that had a tendency to corrode after varying periods of time due to a current leakage from the impulse generators. Many of the patients were paced with externally worn impulse generators for long periods during which some of them accidentally dislodged the electrode by pulling the lead. Accidents also happened to the electrode at the several operations each patient underwent for exchange of their implanted unit. These interventions sometimes caused an infection that could only be controlled by providing the patient with a new electrode.

In the early 70-ties there was a trend to reduce the electrode in size in order both to increase the polarization impedance and thereby save battery life and to decrease the stimulation threshold. A study was therefore initiated with the aim to compare large and small surface electrodes and to find out if a modification of the electrode design would bring about advantages in the anchoring of the electrode onto the endocardium /2/.

The same lead EM 588 but three different electrodes were used. The original platinum electrode (A) with an electrically active surface of 47 mm^2 was given to 54 patients. The same type of electrode but where the active surface had been reduced to 6 mm^2 (D) was given to 268 patients. The third electrode (K) given to 428 patients, was made of two crossed platinum wires formed into an empty cage or basket with an active surface of about 15 mm^2.

		Operation method			Pacemaker surgeons		
Electrode	Number of patients	two-stage		one-stage	unexperienced		experienced
A	54 (11)	50 (10)	NS	4 (1)	13 (4)	NS	41 (7)
	NS	NS		NS	NS		NS
D	268 (39)	210 (34)	NS	58 (5)	94 (26)	S	174 (13)
	S	S		S	S		S
K	428 (18)	139 (10)	S	289 (8)	57 (6)	S	371 (12)
	750 (68)	399 (54)	S	351 (14)	164 (36)	S	586 (32)

Number of early complication in brackets in 750 patients treated with different electrodes by one- or two-stage procedure and by surgeons with different experience. Significant (S) respectively not significant (NS) differences.

The two conventional electrodes A and D did not show any significant difference in the number of early complications (20 and 15 per cent respectively) regardless whether the lead was immediately connected to an implanted pacemaker or for some time first connected to an externally worn impulse generator before it was implanted.

Early complications with the two-stage procedure denotes such which occurred up until two weeks after the patient received an implanted pacemaker and with the one-stage procedure such which occurred within 1½ month after the operation.

The cage or basket electrode had the significantly lowest number of early complications. Among the 246 patients that had been operated upon by experienced pacemaker surgeons with a one-stage procedure and were given a basket electrode, only three early complications occurred, two of them were a rise in the stimulation threshold and one an electrode dislocation.

Late complications occurred among the 750 patients at 23 instances but were unrelated to the type of electrode. These were generally caused by pulling the lead when pacemakers were exchanged or by a defect in the lead insulation. The chronic stimulation threshold 6 months after the operation was not influenced by the size or shape of the electrode.

DISCUSSION

The basket electrode, which was designed with the intention of enlarging the contact area but still keeping the active surface small did not easily dislocate. It is probable that a thrombus is rapidly formed inside the cage and, when it becomes organized, attaches the electrode to the endocardium. A similar occurrence has been suggested for other hollow electrodes /3/. In most other studies, however, the electrodes have been attached to leads of different designs which might influence the results. In this series there is no lead bias and the differences found must thus be attributed to the electrodes. Lead related problems however are important and will need great attention in the future in order to reduce the long-term complication rate /4/.

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A SHORT REVIEW OF THE HISTORY OF CARDIAC PACEMAKER ELECTRODES AND LEADS

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SUMMARY

Authors review the history and development of pacemaker electrodes and leads used for temporary and permanent cardiac stimulation. After the start with external stimulation, needle electrodes and wires the transthoracic, epicardial and myocardial leads were developed. The next step was the transvenous electrode used for endocardial stimulation. Different shapes and materials were used to achieve active or passive fixation /screw-in, helifix, tines, J shape, etc./. Special leads and electrodes became available for stable atrial fixation enabling the widespread use of physiologic dual chamber pacing. New materials and techniques like porous carbon, and flares are tried to ensure lofe long stable electrodes and leads. The are tried to ensure lofe long stable electrodes and leads. The problems associated with unipolar and bipolar stimulation, the advantage of polyurethane versus silicone sheating of the leads, some special diagnostic stimulation electrodes are discussed. The future trends and requirments for ideal electrodes and leads are outlined.

MATERIALS AND METHODS

Introduction

From an emergency attempt to save life temporary and permanent cardiac pacing became routine proceeding with about 2oo ooo pacemakers implanted yearly. This involves a compepetive high technology multi-million $ industry producing constantly newer models with extended capabilities developing safer, more complex, cheaper acessories.

The usual stimulation unit for heart pacing can be divided into 3 parts:

1/ Impulse generator /PM/: energy source and electric circuit
2/ Electrode lead /L/: connects the PM and the heart, through it the electric impulse is conducted via an isolated electrode
3/ Electrode: is defined as the termination of the L in direct contact with the stimulated heart

The relatively simple task of the L and E /generally we understand L and E clinically even if we use either of them/, connecting the heart and the PM electrically is of very great importance, because any failure can result in sudden cessation of cardiac pacing and mortally endanger the pts life. It is interesting to note, that at the beginning of cardiac pacing for a long time the electrodes seemed the most secure part of the pacing system, but with the advent of the long life energy source /lithium powered batteries/ the L is considered the weakest link: electrode-lead rupture, dislocation etc. are predominant in complication statistics.

Our aim was to reviw the history of L and E in cardiac stimulation.

History and development of electrode leads

The clinical hystory of L and E started with the skin electrode in 1952 /1/. This and the esophageal electrode /2/ stimulated the heart indirectly. The first direct stimulation was carried out using needle electrodes and wires. This were no more than emergency life saving techniques.

The first great leap forward was the introduction of transthoracic electrodes. One type of this was the myocardial E, the other the epicardial, placed either into the myocardium or on the epicardium of the exposed heart undre cardiac surgery /3,4/. These were used in nearly all PM implantations initially. Different shapes and structures were brought out early to give stable and safe electrodes. These were the times when the helical coil, the loop was introduced. Cardiac surgery was required this gave it at first safety and stable positioning, but in the relatively old patient group it was one of its major drawbacks, causing lot of complications. To do away with the necessary general anasthesia, to limit the complications of thoracotomy special myocardial corkscrew electrodes were designed and proved to be effective.

Nearly simulatneously with the transthoracic E and L the transvenous E-L was developed and by facilitating a relatively simple introduction via a vein of the E-L and making cardiac surgery unnecess sary became the most widely used technique ina ashort time after some of its initial drawbacks were eliminated /5/. Today except in cardiac surgery and very special cases it is universally used.

From here on we discuss the E and L of temporary stimulation later. With the advent of demand pacing beside the role of transmitting the electric stimuli reliable sensing of the endocardial ECG became an other eqally important factor in E and L design.

Since the introduction of cardiac pacing two electrode systems were used either unipolar or bipolar /one stimulating electrode is applied, the anode is attached to the Pm and is of large surface/ or bipolar /where both electrodes are in or on the heart/. Unipolar configuration is generally favored, but both have advantages and disadvantages /6/.

Till now we spoke only from passive fixation leads. Despite great efforts to find the most optimal shape /cylindrical, balltip etc./ dislocation was the greatest problem for endocardial transvenous pacing. Therefore the so called active fixation leads were developed. Prongs, screw-in appliances were developed. It is the opinion of many published papers that their use significantly reduces the incidence of electrode displacement compared to traditional L-S. Tines were invented giving new preference for passive fixation.

Most PMs implanted are ventricular models, but in recent years a growing interest was directed toward more physiological pacing modes, requiring atrial semsing and stimulating Es. The major problem limiting for many years the widespread use was that to place atrial electrodes required thoracotomy and even so the sensing and/or pacing properties deteriorated often with time. The development of transvenous J shaped ELs, new introduction techniques mode it a safe and routine clinical procedure, enabling implantation of a yearly growing number of physiological, dual chamber PMs.

Electrode and lead materials

At first gold-platinum and other very costly materials were tested. For long time cheaper metal alloys served. Lately porous tip and activated vitreus carbon tip electrodes were introduced to lower chronic threshold and so prolong PM lifetime.

For many years silicone rubber was the only insulation material, lately polyurethane sheating is also used because smaller diameter, low friction coefficient it is excellent for dual chamber pacing.

Newest Electrode-Leads in use

The percutaneous transvenous /subclavian vein/ introduction techniques and sheating opened a new era removing the PM implantation from surgery to cardiology and simplifying the whole proceeding. The newest tested ELs are single-pass leads making only one EL able to pace/sense both ventricle and atria at the same time.

CONCLUSIONS

Future requirment for ideal EL:

1/ Single catheter system integrating atrial, ventricular sensing-pacing into one system, percutaneous introduction technique
2/ Absolute reliability, redundancy in case of lead rupture etc.
3/ Unlimited life-time
4/ Low energy requirments

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NEW PHYSIOLOGIC CARDIAC PACING

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SUMMARY

A new pacemaker that can adapt the heart rate in response to the patients metabolic requirements has been developed. This pacemaker uses breathing frequency (BF) and tidal volume as the indicators of physiological demand. In previous studies we have shown the BF to be a valid and stable physiological parameter with which to control the stimulation rate /1/.
The implantable respiration dependent pacemaker has the advantage that no special mechanical or chemical sensor are needed.
The BF is determined by an electronic autoregulating system which measures the impedance variations between an auxiliary lead and the can of pacemaker. Thirteen units have been implanted in our hospital.
Holter monitoring and stress test were performed every 1-3 months; follow-up ranged 1 to 16 months (total 68m pts). Experience in thirteen pts showed the rate response to exercise to be smooth and progressive strictly related to the oxygen uptake. The respiratoty dependent pacemaker fits the pacing rate to the metabolic needs in all pts during daily activity.

MATERIAL AND METHODS

Patients

We recently described a rate responsive pacemaker that uses the breathing frequency as an indicator of physiological demand /1/ and report here our experience with this pacing system.
A respiratory dependent pacemaker was implanted in twelve patients (mean age 62,7, range 22 - 88 years), with complete, established heart block and in one patient with sick sinus syndrome. Three patients were undergoing routine change of a pulse generator and had ventricular inhibited, fixed rate pacemakers and long term electrodes. The eight other patients were undergoing routine implantation of a pacemaker and had short term electrodes. An auxiliary passive lead was easily inserted transcutaneously by means of an introducer. The sensing electrode is of very simple design and similar to a screw-in intracardiac lead. All patients had unrestricted exercise tollerance corresponding to the 2nd NYHA functional class.

The Pacemaker

In the implantable pacemaker (Biotec S.p.A. Bologna, Italy) it is possible to program the following parameters: 1) respiratory dependency (on off); 2) relationship between respiratory rate and heart rate (8 positions); 3) minimum heart rates 60 and 70 bpm);

and 4) respiratory sensitivity level (8 positions), which selects the minimum sensed tidal volume. By implanting a subcutaneous lead and passing a pulsed current signal across the dipole created between the pacemaker itself and the lead, movement of the thorax can be monitored by the change in electrical impedance which occurs as the dipole length changes. The current drain at 500 ohm, 70 bpm, 100% pacing is less than 25 μA. The detector system for respiratory frequency has a current drain of less than 3 μA. The most important tecnical aspect is the reliability of the detection system since neither a mechanical transducer nor an electrochemical sensor is present.

Assessment Study

Exercise testing - In each patient the effects of ventricular inhibited, fixed rate pacing at 70 beats/min and of rate responsive pacing were comparatively assessed on two separate occassions by measurements of tolerance to treadmill exercise following six minute work load steps.
Studies were performed on average four weeks and three months after implantation of the pacemaker, and the patients were unaware of which pacing mode was being evaluated. Exercise tolerance was reported in terms of metabolic equivalents (METS) and expressed as ml oxygen uptake/min/kg/3.5.
Holter monitoring - The patients underwent Holter monitoring over periods of 24 hours every three months using Anatec S (Ela Medical, Paris) system. From these data a trend analysis (rate v time) was computed.

RESULTS

The results were obtained over a 68 months/patients, range 1 to 16 months, follow-up period. In one patient miopotential inhibition of pacing was observed for few seconds when the patient exercised strongly the right arm. There were no other sensing or pacing problems at this early follow-up stage.
The respiratory sensing of implanted unit was assessed by telemetry and changed to an acoustic signal by an external receiver. The proper sensing level of the respiration pick up system was selected avoiding the side effects of the hyperventilation associated with small tidal volume. The level of respiratory sensing remained stable in each patient for all over the time of observation. The respiration to heart rate regression line was selected for the individual patient. The minimum heart rate and minimum respiratory rate were similar for all patients and in the order of 65-75 bpm and 12 cycles per minute. The maximum respiratory rate of individual patient was checked during maximum exercise at fixed rate pacing. The maximum individual respiratory rate was indipendent of heart rate. Maximum heart rate was defined either selecting an upper rate slightly below the sinus rate at maximum exercise or substracting the age from the number 180.
During treadmill exercise testing with rate responsive pacing the progressive adaptation of ventricular rate was strictly related to the oxygen uptake. Maximum pacing rate coinciding with peak exercise work load attained the peak values of the selected regression line in individual patients. The mean value of maximum pacing rate was 129 $\pm$ SD21 range 118 - 155. The average work time with a fixed rate was 25 $\pm$ 4 (SD) minutes, with rate responsive pacing was 30 $\pm$ 3 minutes ($P < 0.05$). The maximal exercise capacity at the rate 70 beats/min was 5 $\pm$ 2 oxygen uptake/min/Kg/3.5 while at the maximum pacing rate it was 6 $\pm$ 0.9 oxygen uptake/min/Kg/3.5 ($P < 0.01$).
The fluctuations in the ventricular paced rate during various daily activities were documented by ambulatory monitoring; comparison with the patients diary permitted confirmation of appropriate responses to exercise. The predominantly basal rate of

70-80 beats/min during overnight rest is also shown.

DISCUSSION

The optimal rate in any person at rest is not the optimal rate for exercise. Standard ventricular inhibited pacemakers are set at rate fixed 70 beats/min. The two variables that determine cardiac output are heart rate and stroke volume. The compensation to fixed rate by changes in stroke volume achievable on exertion is limited. Intrinsic ventricular function, venous return, peripheral oxygen uptake modified by exercise are important determinants of exercise capacity in patients with pacemakers. The ideal physiological form of pacing is one that responds to the body's needs for varying cardiac output. Of the physiologic parameters with potential, theoretical application in the controlling of the simulation rate for a physiological pacemaker, we considered those originating from the heart or direct reflecting metabolism as unreliable in many clinical conditions. Among respiratory parameters BF offered the most potential of being used with an implantable pacemaker.
The essential advantages of selecting respiratory rate as a control parameter for rate responsive pacing are that the sensor is of simple design and shows excelent longevity, that the open loop regulation makes use of the human body computer to select the proper rate with very quick response, that can be adapted very easily to the individual patient. Therefore this principle is working as well for short term activities like climbing stairs, as for long term activities like walking uphill or aerobics so to say. The respiration controlled rate responsive pacemaker has successfully passed clinical evaluation and is available now.

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EFFECT OF ENFLURAN, ISOFLURAN, KETAMIN AND ETOMIDATE ON MYOCARDIAL THRESHOLD. AN EXPERIMENTAL STUDY IN MINIPIGS.

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SUMMARY

This study was performed in order to evaluate the effect of anaesthesia (inhalation and intravenous) on myocardial threshold.
These investigations were carried out in a group of 24 minipigs in neuroleptanalgesia. Respiration was performed via tracheotomy with a Dräger Spiromat. After a 30 ´ period of waiting for steady state and drawing arterial bloodgases and base exess to maintain equal conditions, the anesthetic agents to test were given. The effect of Enfluran, Isofluran, Ketamin and Etomidate on current and voltage thresholds as well as R-wave sensitivities were measured via a screw in electrode (Bisping, Medtronic). A significant fall in current and voltage threshold in case of Ketamin (to 71 %) and more of Etomidate (to 64,8 %) was seen (zero level 100 %). In case of Enfluran and Isofluran a minor change down to 65,2 % and 68,6 % was observed. A significant decrease in threshold means on one hand a minor A-V conduction on the other a lower fibrillation threshold, a train of thought to think in case of high risk patients.

Myocardial threshold as the presupposition in pacemaker surgery, is always of great theoretical and practical interest. In order to accurately measure changes in cardiac electrical threshold, as evoked by pharmacological interventions, it is necessary to define clearly the term threshold and the method of measuring it. Electrical threshold at any given time is the minimum electrical impulse necessary to stimulate the heart for the specific electrical system being used at that time. The myocardial threshold can be definited as parameter of electric charge, energy, current or voltage. For clinical use is above all measuring of current and voltage practicabel, since electric charge and energy are parameters very difficult to measure directly. Determinants of threshold for any pacemaker system are many and can be thought of as comprising extrinsic and intrinsic factors. Intrinsic factors include the position of the electrode, the electromechanical interface between the electrode and surounding tissue and the intrinsic excitability of the tissue. Extrinsic factors, which are determined by engineering design, include electrode composition, electrode surface area, electrode impedance and the waveform, voltage, current, and the duration of the stimulis. Along with acidosis, alcalosis and the condition of the myocardium the influence of drugs is to mention (4). In the following we will restrict us only on drugs influence and here in particular on effects of inhalation and intravenous anaesthesia.

MATERIAL AND METHODS

These investigations were carried out in a group of 24 minipigs (mean weight $\pm$ 3 kg) after praemedications in neuroleptanalgesia with 0,015 mg/kg body weight Fentanyl and 0,06 mg/kg body weight/h. Pancuronium in 500 ml 5 % Dextrose with isotone electrolyts with a drop speed of 15 ml/kg body weight/h. Respiration was per formed via tracheotomy with a Dräger Spiromat. After a 30 ´period of waiting for steady state and drawing arterial bloodgases and base excess to maintain equal conditions, the anesthetic agents to test were given. The effect of Enfluran, Isofluran, Ketamin and Etomidate on current and voltage thresholds, as well a R-wave sensitivities were measured in groups of 6 pigs via a screw in electrode (Bisping, Medtronic),

which was inserted through the right jugular vein; a controllgroup of additional 6 animals was testet with the same electrode without anesthetic agents. After adding the agent to test measurements were performed immediately, after 5 and after 10 minutes. Range-finder was the thresholdanalyser 5309 Medtronic. Statistics were performed with the paired student t-test.

RESULTS

1. A slight decrease in threshold in the controllgroup was obtained. An even minimal increase in case of 0,2 ms impulse duration.

2. In case of Enfluran a significant fall in current and voltage threshold down to 65,2 %.

3. A similar significant decrease was shown in case of Isofluran. Here the threshold sunk down to 68,6 %.

4. In case of i.v. narcotics the decrease was more significant. Ketamin showed already after 2 minutes a significant decrease down to 71,5 % of current and voltage threshold. Pay attention to the difference between impulse duration and the quick increase of the threshold after the first blood culmination.

5. After i.v. Etomidate the decrease was the deepest. 64,8 % of controll in case of an impulse duration of 1 ms.

DISCUSSION

Myocardial thresholddynamics intra- and imidiate postoperatively are because of the previous mentioned variability and the possibility of drug interactiones of great interest. Beside the new implantation of a pacemakersystem, the imidiate post-cardiopulmonary bypass phase after cardiac surgery with third degree heart block is often the motive to ventricular or sequential pacing (2). Moreover the influence of anaesthesia on pacemakerpatients in case of later surgical operations seems to be important. Decreasing threshold means a decrease in absolutely, relatively and effectively refractory period. In case of ischemic myocardial areas electrical myocardial fragmentation takes place. It means better and quicker repolarication in areas with better blood flow, with the consequence of a devided repolarisation in different areas. It means a lower fibrillation threshold respectively a longer ventricular vulnerability.
A decrease in myocardial threshold was obtained in all tested anesthetics. The straight neutral decrease in connection with small myocardial depression makes Enfluran to the way of choice in case of bradycardia and AV-blocking. Not so the isomer of Enfluran-Isofluran because of the significant fall of blood pressure systemic as well as pulmonary (1).
The effect of Ketamin is dependent on the dosis given. There is a curvilinear relation between duration of the effect and logarithm of the dosis given. The significant decrease in myocardial threshold may be an effect of the sympathomimetic working of the substance.
Etomidate is a modern hypnotic without analgetic component frequently used, because of the alleged missing of effects on the cardiac function. Our observations however show the significant decrease in myocardial threshold,only the duration of this effect is very short.
A significant decrease in threshold means on one hand a minor A-V conduction on the other a lower fibrillation threshold, a train of thought to think in case of high risk patients.

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ESOPHAGEAL HEART STIMULATION IN THE DIAGNOSIS OF SINUS DISEASE

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SUMMARY

Authors used during complex electrophysiologic and pharmacologic testing of the sinus node function /sinus automaticity assesment = sinus node recovery time = SNRT measurement, sinoatrial conduction time = SACT determination, repetition after pharmacologic autonomous nervous system blockade etc./ instead of the usual intracardiac /IC/ electric heart stimulation esophageal /E/ noninvasive heart pacing. The results obtained in 16 pts with both pacing techniques were compared: The values were /$\bar{x}\pm SD$/: SNRT-IC=1825±616 ms and SNRT-E= = 1989±7lo ms; SACT-IC = 114±42 ms and SACT-E = 145±39 ms/ programmed Strauss method/; SACT-IC = 96±25 ms and SACT-E = 119±37 ms /regular atrial - Narula pacing technique/.

Authors conclude that E stimulation gives higher, but correlating values then IC pacing. The simple bedside or ambulatory E stimulation method is a good alternative to invasive IC stimulation. The above mentioned characteristics and the possibility of easy repetition enables a better and simpler diagnosis of sinoatrial node disorders and drug effects on them.

MATERIALS AND METHODS

Introduction

Most pacemakers /PM/ are still implanted worldwide for atrioventricular conduction disorders, while those indicated because of sinus node /SAN/ dysfunction constitute the second largest group. Recognition of the clinical importance of SAN disease is growing. In the last decade different methods of provocative atrial stimulation were developed for electrophysiological testing of SAN function beside other pharmacologic and ECG techniques for better delienation of SAN disorders.

The sudden cessation of rapid atrial pacing was introduced for the measurement of the SNRT, which is assumed to permit the assessment of SAN automaticity /1/. Strauss described the first clinical method for indirect SACT determination /SACT-SM/ using programmed premature atrial stimulation /2/, while Narula presented his much simpler new technique utilizing regular atrial pacing /3/. Volume of scientific reports were published about these methods, their comparison and clinical relevance. All these techniques were described and are still generally performed with IC, invasive stimulation. The noninvasive E pacing technique introduced in 1969 /4,5/ gained acceptance mostly in emergency ventricular heart stimulation. Only a limited number of cardiologists use it routinly for atrial stimulation in diagnostic tests /6,7,8,9,lo,11,12/. We already published papers on the comparison of the different SACT measurement techniques using E and IC

pacing /13,14/. The aim of our present study was to compare the results of the complex electrophysiologic testing of the SAN function obtained by the two stimulation methods.

Complex analysis of SAN function was performed in 16 pts with both E and IC pacing. In all of them SAN dysfunction was suspected according to case histories, clinical and ECG signs. The pts were studied in the nonsedated, postabsorptive state after informed consent was obtained. Cardioactive drugs were withheld at least 48 hours before the study.

For IC pacing 2 bipolar pacing electrodes were inserted percutaneously via the same subclavian vein and guided with intracavitary ECG and fluoroscopy into the right atria. For E pacing a bipolar or hexapolar electrode was introduced orally into the esophagus and positioned under ECG control near the left atrium. The IC electrodes were generally left in position for some time /1-2 weeks/ and so the tests were repeated during this period. E pacing was carried out generally after the IC techniques and was repeated later. In 5 of these pts even after PM implantation /using chest wall stimulation for temporary inhibition of the implanted PMs/ the tests were repeated during follow-up controls for 2 years /15/. A Biotronik USM 3o programmable pacemaker and a self devised and built pacemaker was used.

The test protocol

After regostratopm pf a basoc CG the tests of the following protocol were performed /12,13,14/.

1/ SNRT: For testing SAN automaticity after sudden cessation of rapid atrial pacing /at rates between 7o and 17o/ the SNRT and after deduction of the prepacing cycle length the corrected SNRT /CSNRT/ was determined.

2/ SACT:/SM/: programmed premature atrial extrastimuli were delivered after every 8th spontaneous sinus cycle with decreasing prematurity so that the entire atrial diastolic period was scanned in lo ms increments. SACT was calculated as half the difference of the mean length of the retourn cycles during reset responses and the basic cycle length.
/NM/: after 8 regular atrial paced beats of little shorter cycle length then the spontaneous sinus rhythm cardiac pacing is terminated. SACT is calculated as half the difference of the post-pacing escape cycle and the mean post--pacing sinus cycle length - slight modification of the original technique /11/.

3/ Atrial ERP and the Wenckebach point /assessment of av conduction/ are determined during SACT-SM and the SNRT measurement.

4/ Exerxise testing

5/ Atropine test

6/ Autonomic nervous system blockade after administration of atropine and propranolol enables the determination of the intrinsic heart rate, afterwards repetition of the tests 1 and 2.

RESULTS

Our results are presented in Table I.

	IC pacing /$\bar{x}\pm$SD/ ms	E pacing /$\bar{x}\pm$SD/ms	
SNRT	1825$\pm$ 616	1979$\pm$ 710	/r = 0,86/
CSNRT	712$\pm$ 810	867$\pm$ 600	/r = 0,92/
SACT - SM	114$\pm$ 42	145$\pm$ 39	/r = 0,93/
SACT - NM	96$\pm$ 25	119$\pm$ 37	/r = 0,9 /

We did not list the results of the tests numbered 3 to 6 in the protocol as they are of no consequence for our present study.

DISCUSSION

Using E stimulation generally higher, but correlating values were obtained then with IC pacing during all electrophysiologic tests /SNRT, SACTs/. This is in accordance with other authors /11,14/ that the E technique is perfectly suited for different SAN function tests. Its noninvasivity, giving the ability to perform the tests as a bedside or ambulatory method, the possibility of easy repetition makes it preferable /or at least a good alternative/ to IC stimulation. The causes for its limited application can be explained with a certain reluctance and inexperience of cardiologists to use a "gastroenterological" method, the reluctance of the pts, a certain pain as not experienced with IC stimulation. It is advisable to have the help of a trained assistant with endoscopic experience, this facilitates the introduction of the electrode into the esophagus. The work of Volkmann and Paliege /11/ in calculating and designing the optimal shape and other parameters /electrode distance etc/ of the ideal E pacing electrode-lead, enables the reduction of chest pain, the most frequent complication.

The conclusions of our previous study /14/ were confirmed, that the SACT-SM gives generally higher values then NM, while E pacing gives higher values then IC pacing. Because of this two nonrelated facts the value of SACT-SM-IC can be roughly equated with the SACT-NM-E.

E pacing can also be used to terminate tachycardias /16/.

Our conclusion is that the simple bedside or ambulatory E stimulation method is a good alternative to IC pacing in SAN function tests and is especially suited for screening and follow-up purposes, enabling a better diagnosis of sinoatrial node disorders and drug effects on them.

Care has to be taken to avoid vagal stimulation. Using E stimulation in PM implanted pts is a good method for re-evaluation of SAN function and is useful in determining the need of a new implant /15/.

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A NEW TECHNIQUE USING DC SHOCK AND SUCTION ELECTRODE CATHETER FOR CLOSED-CHEST ABLATION OF HUMAN HIS BUNDLE

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SUMMARY

The purpose of this paper is to describe a new technique for closed-chest ablation of His bundle /HB/ and its application in 3 patients /pts/ with reccurent supraventricular tachycardia /RSVT/ unresponsive to medical management. A self devised and made bipolare suction electrode catheter /SEC/ was introduced through the femoral vein into the right heart and positioned to the HB. When a large His potential appeared, -100 mmHg suction was applied. In this way the SEC was well fixed on the HB. The central terminal of SEC was connected by a switching device to the cathodal output of a standard cardioversion unit. The back paddle was positioned adjecent to the left scapula and connected to anodal output of the cardioversion unit. The defibrillator was discharged synchronously with the QRS complex. Using this technique we were able to induce heart block in all of three pts by passing an average of 150 J one time through the SEC. The procedure was well tolerated without complication. All pts remained free of arrhythmias without medication. This technique is safe and effective in selected pts with drug resistant RSVT.

INTRODUCTION

Supraventricular arrhythmias can be lifethreatening if associated with rapid ventricular response. Usually, these tachycardias can be managed successfully by pharmacological or pacemaker techniques. In refractory cases interruption of atrioventricular /AV/ conduction followed by implantation of a permanent pacemaker has been shown to provide effective therapy /1-5/. Previous attempts to ablate AV conduction have included ligation of tissue near the AV node /6/, injection of formalin into the tissue surrounding the HB /7/, surgical transsection of the HB /8/, cryosurgical ablation of the AV node-HB /2/, and electrocautery of the AV node-HB /5/. The catheter technique for ablation of the HB does not require open heart surgery, with its attendant risk /5/.
The purpose of this paper is to describe a new catheter technique for closed-chest ablation of His bundle, using suction electrode catheter and direct current /DC/ shock.

MATERIAL AND METHODS

Three pts haveing intractable RSVT underwent closed-chest HB ablation using SEC and DC shock. A preliminary electrophysiologic study including recording of HB electrogram and pacing of HB, programmed electrical stimulation and rapid atrial pacing, was performed in all pts to caracterize the functional properties of the AV conduction system. When it had been determined that a patient was candidate for interruption of AV conduction system, the possibility of closed-chest ablation was presented and informed consent was obtained.

During a second catheterization a self devised and made SEC and two F4 electrode catheters were introduced percutaneously into the right heart via the femoral and subclavian veins. One of the F4 electrodes was placed into the right atrium for recording the atrial signal, the other one was used for stimulating the right ventricle. The SEC was positioned under fluoroscopy and ECG control to the region of HB. When an appropriate large HB deflection was recorded by the SEC, -100 mmHg suction was applied through the catheter /Fig.1./. In this way the SEC was well fixed on the His bundle.

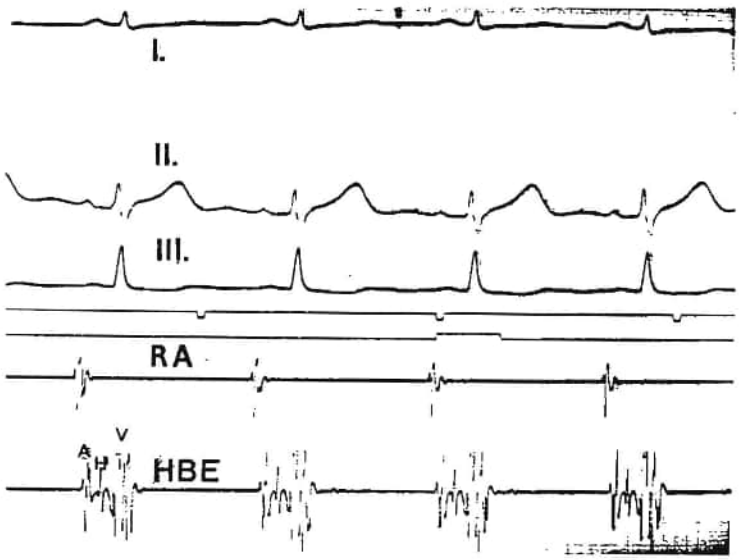


Fig.1. His bundle electrogram /HBE/ recorded by SEC which is under suction. RA=right atrial electrogram

The pts were sedated with intravenous diazepam. The central terminal of SEC was connected to the cathodal output of a standard cardioversion unit. The back paddle was connected to the anodal output. A single direct current pulse from a standard cardioversion unit was delivered between the central terminal of SEC and the back paddle. The delivered energy was 150 J. The DC shock was synchronised to the surface electrocardiogram. After delivery of the shock, demand ventricular pacing was instituted at 35 beats per minute with an external pacemaker.
After the HB ablation the two F4 electrode catheter were remained in the right atrium and ventricle. Serial isoenzymes of lactic dehydrogenase and creatine kinaze were obtained for 48 hours. A repeat study was carried out in every day for a period of two weeks, when we tried to initiate the supraventricular tachycardia by programmed electrical stimulation and rapid atrial pacing. After two weeks of stable AV block a permanent transvenous demand ventricular pacemaker was implanted into two patients.
All the three pts have been followed up by regular visits to the clinic.

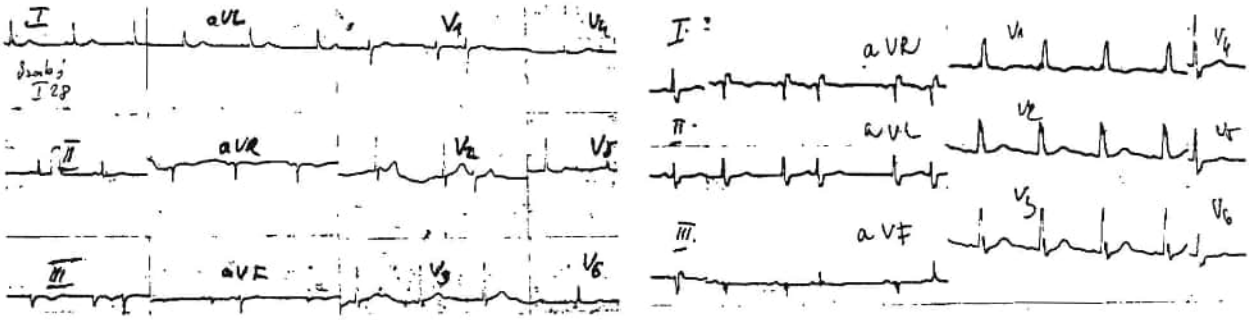
RESULTS

The patient population consisted of three men /45, 47 and 52 years old/. Diagnoses included paroxysmal atrial flutter with rapid ventricular response /in two cases/ and paroxysmal supraventricular tachycardia due to reentry in the AV node-His bundle.
In all of the three pts complete heart block with a stable subsidery rhythm was achieved /Fig.2./. Heart block remained complete and permanent in two pts. In the third patient who had paroxysmal supraven-



Fig.2. Standard ECG and right atrial electrogram /RA/ after HB ablation. Total AV block with 35 beats per minute pacemaker rhythm.

tricular tachycardia, conduction resumed after one day, but right bundle branch block developed in this case /Fig.3./.



A B

Fig.3. ECG recordings of the third patient before /A/ and after /B/ electrocoagulation of His bundle.

Release of the MB fraction of creatin kinaze was observed in all pts, the values ranged from 20 to 138 IU. Enzyme release was limited to the first eight hours in all pts.
The procedure was well tolerated in all cases, and no complications were observed.
During the first two weeks the atrial flutters and the paroxysmal supraventricular tachycardia were impossible to induce by programmed electrical stimulation of rapid atrial pacing.
Complete follow up information on all pts is available for three to five month. No adverse sequalae have been observed, and pts have remained free of arrhythmia, without medication.

DISCUSSION

The need for complete heart block has resulted in the developement of several open-chest techniques to interrupt AV conduction at the HB or AV node/1-4,8/. Recently Gallagher et al. reported the application of catheter technique for closed-chest ablation of the AV conduction system in humans/5/.
The catheter technique for ablation of HB does not require open-heart surgery, with its attendant risk. Dislocation of the catheter could have serious consequences. We thetefore used a self devised and made suction electrode catheter for HB ablation. Application suction through the catheter fixes the electrode in a stable position on the HB and dislocation can be avoided.

Our studies in dogs had suggested that this method is safer than the simple catheter technique /9/.
We applied the described technique in three pts haveing intractable RSVT. In the first two pts with paroxysmal atrial flutter, the induced total AV block remained comlete and permanent during the follow up period. In the third patient who had RSVT, conduction resumed after one day, but right bundle branch block developed. In this case presumably only the superficial part of the HB was damaged, which was a structural part of the reentry. After the procedure tachycardias were impossible to induce. No adverse reactions have been observed, and pts have remained free of arrhythmia, without medication. This technique is an improvement of the method for electric HB ablation /5/. Using this method the dislocation of catheter electrode - which could have serious consequences - can be avoided. The technique is simple, safe and quick, requires no special apparatus, and can produce stable chronic AV block in selected pts with drug resistant RSVT.

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COMPLEX ARRHYTHMIA ANALYSIS IN UREMIC, HEMODIALYSED PATIENTS

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SUMMARY

Impulse formation and conduction disturbances of the heart were investigated in 23 uremic patients with transvenous and oesophageal electrodes. Utilising regular atrial pacing the sinoatrial conduction time /SACT/ was obtained and sinus automaticity was evaluated by measurement of the sinus node recovery time /SNRT/. The atrial effective refractory period and the Wenckebach point was also determined. The effects of regular hemodialysis treatment on impulse formation and propagation disorders caused by uremia were observed. In 16 patients transitory or permanent cardiac stimulation had to be carried out because of 2nd and 3 rd degree AV block.

No complication was observed during simultaneous hemodialysis and pacemaker treatment.

Authors conclude that the non-invasive, simple bedside oesophageal atrial stimulation method is a good alternative and should be used in the exact diagnosis of heart conduction disturbances of hemodialysed patients.

INTRODUCTION

In uremia there are many known causes of cardiac failure; anemia, hypertension, toxic metabolites, uremia, precipitation of calcium in the myocardium. The principle faetures of cardiomyopathy are heart failure, arrhythmias of both supraventricular and ventricular origin, bundle-branch block, pleuritic chest pain, sensitivity to digitalis glycosides, syncope, emboli-both systemic and pulmonary. /2-5,9/

The first description of uremic cardiomyopathy was made by Bailey et al. /1/ There patients suffered from global cardiomegaly, arrhythmia, ECG changes including ventricular extrasystoles, wandering pacemaker, ventricular ischemia, and all had either a history of hypertension, anemia or abnormaly high plasma /Ca x P/ products, all of which are factors possibility causing heart failure.

Generally it is not known whether altered cardiac function in uremia is primarily due to the accumulation of retained products of protein breadkown such as urea, creatinine or guanidine or whether /hormones-parathormone; middle sized molecules/ it is secondary to related factors such as anemia, hypertension, hypervolaemia or electrolyte disorders /hyperkalemia, hypolcalcemia, hyperphosphatemia/.

The generally used methods for electrophisiologic analysis of sinus node /SAN/ function and impulse propagation disorders can be applied in hemodialysed patients only will caution /anticoagulation/.

METHODS

23 patients with chronic renal failure undergoing chronic hemodialysis were studied /9 males, 14 females, mean age 37 ± 14 years/. Mean time on hemodialysis of 37,6 months /range 13-106 months/. There was no predominant type of nephropathy.
Hemodialysis treatment were 3 times per week for 4,5-5,5 hours using Bellco type /VITA-2/ single pass, coiled dialysators of 1-1,2 m^2 surface. The patients diet contained approsimately 1g protein/kg body weight and day or more /7/.

The complex electrophysiologic analysis of sinus impulse initiation and propagation was performed in these patients because either SAN dysfunction was suspected or other conduction disorders and different types of arrhythmias were observed.

The patients were studied in nonsedated, postabsorptive state, after informed consent was obtained. Cardioactive drugs were withdrawal least 48 hours before the study. In those 16 patients where intracardiac /IC/ pacing was performed a bi-, or tripolar electrode was inserted via a subclavian vein into the right atrium /in these patients cardiac pacing was necessary because of therapeutic reasons/.

The nonivasive, oesophageal /OE/ stimulation was done in all 23 patients.

Recording was made on a multichannel electrocardiograph with paper speeds of 50 and 100 mm/sec.

After registration of a basic ECG the tests were performed by the following protocol /6/.

1. SAN automaticity was tested by obtaining the sinus node recovery time /SNRT/ after cessation of rapid atrial pacing both IC and /OE/ at rates between 70 and 170 beats per minute.
2. Sinoatrial conduction time /SACT/ was measured by the programmed premature - Strauss /SM/ and the regular atrial pacing - Narula /NM/ methods /both with IC and also OE/ /8,10/.
3. For testing nervous influences, carotid sinus massage were carried out.
4. The effectiv refracter period of the atria and other structures were determined.
5. The Wenckebach point was determined to test of conduction.

RESULTS

Our results are presented in Tabl.1.

n = 16	n = 16	n = 16	n = 16	n = 15
SNRTc /$\bar{x}$±250/ms	SACT SM-IC	SACT SM-OE	SACT NM-IC	SACT NM-OE
426 ± 52	119 ± 38	129 ± 43	105 ± 25	115 ± 31

In 16 out of 23 hemodialysis patients transitory -, in 1 patient permanent cardiac stimulation had to be carried out because of 2nd and 3 rd degree av.-block.

CONCLUSIONS

1. The non-invasive, simple, bedsied oesophageal atrial stimulation method is a good alternative and should be used in the exact diagnosis of heart conduction disturbances of hemodialysed patients.

IMPORTANCE OF PROGRAMMED CHEST WALL STIMULATION IN THE STUDY OF UNDERLYING HEART RHYTHM IN PACEMAKER IMPLANTED PATIENTS

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SUMMARY

187 patients /pts/ having VVI pacemakers /PMs/ were investigated during follow-up examination. The underlying heart rhythm was evaluated in 3-6 month intervals by three different techniques: 1. Spontaneous heart activity when it is faster than PM rate; 2. Chest wall stimulation by Barold et al.; 3. Programmed chest wall stimulation by Marinato et al. using a Biotronic USM 30 programmable stimulator. Spontaneous heart activity was found in 54 pts. The underlying heart rhythm of remaining 133 pts was studied by the suppression of the implanted VVI PMs with chest wall stimulation /Barold/. During chest wall stimulation the pt was asked to count slowly, chest wall stimulation was stopped if the patient became symptomatic /dizzy/ or stopped counting. In this way 42 PM dependent pts were found. Afterwards, these 42 pts were examined by programmed chest wall stimulation. It was used in order to decrease gradually the PM rate before its complete inhibition. 6 of 42 pts could not be weaned off the PM with programmed chest wall stimulation. It is especially suited for absolute PM dependent pts. This technique avoids the disadvantages of conventional chest wall stimulation which causes abrupt PM inhibition.

INTRODUCTION

The evaluation of the underlying heart rhythm in PM implanted pts is a routine part of the follow-up procedure. The sudden failure of an implanted PM and electrode have serious consequences in pts whose underlying heart rhythm is inadequate. In pts with R-wave inhibited, demand /VVI/ PM two conditions can exist: 1. Spontaneous heart activity or 2. PM rhythm. The PM rhythm can be inhibited by chest wall stimulation /2/, so that the intrinsic heart rhythm can appear. This procedure is quick, safe and simple to reveal this rhythm. The conventional chest wall stimulation can cause discomfort to the pts, because the heart rate suddenly decreases. Marinato et al. suggested a programmed chest wall stimulation, which, by gradually decreasing the rate, prevents this discomfort /9/. The purpose of the present study was to compare the use fullness of the two different chest wall stimulations methods in the examination of PM dependent pts.

MATERIAL AND METHODS

187 pts having VVI PMs were investigated during follow-up examination, /107 males, 80 females/. Ages: 17-94 years, averages: 61±4.5 years. The indication of PM implantation was atrio-ventricular block, sinus bradycardia, sick sinus syndrome, bi-or trifascicular block with Adams-Stokes attacks, intractable tachyarrhythmias and carotis sinus hypersensitivity. The rhythm abnormalities were caused

by chronic ischaemic heart disease arterial hypertension, valvular cardiac disease, cardiomyopathies and congenital atrioventricular block. During every examination ECG's were recorded in the supine position with direct writing electrocardiograph at a paper speed of 25 mm per second. The conventional chest wall stimulation was carried out according to Barold et al, modified by the authors /2,8/. Two metal electrodes were placed over the anterior chest wall. Electrode paste was used between the skin and the electrodes. The electrode terminals were connected to the external stimulator /Cordis, Medtronic/. External chest wall stimulation was initially applied at a rate 10 to 20 beats a minute faster than the frequency of the implanted PM. During chest wall stimulation the pt was asked to count slowly. The test was stopped if the pt became sympthomatic /dizzy/ or stopped counting or the ventricular asystole was longer than 5,000 mseconds /10/. During each follow-up visit chest wall stimulation was repeated for reproducibility. When the pts had longer than 5,000 mseconds ventricular asystole, chest wall stimulation was repeated subsequently /up to 10 to 20 tests/, and in this way, the underlying heart rhythm could be recovered /8,10/. Sometimes the position of the electrodes had to be changed to find the optimal site for inhibition, but with 10-15 volt stimuli the suppression of implanted PMs was successful. A defibrillator and resuscitation equipment were on hand for immediate use in our coronary care unit. All currently used PMs /Cordis, Medtronic, Biotec, Devices/ could be inhibited without difficulty. Programmed chest wall stimulation was carried out according to Marinato et al, /9/. The skin electrodes were connected with Biotronic USM 30 programmable stimulator, which is used for electrophysiological examinations. The PM spikes were sensed by the Biotronic USM 30 stimulator amplifier, and one or two programmed chest wall stimuli capable of resetting the PM oscillator were elicited after each PM spike. According to the coupling intervals of chest wall stimuli and to the PM escape interval, the PM rate could be exactly determined. In such a way the PM rate was reduced step by step from 81 to 54,42,35,30 and 28 beats per minute in 5 minutes /Fig.1./. After stimulating at 28 beat per minute for 3 minutes, the PM was completely inhibited for 5 minutes if a ventricular rhythm emerged without giving discomfort to the pts. The underlying heart rhythm can appear during step by step programmed chest wall stimulation /Fig.2./.

RESULTS

Spontaneous heart activity was found in 54 pts. The underlying heart rhythm of the remaining 133 pts was studied by the suppression of the implanted VVI PMs with conventional chest wall stimulation /2/. In this way 42 PM dependent pts were found. They were sympthomatic /dizzy/ before 5,000 mseconds ventricular asystole or had longer than 5,000 mseconds ventricular asystole. After repeated conventional tests 36 of the 42 pts could be weaned off the PM. During the weaning off the pts often complained of discomfort, dizziness, weakness. Afterwards these 42 pts were examined by programmed chest wall stimulation. It was used in order to decrease gradually the implanted PM rate before its completes inhibition. 6 of the 42 pts could not be weaned off the PM even with programmed chest wall stimulation. During programmed chest wall stimulation pts did not give any sign of discomfort.

DISCUSSION

The evaluation of underlying heart rhythm is very important in PM implanted pts. The temporary inhibition of permaently implanted VVI PMs is valuable in a veriety of clinical situations such as a- diagnosing morphologic or rhythm changes in the spontaneous electrocardiogramm /4,7,13/, b- monitoring the progress of disease of conduction system /4,7,12/, c- assessing the PM and conduction system interac-

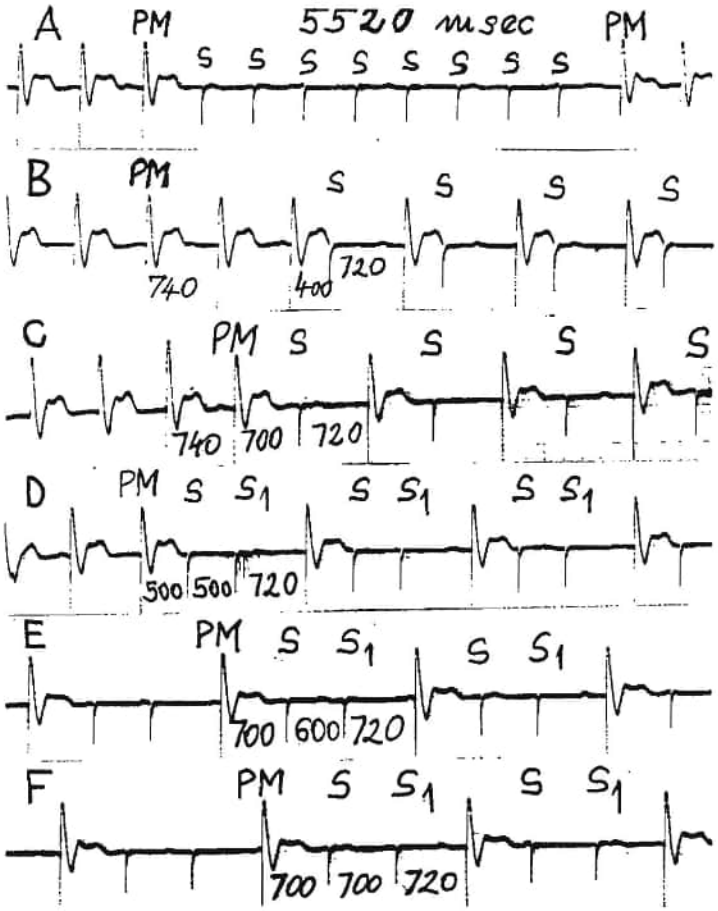


Fig.1. ECG of an absolute PM dependent pt with 5520 msec ventricular asystole during conventional chest wall stimulation /A/. This ECG shows the decreasing of implanted PM cycle length using single programmed stimuli /S/ with a coupling interval of 400 msec increased gradually to 700 msec is capable of reducing the PM rate from 81 to 54 bpm /B/; 42 bpm /C/. Paired programmed stimuli /PM-S/ of 500 msec with coupling intervals /S-S_1/ of 500 msec decreasing the PM rate to 35 bpm /D/; 30 bpm /E/. The last line shows that with paired stimulation /700 and 700 msec/; the pt was not weaned off the implanted PM even as the PM rate decreased to 28 bpm /F/.

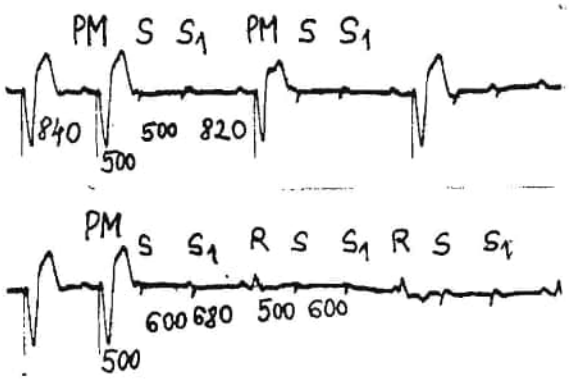


Fig.2. ECG recording of an other absolute PM dependent pt. Using paired stimuli /coupling intervals were 500 and 500 msec/ the underlying heart rhythm did not appear, but using coupling intervals 500 and 600 msec the underlying heart rhythm appeared.

tion /13/, d- identifying high risk /absolute PM dependent/ pts /8, 10/, e- evaluating the "PM syndrome" /1/, f- PM induced arrhythmias /1,13/, g- assessing the PM's sensing function and refracter periods /3,5/, h- evaluation effects of different drugs on the underlying heart rhythm /6,8,11/.

The conventional chest wall stimulation technique, however, has a number of drawbacks. First, the sudden decrease of heart rate may cause discomfort to the pts. Second, soon after PM inhibition the intrinsic heart rhythm may be absent or too slow, and pacing must be promptly restored /7,8,9/, thereby hindering accurate analysis of the underlying heart rhythm. Third, the PM stimulation itself may cause the suppression of both automaticity of ventricular foci /6,7,8/, and conduction of impulse through the HIS bundle and its branches /9/. In the present study a simple method of programmed chest wall stimulation was used in order to decrease gradually the implanted PM rate before its complete inhibition in absolute PM dependent pts. This technique of progressive PM inhibition avoided the disadvantages of abrupt PM inhibition and allowed the investigation of the underlying heart rhythm in pts with PM without undesirable effects. This is particularly applicable to the screening of PM dependent pts. The examination causes less discomfort to the pts and its use is safer. A PM dependent pt must be examined more carefully and special care must be taken during generator replacement for the prolonged ventricular asystole.

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SAFETY AND RELIABILITY MEASURES IN NERVE PACEMAKER TECHNOLOGY*

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SUMMARY

Electrical carotid sinus nerve stimulation is therapeutically applied in cases of severe coronary heart disease and/or hypertension when patients are not responsive to pharmacological therapy. Electrodes around both carotid sinus nerves are connected to an implanted passive receiver, which is activated by an external stimulator via radiofrequency transmission.

Both feedback-controlled devices (intensity of stimulation is controlled by the patient's actual heart rate derived from the continuously recorded ECG) and conventional stimulators (fixed frequency and fixed intensity of stimulation) are in use. In both stimulators certain disturbances in function may occur due to battery exhaustion, antenna breakage or failure, etc. Additionally, in the feedback-controlled device, the ECG signal may be distorted or absent. Therefore all stimulators have a built-in automatic self-check system. A special hybrid circuit monitors the power supply, the function of the antenna and the ECG transmission. Malfunction is signalled via a beeper. Correct ECG transmission is signalled by pulse synchronous function of the beeper, which may be activated by a push-button. The attending physician is supplied with a pocket-size check system which allows monitoring of the actual stimulation frequencies and intensities on a digital display.

MATERIALS AND METHODS

Technological Methods

Nerve pacemakers used for electrical carotid sinus nerve stimulation are controllable stimulation systems which consist of two separate electronic devices. A passive receiver, implanted subcutaneously, is driven by energy transmitted inductively through the skin. An external battery-driven stimulation transmitter and its antenna are carried by the patient in a small pocket in his clothing.

The external stimulation transmitter of the nerve pacemaker system, called nerve pacemaker in the following, may be one of two different designs. One type is a further development of the conventional stimulator with constant but patient-adapted stimulus parameters. This type of stimulator has a built-in self-check system which indicates battery exhaustion and antenna breakage or failure. Additionally, there is the option to modulate the optimal stimulation frequency for each patient in a sine-shaped manner with low frequencies around 0.1 Hz.

The second type of pacemaker uses the principle of feedback-controlled stimulation. Dependent on the R-R interval, the pacemaker increases pulse-synchronously the electrical stimulation of the carotid sinus nerves. A decrease in heart rate causes a reduction of the stimulus intensity. Since a certain intensity of electrical stimulation results in a certain decrease of heart rate, a feedback results which supports the compromized physiological cardiovascular regulation. The nerve pacemaker can be programmed for each patient individually to provide the therapeutically desired stimulation

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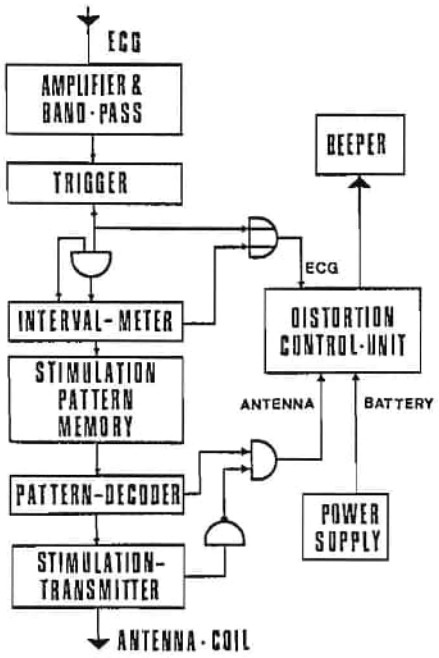
intensity. Thus overstimulation may be avoided. The carotid sinus nerves are activated pulse-synchronously with impulse patterns optimized for each patient. Specifically optimal ranges of impulse frequencies and amplitudes of stimulation impulses, that means the parameters with the strongest haemodynamic effects, are estimated for each patient in a special test. The optimal stimulus frequency, highest amplitude of stimulation and the best impulse width are programmed with potentiometers, setting the range-limiting values. Within these limits, up to 128 different stimulation patterns can be stored in the nerve pacemaker's PROM (programmable read only memory). This covers an effective range of heart frequency between 46 and 192 BPM. Each pattern consists of sixteen four-bit words and specifies the envelope of the pulse amplitude and frequency of stimulation. Thus the pacemaker can be particularly programmed to respond to increasing heart rate with increases of the amplitude or constant of stimulus pulse envelope.

It is also possible to inactivate the stimulation transmitter at a given heart frequency. A detailed introduction has been given elsewhere /1/. For therapeutical considerations, see in this volume: "Carotid sinus nerve pacemaker in angina pectoris and severe hypertension".

RESULTS

Problems of Control

The nerve pacemaker is intended for continuous application and is designed to pick up reliably the heart rate of the patient in order to monitor his neurovegetative situation and supply the necessary stimulation when needed. Thus, the apparatus has to have a system for automatic control of its functions to call the patient's attention in case of problems. Therefore, three functional aspects of the system have to be controlled by internal electronics:



1. The ECG has to be fail-safe to assure the evaluation of signals by the electronic system.
2. The transmitter has to emit a high-frequency signal over the antenna of the nerve pacemaker system when stimulation is called for.
3. The voltage of the battery has to be sufficient to assure safe function of the stimulation

This control system is designed in the following way.

Fig. 1. Block scheme of feedback-controlled nerve pacemaker. Distortion control-unit watches over ECG signal, battery voltage and antenna failure.

Control of ECG Uptake

Pressing a push-button on the transmitter makes the ECG signal audible via an internal

beeper. The electrical ECG signal must be conditioned in such a way that only the characteristic form of the signal is identified and background noise is filtered out.

Trigger signals beyond the physiological range of 40 to 190 BPM must be recognized as noise. If, for example, an ECG recording electrode has no contact, the input loop of the preamplifier is not closed. Strong high-frequency impulse noise will be transmitted additionally or the trigger signal will fail to appear. In both cases a failure detection must occur.

A relatively safe solution has been found in using the following signal shaping and transmission:

The ECG is amplified by a differential amplifier. An input filter suppresses high frequencies which, for instance, may occur with muscle activity. Strong electrical fields of house current are suppressed by a 50 Hz Notch filter. This is followed by an active band pass filter which passes and amplifies the R-wave in the ECG. This filtered signal is transformed to a rectangular pulse by a modified Schmitt trigger circuit. In this circuit, a triggered output sets the threshold to the level of the triggering input which then decays with a 2 s time constant. Thus potential shifting and motion artifacts are largely ineffective. The trigger impulse finishes the preceding measuring period of the R-R interval, starts a new period and, after a delay time of about 60 ms, causes the selection of the impulse pattern related to the interval time from the pattern memory. After transformation it is transmitted by the stimulation transmitter.

When the trigger impulse is activated, the trigger input is disabled for 315 ms, so that interference can have no effect in this period. Nevertheless it will be recognized and many artifacts result in a failure indication via the beeper. The trigger signal controls a programmed counter that counts the cycle of the central clock frequency of the nerve pacemaker. The counter starts to send impulses after an interval time of 315 ms. If the counter was reset before this time by a trigger signal, it starts again and no pulses will be activated. After a delay, this is indicated by the fault detector. A logical circuit will block conduction of impulses of the counter if the estimated interval time is below the working range of the nerve pacemaker, i.e. below 40 BPM. This also leads to a failure detection. This signals the patient to look after the fit or right location of the ECG electrodes.

Control of Transmitter Function

Experience of the past years has shown that the antenna and cables have to resist a strong mechanical strain. Malfunctions or defects which occurred in this part of the system have not been easy to recognize. That is why a control system supervises the function of the stimulation transmitter and the antenna coil, which is an active element of the transmitting oscillator. A small part of the oscillator voltage is coupled capacitively and drives a retriggerable monostable multivibrator. If there is a short-circuit or an interruption, the oscillator of the transmitter cannot work. In this case, the trigger signal is missing and an acoustical failure indication is given. The nerve pacemaker may be programmed in such a way that there will be no activation in stimulation at certain heart frequencies. This means the stimulation transmitter of the nerve pacemaker is switched off by the program, as in this special case there is no demand for stimulation. A logical circuit guarantees that the defect of the oscillator voltage is recognized as interference only if impulse patterns are activated by the pattern memory for the stimulation.

Control of Energy Supply

The nerve pacemaker is equipped with a 9 V rechargeable battery with a capacity of 100 mA. It is sufficient for continuous supply over more than 2 days. Any commercially available non-rechargeable 9 V battery may also be used. The stimulation transmitter needs about 2 mA. The measurement circuits and the control and processor units are supplied with stabilized voltages of 4 and 5 V respectively and need together about 0.6 mA.

The driving voltage for the stimulation transmitter is directly shunted by the battery voltage and allows a correct modulation of the stimulation amplitude down to a battery voltage of about 7 V. The battery charge is monitored by a micropower voltage detector. It switches on a beeper when the battery voltage sinks to 7 V, at which point most batteries are nearly discharged.

Control of Overall Stimulation Program and Function

For the physician in the hospital it is important, especially in the routine check-up, to get a quick and uncomplicated survey of the functions of the nerve pacemaker. For this purpose, a handy, pocket-sized tester was developed. It is designed to measure the stimulation intensity and frequency of the nerve pacemaker under natural and test conditions. The characteristic of stimulus parameters results from the relation of certain stimulation impulse patterns to certain heart frequency values.

When the patient is using his nerve pacemaker, the physician can obtain a general view of the function of the pacemaker by holding the tester flat on the back of the antenna coil and pushing the storage button. The impulse frequency and stimulation amplitude, respectively, are measured and stored by the tester and shown on a digital read out.

To carry out an exhaustive test of the function, the patient has to take off the external part of the pacemaker. The ECG electrodes of the nerve pacemaker are connected with the tester and the stimulation antenna coil is positioned at the tester. This check-system can simulate a heart rate in calibrated steps of frequency range from 40 to 200 BPM. The resulting stimulus parameters are shown on the display of the tester.

DISCUSSION

The practical application of the electrical carotid sinus nerve stimulation with "simple constant stimulators" has shown in the past 12 years that testing of the stimulators by the patient or by the physician was limited. Failure indication and control by the stimulator itself was not possible. No practical testers were available for the physicians and malfunction was recognized merely incidentally. Thus many clinicians were reluctant to use the system. The new generation of conventional and feedback-controlled stimulators has been developed to assure a safe signal pick-up and transmission of stimulation. Since the built-in monitoring of important functions allows a safe and continuous control of the pacemaker, there should be no failure in therapy with electrical carotid sinus nerve stimulation by undetected malfunction of the nerve pacemaker system.

The feedback-controlled nerve pacemaker allows the patient to control the function of his stimulator everywhere and at any time. The clinician will have no problems checking the parameters of the nerve pacemaker with the newly developed tester.

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CAROTID SINUS NERVE PACEMAKER IN ANGINA PECTORIS AND SEVERE HYPERTENSION*

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SUMMARY

Carotid sinus nerve stimulation via implanted electrodes has been effective in controlling angina pectoris and/or hypertension in patients being unresponsive to other therapeutical means (medication, surgery). Stimulation is transmitted transcutaneously via radiofrequency. Four patients being equipped with conventional carotid sinus nerve stimulators for 10-12 years, have been newly equipped with a nerve pacemaker system. Intensity of stimulation is controlled by the R-R interval, derived continuously from the patient's ECG. As the carotid sinus nerve stimulation electrodes and a passive receiver unit are implanted, only the external stimulator and transmitter had to be exchanged. Patients were followed up for another period of 12-30 months with the new system. The patients had to perform dynamic exercise, and their haemodynamic response was compared with and without stimulation intraindividually. Twelve to fourteen years after implantation, carotid sinus nerve stimulation via a nerve pacemaker system leads to haemodynamic responses as one sign of therapeutic efficiency. Two patients newly implanted for their severe hypertension, being non-responsive to pharmacological therapy, were followed up for 6-9 months. Conventional and feedback-controlled stimulation lead to substantial blood pressure reduction at rest and under exercise conditions.

MATERIALS AND METHODS

Functional Significance of Carotid Sinus Nerves

The carotid sinus nerves emerge from mechanoreceptive nerve endings, the so-called baroreceptors, which are excited by distensions of the carotid arterial wall. Entering the central nervous system's neuronal network, the activity of those afferent fibres interacts in a complex fashion by multiple connections with other functional pathways of circulatory and respiratory control. Briefly, the activation of the baroreflex pathways (as would be seen with a rapid rise in blood pressure) leads to an increased vagal nerve activity to the heart and a decrease in the sympathetic activity to the heart, peripheral vasculature, kidney and adrenal glands.

Nerve Stimulation

Bipolar platinum-iridium electrodes are connected surgically to both carotid sinus nerves. An equally implanted passive receiver, which is placed subcutaneously in the subclavicular region of the patient, is connected to both electrodes. Nerve stimulation is activated by a battery-powered transmitter consisting of a signal generator, power supply and an induction coil which is placed over the implanted receiver. Thus, both systems, i.e. the implanted unit and the external stimulator, are inductively coupled. The stimulation of the carotid sinus nerves leads to a reduced stroke volume and a reduced heart rate causing a decrease in cardiac output with a reduced peripheral resistance concomitantly resulting in a decrease of blood pressure. Thereby carotid sinus nerve stimulation exerts the same effects as, or intensifies the effects of natural excitation of the baroreceptor nerve endings.

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Therapeutical Considerations

Electrical stimulation of the carotid sinus nerves simulates a higher blood pressure than is originally "measured" by the baroreceptors. The resulting haemodynamic changes decrease the blood pressure in hypertensive patients to the therapeutically desired level. As it is a form of therapy which requires surgery, electrical carotid sinus nerve stimulation is reserved for the severely hypertensive patient highly resistant to pharmacological therapy. Extensive case reports on stimulation in hypertensive disease can be found in: /1,2/.

In severe drug resistant angina pectoris, a better balance of supply and demand of the heart's metabolism is reached by simultaneously decreasing contractility, heart rate, and blood pressure (afterload) via the nerve stimulation. For case reports see e.g. /3/.

Experiences

For almost two decades, electrical carotid sinus nerve stimulation has been performed in patients successfully using the former MEDTRONIC system. For literature see /4/. Beginning in 1968, patients with severe coronary artery disease and a history of one or more myocardial infarctions have been treated by electrical carotid sinus nerve stimulation. Details on these patients can be found in the literature /5/. In a close cooperation with the Department of Cardiology, Medical Clinic, Bonn University, it was possible to develop a new nerve pacemaker for chronical carotid sinus stimulation where the intensity of stimulation is controlled by the R-R interval of the patient. Equidistant fixed frequency stimulation is applied with the former MEDTRONIC system. Our investigations in patients led to impulse patterns where the R-R interval controls both frequency and amplitude of the stimulation impulses. This method of stimulation is applied with the nerve pacemaker system which is described elsewhere in detail /4/. For technical details see in this volume: "Safety and reliability measures in nerve pacemaker technology".

The nerve pacemaker system is programmed with impulse patterns for each patient specifically. Thus, the patient's heart rate controls the intensity of stimulus impulses which are applied pulse-synchronously to the carotid sinus nerves. The patient has no longer to switch on or off the stimulation as in the former system.

Recent Developments

Four patients with severe coronary artery disease and frequent anginal attacks who where treated with electrical carotid sinus nerve stimulation for more than a decade have been equipped with the heart rate-controlled nerve pacemaker system. This change in method of stimulation is achieved by only changing the external transmitter plus antenna coil without touching the implanted parts (electrodes plus passive receiver). In two patients this exchange was performed 12 years after the original implantation procedure for initiation of carotid sinus nerve stimulation therapy. In the other two patients it was 11 years after implantation surgery. Two more patients underwent exchange of the external unit. One patient was not available for follow-up yet, the other patient kept his former stimulator and gave back the new one as he could not familiarize with the new self-controlling system and the technique of applying ECG electrodes for permanent ECG pick-up, which is necessary in the nerve pacemaker system.

Two patients treated for severe hypertensive disease being unresponsive to pharmacological therapy have been implanted recently. A follow-up on therapy was possible for 6-9 months. Both patients are prepared to receive the feedback-controlled nerve pacemaker in the near future.

RESULTS

Angina Pectoris Patients

All patients have a history of 1-4 myocardial infarctions prior to implantation surg-

ery. No patient had a reinfarction for the 12-14 years of follow up.

1. Patient 17-2, age 57, male; 3 investigations (8, 12, 30 months after exchange): Normotension at rest. Peak systolic blood pressure reduction by 10-15 mmHg with light treadmill workload (2 kmh/10-15% slope) was seen 8 and 30 months after exchange when compared to controls. Working capacity was 80 W for 2' vs. 60 W for 1' when compared to controls on the bicycle ergometer 12 months after exchange.

2. Patient 19-2, age 72, male; 3 investigations (8, 12, 30 months after exchange): Peak systolic pressure reduction by 15 mmHg (treadmill, 2 kmh/10% slope) was seen 8 and 30 months after exchange. Working capacity increased by one step to 80 W for 1' when compared to controls on the bicycle ergometer 12 months after exchange.

3. Patient 10-9, age 64, male; 2 investigations (12, 22 months after exchange): Peak systolic blood pressure reduction by 35 mmHg (bicycle ergometer) when compared to control was seen 12 months after exchange. Peak systolic blood pressure reduction by 20 mmHg (treadmill, 2 kmh/5% slope) was seen 22 months after exchange. Due to peripheral occlusive arterial disease, ergometry is severely hampered in this patient by premature interruption of work.

4. Patient 29-6, age 66, male; 1 investigation (12 months after exchange): Investigations under workload conditions led to immediate interruptions of work due to other factors than fatigue and/or angina. At rest systolic blood pressure can be reduced by 36 mmHg and diastolic pressure by 12 mmHg when compared to controls 12 months after exchange. No blood pressure reduction was seen with stimulation at a 4' workload (treadmill, 1.75 kmh/5% slope). Immediately after work systolic blood pressure and diastolic blood pressure were reduced by 20 mmHg with stimulation.

Hypertensive Patients

1. Patient K.A., age 33, female; 4 investigations (1, 4, 7, 9 months after implantation surgery): Light treadmill exercise (5%, 2 kmh): Average systolic blood pressure reduction was 23 mmHg, average diastolic blood pressure reduction was 19 mmHg with stimulation prior to initiation of workload. During workload systolic blood pressure under stimulation was reduced by an average of 22 mmHg, diastolic blood pressure was reduced by 17 mmHg.

2. Patient H.B., age 43, female; 3 investigations (1, 3, 7 months after implantation surgery): Stimulation reduced systolic blood pressure by an average of 45 mmHg in the phase prior to initiation of workload. Diastolic blood pressure was reduced by 25 mmHg. Stimulation reduced systolic blood pressure during workload (bicycle ergometer, 25 W) by an average of 43 mmHg. Diastolic blood pressure was reduced by 27 mmHg.

DISCUSSION

Electrical carotid sinus nerve stimulation exerts its effects mainly by neural or neurally transmitted mechanisms. Therefore, therapeutic efficiency can be tested by intraindividual comparison of the haemodynamic response to stimulation. Unlike pharmacological therapy, this type of therapy can be "switched off" or "switched on" very easily depending on the therapeutical or investigational needs (see Fig. 1). Because frequent blood pressure measurements are necessary, a non-invasive method of blood pressure measurement was chosen. An automatic sphygmomanometer (D 4000, supplied to us by Puritan Bennett Corp.) was used in most conditions. After it had been checked against the patient's intraarterial blood pressure, which was recorded in parallel during one investigation, an intraindividual correlation proved the D 4000 to be reliable for those intended intraindividual comparisons necessary in the control of carotid sinus nerve stimulation therapy.

In contrast to the formerly used conventional carotid sinus nerve stimulation in those four patients, the nerve pacemaker therapy does not lead to strong haemodynamic effects

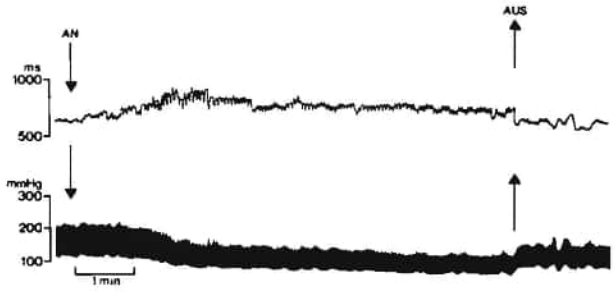


Fig. 1: Typical "on-off" response with electrical carotid sinus nerve stimulation. Upper trace: R-R interval derived from the ECG. Lower trace: Intraarterial blood pressure. Original registration in a hypertensive patient. Stimulation between arrows.

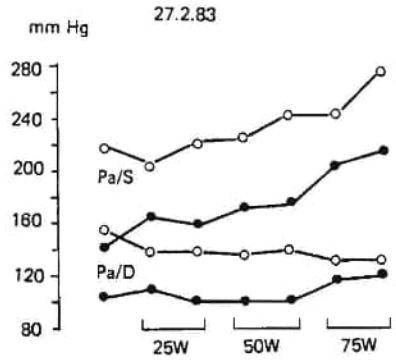


Fig. 2: Impressive effect of stimulation upon systolic and diastolic blood pressures (ordinate) in a hypertensive patient. Bicycle ergometer workload was increased by steps of 25 W for 2'. One measurement per minute. (Pat. H.B., 3 months after implantation) Open circles: Control, filled circles: stimulation.

during rest conditions. As the stimulation intensity is a function of the patient's heart rate, it has to be programmed individually for the patient. Intensive stimulation in angina pectoris patients should only occur with physical or emotional exertion, as signalled by the heart rate. - Three of the four angina pectoris patients report a reduced frequency of anginal attacks since they had been equipped with the heart rate-controlled nerve pacemaker. The two patients with essential hypertension being unresponsive to pharmacotherapy are currently treated with the constant frequency - constant amplitude continuously working stimulation device. It is planned to equip both patients with a feedback-controlled nerve pacemaker system in the near future. In combination with formerly ineffective pharmacotherapy, normotensive blood pressure values have been measured in those patients under carotid sinus nerve stimulation. The individual blood pressure reduction is sometimes dependent on the accompanying medication and the patient's compliance with this medication. For an example of a patient's blood pressure during workload and stimulation see Fig. 2. - It could be shown that electrical carotid sinus nerve stimulation is effective even 12-14 years after implantation of the electrodes and the receiver. In two hypertensive patients, earlier observations and reports can be confirmed that it is possible to treat severe, pharmacoresistant hypertension with electrical carotid sinus nerve stimulation.

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IMPORTANT CONSIDERATIONS FOR THE USE OF FES IN THE REHABILITATION OF PARAPLEGIC PATIENTS x)

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SUMMARY

A 34 year old woman, paralysed in a trampoline accident fourteen years ago with a complete lesion at C6/7, has received treatment with functional electrical stimulation (FES) since September 1982. She now uses her own equipment to stand and walk at home, in the street and in the park.

This work has highlighted special needs in cardiovascular fitness, nutrition and even chiropody as well as special techniques of stimulation.

MATERIALS AND METHOD

The apparatus used for FES consists of two separate devices. The first being for exercising the patients up to the point where they have the strength in their leg muscles and bones to stand and the second device is the one that the patients can wear on a belt around their waists for standing and walking.

The exercise device consists of two electronic power supply units whose frequency and amplitude of pulse output can be tuned to the patient's requirements; a distribution computer which sends the pulses to the respective muscle groups and can vary the strength of signal to each group; an exercise computer which can be set to sequentially stimulate each muscle with a fixed period of stimulation and rest. A special harness, made to measure, is fitted with suitably positioned electrodes and is used in conjunction with both devices.

It is obviously important to start with a medical examination of the paitent especially regarding any cardiovascular problems which might inhibit or even prohibit the use of the equipment.

Many paraplegic patients have a problem with calcium transport and balance resulting in calcium deposits in joints which will limit the movement of these joints. A further problem which applies to long term paraplegics is demineralization of bones and it is very important not to place excessive bending stress on bones in this condition.

A more unusual observation is that persons confined to a wheelchair lose all the padding over the bones on their feet so chiropody and correctly designed and fitted shoes and supports are necessary once the patient starts to stand. Initial standing times with close monitoring of the condition of the feet is necessary to avoid problems which would delay the rehabilitation process.

Once large muscle groups such as those in the lower limbs are exercised after many years of disuse the cardiovascular system has to increase its work-load. There is therefore a great need to include a cardiovascular fitness programme in the rehabilitation.

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The science of nutrition, similar to the science of exercise physiology, is in a major growth period and we are just beginning to understand the subtle alterations of diet needed to match different states of human activity. At this stage in our knowledge some uncertaintly still exists about the exact quantities of proteins, minerals, vitamins, needed for good health.

A high protein diet has been recommended for building muscles and improving cardiovascular fitness /1/ Certain mineral and vitamin requirements are worthy of mention. Obviously calcium is important in rebuilding bone structure and this must be considered in conjunction with phosphorus. Vitamin C provides an intercellular cementing substance that is necessary to build supportive tissue. Difficulties in establishing requirements for Vitamin C involve questions concerning individual tissue need. Doses as high as 80 mg. daily are required by lactating women and could serve as a guide for tissue building in paraplegia. In fact it has been proposed that the needs of pregnancy could serve as a guide for the rebirth of muscle and bone structure in paraplegics. The U.S. National Research Council recommended allowances (1974 Revision) for calcium are 800 mg. daily for adults, increased to 1.2 gm. daily during pregnancy and lactation. Petrosfsky /2/ has reported dosing patients during FES with $\frac{1}{2}$ gm. calcium in morning and $\frac{1}{2}$ gm. calcium at night and 1-2 gms. of Vitamin C (ascorbic acid) daily.

Tracer studies with radioactive isotopes has shown that Vitamin D directly increases the rate of mineral accretion and resorption in bone, by which the tissue is built and maintained.

Respiration plays a very important part in FES rehabilitation. The more strenuous the exercise, the greater the amounts of oxygen used and carbon dioxide produced. Rates of gas exchange in a muscle can be increased over 30 times the resting level in a sedentary person. From resting values of 5 litres of air per minute, maximal exercise efforts cause a sedentary person to increase lung ventilation 20 times the resting amount. It is generally held that, in a healthy person, neither the muscles of ventilation nor the lungs themselves place any restriction on activity. In paralysed patients however it may be necessary to use specific developmental exercises to increase ventilation.

The overall schedule and the daily programme of exercise will greatly influence the progress a person makes, whether strength or CV fitness is the consideration. The recommended regimen is :

* a relatively high intensity of exercise in each day's session
* a minimum total time investment of 45 minutes a day
* a minimum of three days a week

In the case of CV fitness, it would appear that the highest exercise intensity a person can endure for periods lasting three minutes but not much longer than six minutes brings about optimum development of the factors related to the uptake of oxygen. With a few minutes rest between each bout, this would allow between four and eight repetitions of the exercise bouts in a 45 minute period.

Continued medical assessments are necessary for these programmes.

The following exercises have undergone preliminary assessment to improve both muscle strength and cardiovascular fitness in the long term paraplegic :-

Exercise 1	FES 4 secs on 8 secs off one leg at a time - quads only isometric
Exercise 2	FES 4 secs on 4 secs off both legs together- quads only isometric
Exercise 3	FES 1 sec on 1 sec off both legs together- quads only isometric
Exercise 4	FES cycling on ergometer
Exercise 5	FES walking
Exercise 6	Arm cycling with ergometer

RESULTS

Patient

Female, trampoline accident, C6/C7 complete lesion, 1968, FES from September 1982 - limited to just sufficient to get the patient standing and walking by February 1983 and barely sufficient to maintain this position up to May 1983. Other exercises were carried out at end August, 1983.

Table 1 - Analysis of Metabolism for Different Exercises

Exercise	VE L/M	FR BR/M	VT L	% O2	% CO2	VO2 L/M	VO2/Kg ml/Kg	VCO2 L/M	RQ	HR	Lactate mmol/L
Rest	5.5	16	0.35	3.6	2.7	0.16	2.7	0.12	0.73	80	
1	20.1	33	0.61	3.2	2.8	0.53	8.8	0.47	0.89	124	4.7
2	23.1	24	0.96	2.7	3.7	0.52	8.6	0.69	1.34	115	
3	29.5	38	0.78	2.5	2.9	0.59	9.9	0.70	1.17	134	
4	37.5	55	0.68	2.7	2.3	0.85	14.2	0.73	0.86		8.2
5	23.1	36	0.64	3.8	2.9	0.71	11.9	0.56	0.78		
6	42.0	71	0.59	3.1	2.4	1.08	17.9	0.85	0.79		
6B	24.3	41	0.59	3.0	2.5	0.60	9.4	0.49	0.83	132	7.5

Maximum force obtained by FES was 112.2 Newtons in right quadruceps and 157.5 Newtons in left quads. Maximum relaxation rate (% force loss in 10 msecs) was 7.60 (Normal range 8.43-14.43% mean S.D.$\pm$ 2). Index of fatigability 54.76% of force loss after 2 mins. stimulation at 0.25 sec. on 0.75 sec. rest was within normal range. Myogram /3/ was also normal.

Muscle biopsy showed thirty percent of the fibres had internal nuclei. The fibres were of normal area but were all of one fibre type. MyosinATPase at acid pH showed them to be Type IIA and IIB. Some of the fibres showed diffuse intracellular acid phosphatase. Electron microscopy showed all fibres had a large excess of sub-sarcolemmal and inter fibrillar glycogen. In many fibres there was very extensive myofilament loss, the lost filaments being replaced by glycogen. A few small focal areas of Z-line streaming were seen and one fibre had a large area of architectural disorganisation in which some Z-lines were absent. There was one atrophic fibre which had viscular mitochondria but was otherwise undamaged.

Computer axial tomography scans were taken and quads muscle area found to be 35.1 sq.cm. on right leg and 35.8 sq.cm. on the left leg while the right and left femurs were both 5.04 sq.cm. giving a quads/femur ratio of 6.9 and 7.1 (normal 11.7$\pm$ 1.4).

In July and August, 1983, eight weeks of intensive exercise using FES were carried out by the patient using 4 secs. on and 8 secs. off for a total of 60 mins. every day. After this period the relaxation rate had increased to 8.62% which is within the normal range and muscle strength had increased by about 18%.

DISCUSSION

The patient's normal myogram and fatigue rate showed that the atrophy of 14 years was being corrected. The intensive exercise period also showed promise for improving muscle strength and relaxation rate. The electron microscopy shows evidence of glycogen replacement of myofilaments and the Z-line streaming is what is seen after eccentric muscle damage /4/ but it is thought that both these effects could be part of the long term process of atrophy and it is intended to verify this by further research.

The tests on cardiovascular fitness show that life in a wheelchair reduces CV fitness considerably. The patient was a Welsh International gymnast prior to her accident and had led an active life since, trying to keep herself in reasonable condition by daily exercise and swimming considerable distances once a week. Exercise 6B, arm pedalling on an ergometer showed that prior to extensive FES exercise her ventilation (VE) could only be raised to 24.3 litres/min and breathing frequence (FR) was 41 breaths per min. tidal volume (VT) was 0.59 litres. The volume of oxygen used per Kg of body weight (VO2/Kg) of 9.4 mL/Kg is extremely low, this is only three times the resting rate. After the eight weeks exercise this increased to 17.9 mL/Kg which is still very low indeed. The respiratory quotient (RQ) changed from 0.83 to 0.79 which means that the patient was burning off more fat. Maximum heart rate (HR) during exercise of 134 was the highest the patient could achieve and was obtained during rapid FES stimulation.

Qualitative observations have been made on Patient 2 over the period prior to and after stimulation which are worth recording. Patient 2 had suffered for some time from typical circulation problems of paraplegics, lower extremities were extremely cold and had to be well wrapped in winter, skin was shining and cracked and had to be frequently rubbed with cream containing lanolin, soles of the feet were hypersensitive. Since stimulation her feet are warm, the skin is normal and no longer needs to be rubbed with lanolin.

Psychological improvements have made the patient state that from this point alone the FES has been very worthwhile especially since results have shown improvement in a relatively short time, though it must be pointed out that the patient herself has worked extremely hard at the exercises.

Cardiovascular fitness tests were carried out at the Human Performance Laboratory at Salford University and muscle force analysis, biopsies and CT scans were carried out at University College Hospital, London, and our thanks are due to all concerned.

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COMPUTER CONTROLLED MOVEMENT OF PARALYZED MUSCLE: THE MEDICAL PERSPECTIVE*

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SUMMARY

Electrical stimulation causes muscle to contract by the generation of action potentials on nerve and muscle following the application of electrical current to the skin, motor nerve, or the muscle directly, e.g. (2),(15),(17),(18). Current design of microprocessors allows multi-channel control through standard feedback control techniques for movement in muscle,(6),(7),(8),(16). Using these techniques, it is now possible to control movement in muscle. However, one problem that may not be apparent is the deconditioning of the body following spinal cord injury (SCI). Following SCI, muscle is not used and atrophies. This is disuse atrophy and is similar to the atrophy that occurs in muscles after prolonged hospital stays, or the atrophy that occurs when a leg or arm is put in a cast for a few months. Associated with disuse atrophy is demineralization of bones. This is analogous to the demineralization that occurs with prolonged bed rest and with prolonged stays outside the earths atmosphere. When bone is not stressed in a normal manner, calcium leaves the bone and is excreted by the body. This makes the bone fragile and predisposes to injury. The fragility of bones creates a long-term medical problem for people who have been in wheelchairs for many years. The lack of use of part of the body also results in deconditioning the heart, cardiovascular and pulmonary systems. This predisposes SCI individuals to coronary artery disease, cardiovascular disease, renal disease and pulmonary disease (such as pneumonia). Consequently, before wide-scale computer controlled technology can be applied to wheelchair-bound individuals or before any successful reversal of SCI can be attempted, the body needs to be reconditioned to normal physical fitness or as near to normal as possible.

During normal, voluntary activity, strength and endurance are trained for by two different mechanisms. To train for muscular strength, a type of exercise is used called isokinetic exercise(1). This type exercise requires lifting weights at a very slow rate up and down. The rate is one important variable, while the second variable is the amount of weight lifted. To optimize this type of training, the weight should be approximately 25% to 50% of the person's maximum voluntary strength. When this is accomplished, strength builds very rapidly. This type of training is used to cause muscular hypertrophy and increase the strength of muscle (e.g. weight lifters). However, this type of exercise does not train for muscle endurance. To train for endurance, both the blood supply and the also oxidative capacity of the muscle must be increased. This type of training is aerobic training because it involves the utilization of oxygen extracted from the blood by active muscle. Aerobic training is entirely different from anaerobic training such as weight lifting. Aerobic training is typified by bicycling, running or swimming. With aerobic training, muscles work under a light load but at a high rate. When the rate is set to stress the muscle in the proper manner, (the muscle must work near its anaerobic threshold), the muscle develops

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increased circulation. As a secondary benefit, the stress on the body improves cardiovascular and respiratory fitness. A good balanced training program is a combination of both aerobic and anaerobic exercise. This type of balanced training program is used for normal physical conditioning of the body. Over the last twenty years, a number of techniques have been used to exercise paralyzed muscle. These typically involve stimulating muscle at various rates with an undetermined weight. Although the neural traffic is similar to what occurs during voluntary activity, stress on the body is not. Basically, muscle metabolism must be stressed in a precise manner to be a stimulus for muscle growth[19]. Over the last few years we developed in our laboratory a computer controlled stimulation system used to stress muscle in a manner similar to what would occur during voluntary exercise training. This is termed "Active Physical Therapy," which required two different types of devices.

MATERIAL AND METHODS

Weight Trainer System

The first device was a weight trainer, similar in many respects to the types of weight lifting equipment available at a modern gymnasium. This equipment utilizes a weight tray where weights can be added and lifted. The weights are connected through a cable system to a harness that could be placed around the appropriate appendage and allow muscles to operate. When a given muscle (such as the quadriceps muscle of the leg) contracts, the weights are lifted up and down. Operationally, a strap can be placed around the ankle of the subject and secured by velcro fasteners. The leg is connected (through a steel cable connected to the strap) to the weight tray under the back of the chair. The subject obviously cannot feel the limb, nor can he/she see the weights that are being lifted. Therefore, a sensor is provided along the length of the cable to provide information utilized by a computer as to the position of the leg. The computer used in these studies was an Apple II microcomputer (Apple Computer Company, Berkeley, California). To interface the computer to the sensor, an A/D convertor was utilized[4],[5].

The programs to operate the chair simply involve a tracking algorhythm which continually changes the stimulation voltage applied through the D/A convertor and then senses the position of the leg to determine if the leg is going up or down at the appropriate rate. The rate is determined by a ramp generator to provide a triangular wave with a rise time of three seconds and a fall time of three seconds. The output of this ramp generator is set to match the gain of the sensor for the leg so that the computer program tries to match the target analog voltage to the actual input of the A/D convertor. The computer program matches the synthetically generated ramp and tries to have the leg do the same thing. If the ramp voltage is going up faster than the leg is moving, stimulation voltage is proportionately increased. If the ramp voltage is going up slower than the leg voltage, stimulation voltage is proportionately reduced.

Dynamic Exercise Trainer

One common form of dynamic exercise used in physical fitness training is bicycling. For the paraplegic or quadriplegic subject, bicycling offers the advantage of supporting the body weight while allowing the muscles to exercise in a manner similar to what would occur during normal voluntary walking. Computer controlled bicycling is accomplished by a modified Monark exercise

bicycle ergometer system[14]. The bicycle ergometer was modified by a pedal sensor that indicated the position of the pedals. The bicycle ergometer was also modified by a high back seat, shoulder harness and seat belt to allow subjects to maintain balance. This is especially critical for quadriplegic subjects who have no discernable upper body balance. To operate the system, an Apple II microcomputer was again utilized. The Apple II microcomputer was modified with a hardware interface. This required that four channels of stimulus control be built similar to the leg trainer (vide supra). These four channels were controlled through four D/A convertors, i.e., a DAC0832 solid state eight-bit D/A convertor chip. The interfaces were identical except that four discreet addresses were decoded from the Apple address bus. Data inputs were provided from a single A/D convertor. Additionally, Apple game paddles were used as analog inputs. Because of the use of multiple muscles, it was possible to develop a high level of force on the legs and joints during pedaling. In order to protect both muscle and bone, only the quadriceps and iliacus muscles were used. The timing was set assuming that the very top rotation of the pedal was at 0° rotation. For the first 90° of rotation of each leg, the appropriate quadriceps muscle was activated. For the last 180° of rotation, the appropriate iliacus muscle was activated. By thus adjusting the stimulus voltage on these two muscles (on each leg), pedaling could be sustained on a standard Monark exercise bicycle.

RESULTS

The training on the leg exerciser resulted in a significant increase in muscular strength[9]. A group of four subjects were exercised for fifteen minutes a day, three days per week, for a period of one month, lifting weights equivalent to 25% of their maximum voluntary strength. Each of the four subjects lifted upward slowly at uniform velocity over a three second period, and then lowered downward over the same period. Six seconds were allowed between the exercise cycles. The results of these experiments showed an average increase of one and one-half inches in leg size and an average increase of almost 100% in strength (13 lbs. to 25 lbs.). While increasing strength significantly for the minimum workout being used, the leg trainer was only partly effective in stabilizing blood pressure. Bicycling at fifteen kilometers per hour (at a load which would fatique the muscle in fifteen minutes) was performed three days per week for a period of one month and resulted in a significant increase in muscular endurance. In a group of four subjects endurance increased ten fold during exercise bicycling (2 minutes to 20 minutes).

During bicycling on the exercise ergometer, there was a significant elevation of mean resting blood pressure at rest and increased stability during exercise. Quadriplegics are very sensitve to changes in body position from damage of the sympathetic nervous system. In quadriplegics, for example, orthostatic hypotension makes it difficult to change body position rapidly without losing consciousness. The average resting blood pressure for a group of four untrained quadriplegic subjects in the laboratory was 90/60mmHg. After one month of exercising on the bicycle ergometer, mean resting blood pressure was increased by 11mmHg. Additionally, the mean exercising blood pressure during exercise became much more stable being reduced by 22mmHg. Consequently, the exercise bicycle provides both an increase in blood pressure stability and muscular endurance [3],[12].

Bone density changes have been evaluated in order to determine if active physical therapy is effective towards reversing the osteoporosis seen in SCI patients. In principle, we have found that mechanical stressing of previously unstressed bone, promotes the remineralization of such bone. Bone density changes have been determined serially by computer averaged tomography (CAT) scans of the leg bones (proximal tibia and distal femur). Impact loading (primarily vibration) in two SCI patients over a three month period resulted in an approximate 50% increase in bone density (0.75 gms/cm^3 to 1.10 gms/cm^3). These results indicate that the reversal of disuse osteoporosis compared to the reversal of disuse muscle atrophy (vide supra) is positive but distinctly slower. This is consistent (in part) with the relatively lower bone turn-over rate (28 days) as compared to muscle turn-over rate (14 days).

DISCUSSION

Although the primary goal of active physical therapy was the physical reconditioning of the SCI individual, it is also a necessary antecedant for the SCI subject to withstand the stresses associated with active ambulation. Once the subjects had their bodies physically reconditioned, it was possible to use the same feedback control technology to coordinate movement during standing and walking (initially in a paraplegic subject). The system involved six sets of sensors placed on hip, knee and ankle joints along with contact sensors on the shoes to provide feedback information to the computer. The computer used this information to coordinate balance and muscular movement through feedback control. The computer control algorhythms sample the individual joint sensors approximately every four milliseconds and then control movement joint by joint. Each joint was set to maintain its position by muscle control at an angle which was defined by a look-up table [10],[13]. By changing the look-up table rapidly in memory, movement was accomplished through piecewise linear analysis of the gait cycle. Obviously, such a system is complex and required much development. A final system for controlling movement in walking would involve the automatic determination of the upper body gravity vector. In quadriplegics and paraplegics, this provides a mechanism for correcting balance. This would require the use of gyroscopes to assist in coordinating movement. Such adjustments are the object of current research in our laboratory. Finally, the system must be miniaturized if it is to be implanted. Miniaturization requires developing implantable electrodes [11] that are biocompatible and biochips that can be used in the body for extended periods and still be biocompatible. Such developments may take ten years or more before practical application of a portable walking system can be realised. Meanwhile, the "active physical therapy" system described in this paper can form the basis for a new type of physical therapy to physically condition paraplegic and quadriplegic subjects in order to prevent additional disabilities associated with life in a wheelchair.

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EPINEURAL ELECTRODE IMPLANTATION FOR ELECTRICALLY INDUCED MOBILISATION OF PARAPLEGICS.

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SUMMARY

After investigation of the optimal stainless steel electrodes for long time application, the optimal electrical impulse form to gain a smooth, strong and constant muscle contraction, the electrochemical and mechanical influence of the electrodes on to the nerves and the muscles in animal experiments a battery driven, portable 16-channel extracorporal control device was constructed together with an implant with the size of a commercially available cardiac pacemaker and electrodes were developed for electrically induced mobilisation of the lower extremities of paraplegics.

In October 1982 this system was implanted in two paraplegic patients. The electrodes were connected to the femoral and infragluteal nerves to stimulate the gluteus maximus and rectus femoris muscle with the purpose of stretching hip- and knee-joint by electrical stimulation. In the postoperative period the patients were told to train their connected muscles by daily exercises with a stimulating device and 6 months after the operation both patients learned to walk with crutches using the stimulating system.

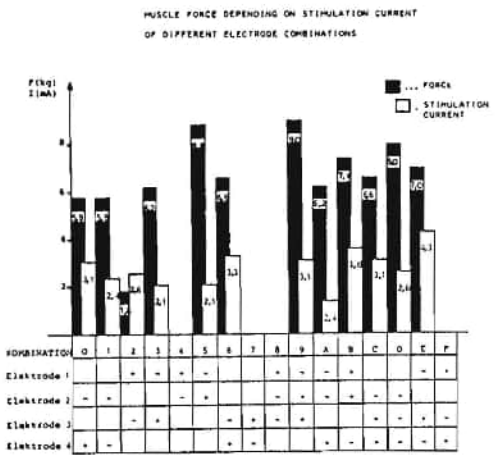
MATERIAL AND METHODS

Since the nerve- and muscle-units of the legs in paraplegics with a cord lesion above Th-12 are still functioning, but are out of control of the patient's will, the idea of overbridging the spinal cord defect by an artificial electrical device seems to be obvious. The phenomenon of muscle contraction by electrical nerve stimulation is well known, but not introduced into the therapy of paraplegics because of several disadvantages, such as for instance a progressively diminished contraction of the muscles with significant relationship to pulse parameters.

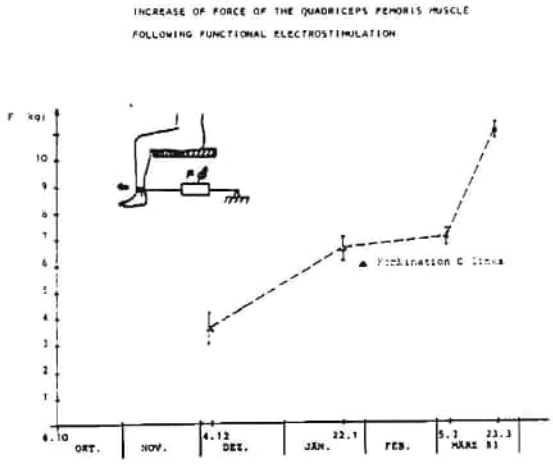
1971 a fatigue-free stimulation method of nerves was developed in our Department with the so called "Karusell-Stimulation". By periodically switching the electrical current between 4 electrodes placed around the nerve, a marked time prolongation of fatigue-free nerve stimulation could be gained. The principle of the system is the periodically different stimulation of fiber groups and the possibility of recover of the not activated nerve fibers. In animal experiments the development of stainless steel electrodes for long-time application as well as the development of electrical impulse forms to gain a smooth, strong and constant muscle contraction were investigated. In other experiments the electrochemical and mechanical influence of the electrodes and the long time electrical stimulation to the nerves and muscles was investigated. As the result of these experimental investigations a battery driven, portable, 16-channel, extracorporal control device measuring 170-180mm was constructed and this extracorporal control unit connected with an

inductive transmitting coil. An implant in the size of a commercially available cardiac pace maker, called "transcutor", consisting of a receiver coil, electronic management and a connection leading to the electrodes was constructed. All parameters for optimal functional stimulation of peripheral nerves, which are impulse duration, frequency, current amplitude and shape of the pulse series can be programmed in the external control device. Stainless steel electrodes consisting of 19 monophiles with a diameter of 0,05mm and isolated with silicone rubber,are performed for clinical use.

The first clinical application of this stimulation device for functional electrostimulation for mobilisation of paraplegic patients took place in Octiber 1982. In 2 paraplegic patients 2 stimulation units each were implanted. The age of the patients was 41 and 22 years. The trauma causing the spinal cord lesion occurred 21 years in the first case, and 4 years ago in the second case. In both patients a complete spinal cord lesion was located between Th-9 and Th-12. In both patients the femoral nerves and infragluteal nerves were connected with 4 electrodes each to stimulate the quadriceps femoris muscle for knee-joint extension and the gluteus maximus muscle for hip-joint extension. The transverse incision was made in the gluteal region just above the foramen infrapiriformae. The infragluteal nerves were located and 4 electrodes were fixed to the epineureum of the nerve branches with 8/0 nylon. The electrodes were connected subcutaneously with the implant placed in the lower abdomen, 5cm medially of the iliac spine. Through another vertical incision in the groin the femoral nerve was isolated and again connected with 4 electrodes in the same way. The fixation of the 4 electrodes on each nerve was done in a square position to perform a so called "Karusell-stimulation". The postoperative period in both patients was uneventful and on the 10th postoperative day electrostimulation of increasing duration was started. The patients were told to stimulate their muscles 3 times daily for about half an hour. In regular intervals both patients were called to the hospital for follow-up studies. With the control part of the stimulation device the patients have the possibility to chose between 16 different combinations of nerve stimulation by changing the electrical field between the 4 electrodes. Doing so different parts of the stimulated muscles are activated and fatigue is retarded. During the first 3 postoperative months the stimulation currents of the different combinations changed markedly, but after 3 months in both patients the stimulation currents for the different combinations became stable. In Figure 1 a diagram of stimulation current and muscle power between the 16 stimulation combinations is demonstrated.



During the postoperative training the muscle power increased markedly as it can be seen in Figure 2.



5 months after the operation both patients were called to the Rehabilitation Center in Häring to learn and train the use of the implanted system to stand up and walk with crutches. Both patients are now able to stand up from their wheel chair and walk about 100m with crutches, in which the control-switch for their stimulation system is integrated. One patient is able to get out of her car without foreign help and walk certain distances using functional electrostimulation of the legs.



DISCUSSION

There are still a lot of problems, for instance spasticity of the muscles interfering with the functional stimulation. The achieved results are encouraging. A main advance for the paraplegic patients would be the possibility to walk up a staircase, which needs active flextion of the hip joint. To realize this purpose, the functional stimulation device has to be extended.

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FUNCTIONAL ELECTROSTIMULATION MAKES PARAPLEGIC PATIENTS WALK AGAIN *)

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SUMMARY

In most cases of paraplegia (e.g. caused by accidental lesion of the cord) muscles and nerves of lower extremities are still in order. If this precondition is fulfiled electrostimulation might be a proper way to give arbitrary motion again. In 1977 our group founded a research project aiming to solve this thrilling task. Main problem is that - in contrast to a heart pacemaker - not only one stimulation impulse is necessary to cause complete movement but a whole series of impulses adequate in strength, frequency, polarity, duration etc. and that fatigue of the nerve muscle complex can restrict function of stimulation after short time. Beside this there were a lot of unsolved questions concerning material and type of electrodes, implantation technology and control of movement. Most of the problems could be solved in hundreds of animal experiments and excessive development of electronic devices, so that in September 1982 we were able to implant electric stimulation devices in 2 patients worldwide for the first time. As a result of excessive training the patients are now able to stand up and walk short distances using crutches.

INTRODUCTION

Electrostimulation is known at least since Galvani has made his exciting experiments with frog legs. Nevertheless continuous application of artificial control of extremities was not successful up to now. Even more the only field where electrostimulation is used in practice for extended periods is the heart pacemaker. The decisive difference between electrostimulation of the heart and stimulation of extremities is, that only one impulse causes the heart to contract while a continuous and well adjusted series of stimulation impulses is necessary for functional electrostimulation.
Stimulation of extremities can be done either by stimulation of muscles or nerves. Using the nerve for innervation offers some advantages compared to muscle stimulation:

- % lower currents are needed, so effectiveness is higher
- % electrodes can be fixed in non moving areas
- % one complete muscle function can be controlled by one nerve

The main difficulty in case of long-term stimulation of nerves is fatigue at the neuromuscular junction. To overcome this fatigue we developed the so-called "roundabout electrode" (German: Karusellstimulation) /1/. With this new method the natural rotation of activity in a nerve is simulated by varying the electrical field distribution in the cross section of the nerve. To obtain the desired effect the stimulation current has to be low enough to prevent stimulation of the whole nerve (no electrical variation would be possible) and high enough to stimulate a sufficient number of fibres. In practice the inhomogeneous field is obtained by placing several electrodes (so for instance 4 electrodes) close to the nerve to be stimulated. According to the electrodes which are active a varying activity in the nerve is gained. Animal experiments have proved the possibility of this method there is a different muscle reaction in relation with different electrode combinations.

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DEVELOPMENT OF ELECTRODES

Some hundreds of animal experiments and in vitro tests were carried out to find an optimum design of nerve electrodes. Main problem is the material. It has to withstand electrolytic effects, to be as less injuring to the nerve as possible and to be reproducible easily (question of price). All our experiments proved that simple stainless steal electrodes are quite sufficient for all of our demands. As long as a certain electrical field strength is not exceeded the thin oxide layer of the electrode protects against desintegration. The electrode is even stable to practically unavoidable low DC-currents (leak currents). Histological findings of examinations of the cross section of stimulated nerves did not show excessive damages /2/. Stainless steel electrodes offer the advantage to use the same material even as lead-in wire. So electrochemical effects are prevented. To obtain high resistance to lead break the wire is coiled and embedded in silicon. The electrode itself is made of stranded wire (17 x 0.05 mm, ETHICON type EH 6129). The end is wound to a small loop (diameter 1 mm) which is fastened to the nerve using micro surgical methods with thin suture.

THE ELECTRONIC EQUIPMENT

First clinical applications of the fatigueless method of nerve stimulation were carried out in 1974 for stimulation of the phrenic nerve in cases of respiratory malfunction of tetraplegic patients /3/. Application was done at the intensive care unit, so it was justified to use passings through the skin for connection of the electrodes to the extracorporal stimulation unit. But for routine an implantable device is unavoidable.

Demands to an implantable nerve stimulation device are very high:

- all stimulation parameters have to be adjustable in real time
- the system has to have the ability to stimulate several electrodes
- battery supply is impossible because of the high current demand

Because of the high electronical expenditure of the implant and the question of safety we aimed at a solution using hybrid technology.

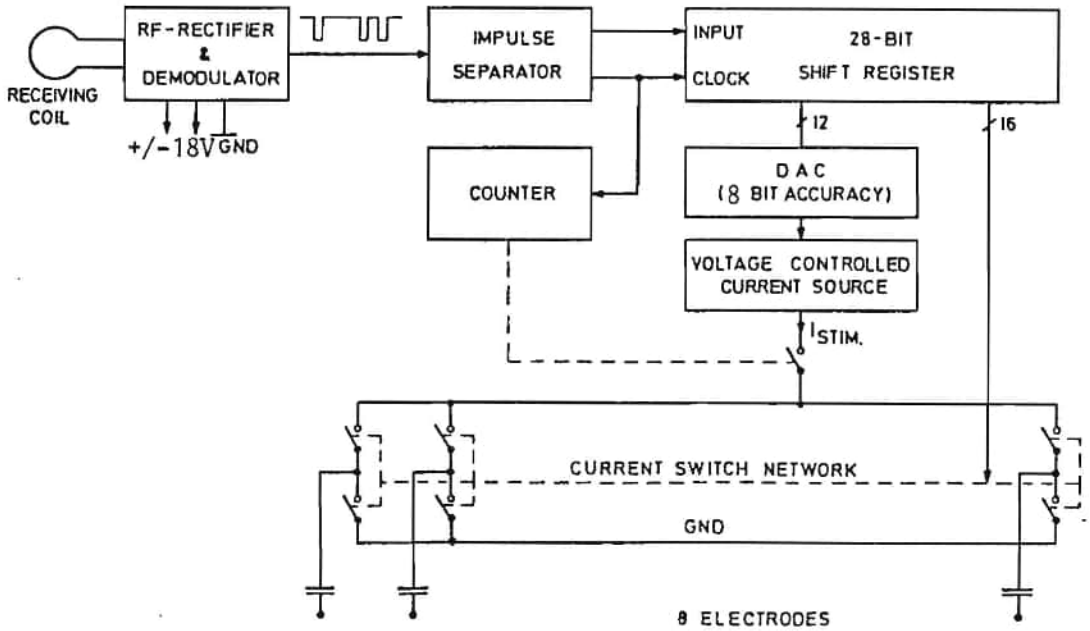


Fig.1: Blockdiagram of the 8-channel nerve stimulator which was implanted in two patients twice in October 1982

Up to now the result of our developments is an 8-channel stimulation device which is able to stimulate two nerves via four electrodes each. Fig.2 gives an impression of the complexity of the implant. Technical data are the following:

% stimulation current adjustable up to 8mA in 256 steps (quarter percent resolution);
% constant current stimulation (so voltage drops at the nerve-electrode connection is neglectable);
% max. voltage is 15 Volts;
% polarity of stimulation impulses is chooseable;
% stimulation impulse width is adjustable continuously up to 2msec;
% stimulation frequency is also adjustable (e.g. 20Hz - 100Hz);
% selection of active electrodes is arbitrary;
% voltage supply of the implant as well as information transmission is done by RF-coupling transcutanuously using an extracorporal transmission coil;
% exact positioning of the transmission coil is not important, all parameters are independent of distance.

It is very important to point out, that all necessary information concerning stimulation parameters is transmitted anew preceding each stimulation impulse. This is essential for functional electrostimulation where movement has to be adaptable at any time. Beside this we are using a time multiplexing method, the two nerves connected to one implant are stimulated alternating each impulse. Information transmission is done by means of a digitally coded sequence (fig.3) which is modulated on the RF-carrier (27MHz). Decoupling capacitors in all output lines to the nerve prevent any DC-current. The size of the implant is compareable to a heart pacemaker.

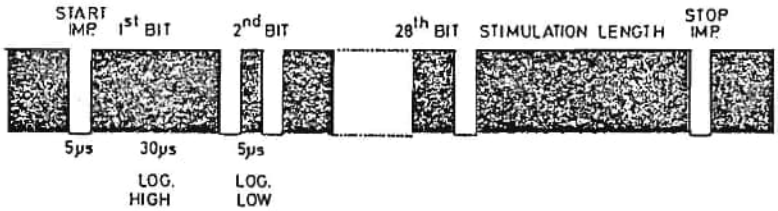


Fig.3: Modulation sequence of transmission of parameters preceeding each impulse

The external control unit is battery powered (rechargeable) and is able to supply two implants via two transmission coils. Control is done by means of a CMOS-microprocessor. According to the principle of the "roundabout electrode" all electrode combinations have to be stimulated with adequate current. To allow easy programming there is an alphanumeric display. Electrode combinations which are not working sufficiently can be deleted. Once programmed, all data remains stored using a CMOS-RAM. The size of the control unit is 17x12x6 cm. We developed two versions of these control units. One is for electrostimulation of extremities (control is done by an especially designed joy-stick), the other one is for electrophrenic respiration (built-in generator for breath frequency and inspiration duration).

CURRENT DEVELOPMENTS

For future application of the system with regard to mobilisation of paraplegic people it is absolutely necessary to expand the number of nerves stimulateable. Because of the complexity of the electronic circuit we chose a custom-designed integrated circuit solution (gate array). The whole implanted system consists of several "satelites" which are positioned near the nerve to be stimulated, (each satelite can stimulate two nerves via five electrodes) and one "master" which is supplying all the slaves (fig.3). This master is implanted centrally and power supplied and controlled similarly to the present system. The new system offers several advantages. So for instance 16 nerves (8 on each side of the body) will be able to be stimulated, but only one transmission coil will be necessary. Because of concentration of electronic parts power consumption is not increased essentially giving longer life to batteries. Beside this we are developing a new extracorporal control unit which is packed in a belt for easy application of the patient.

RESULTS

In October 1982 two 8-channel units were implanted in two paraplegia patients, 41 and 25 years old. The trauma causing the spinal cord lesion occured 21 and 4 years previously. In both patients the complete spinal cord lesion was located between TH-9 and TH-12. The implanted stimulation devices allow activation of the m.gluteus and the m.quadriceps via the inherent nerves. Stimulation currents necessary for desired activation is less than 3mA for the m.quadriceps and less then 5mA for the m.gluteus. Stimulation frequency is 30Hz, stimulation impulse duration is 0.6msec. The last training stage was focused on stand-up and walk exercises. As a result of this the patients are able to stand up with one hand on a mechanically fixed point. Using normal crutches equiped with control switches, they are able to walk short distances.

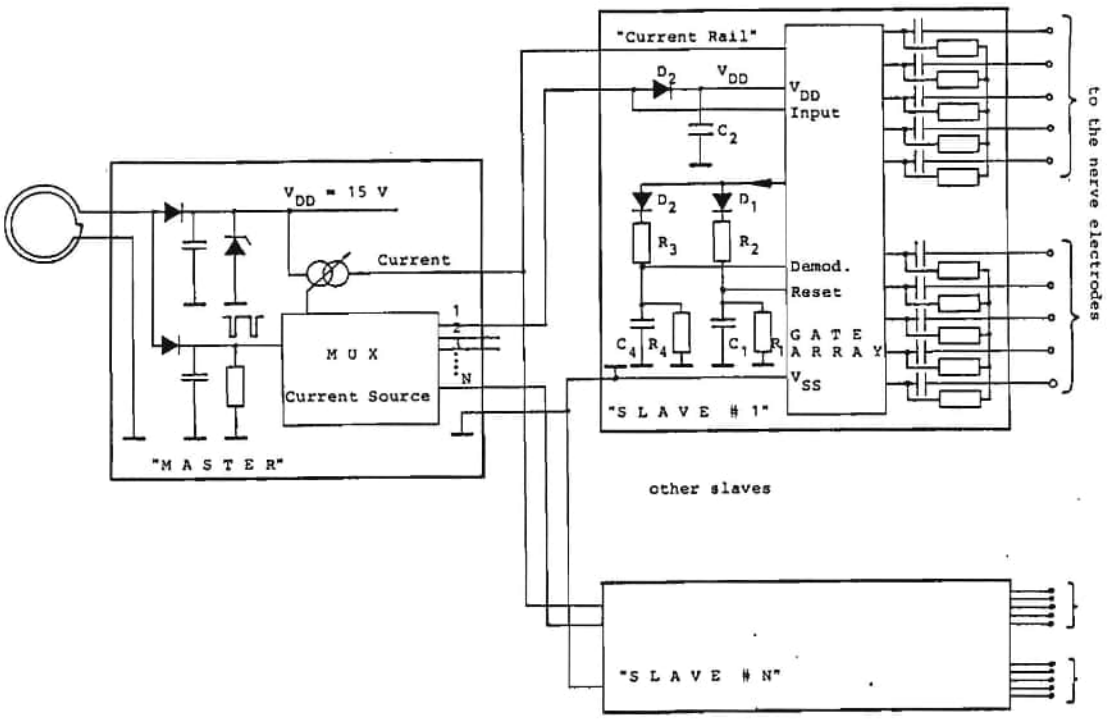


Fig.3: Blockdiagram of the master-slave stimulation system which is presently developed

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FUNCTIONAL ELECTRIC STIMULATION OF PARAPLEGIC PATIENTS - A CHALLENGE TO REHABILITATION

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SUMMARY

Excellent results and achievements in the therapie of spinal cord injuries, influenced by the pioneer work of Sir L.Guttmann,have helped paraplegic patients to master their life with the wheel chair. Although the progress in the field of physical medicine,internal and urological care,orthopedic technology etc is enormous, minor details,unimportant for healthy person,cause invincible difficulties to the paraplegic patient.
our aim is not the locomotion without the wheel chair,but the wheel chair combined with going with crutches.Check in busses,narrow staircases,the distance apartement-car and car-job are up to now open questiones in the rehabilitation.
As the result of implantation of a 16-channelelectric stimulation device in October 1982,the basic requirement was produced.After a few months of muscle and coordination training a paraplegic patient was able to climb the first stair with electric stimulation in June 1983.
We think we can offer a big "step" forward in the rehabilitation of paraplegic patients.

About 3000 patients with spinal cord injuries are an important challenge for medicine, especially for those involved with rehabilitation care. It is of additional importance,that the number of patientsper year is increasing because of more traffic of both cares and motorcycles.
Sir Guttmann had the first big success in Rehabilitation of paraplegic patients by including all parts of medicine in the treatement and set the moving using the wheel chair as a goal of the Rehabilitation.Thus he enabled patients a better "chance to survive" and

a possibilty of integration in society. This has become standard and every other method to decrease the handicap of patients has to measure itself with it.
Using the wheel chair alone, one has only limited possibilties. A small stair for example, or a check in to buses can represent a decissive obstacle for a certain job.
Every possibilty, wich leads to an increase of communication, is of great importance for occupational and social rehabilitation.And though it may take a long time and be very expensive, it can be decissive for the life of the patient.
Therefore one has to put the accent on the selection of patients. Only when a complete rehabiltation with the wheel chair has occured, one can consider whether an increase of communication and therefore an improvement of the whole situation of the patient could be obtained by Functional Electric Stimulation.
This improvement is possible because the patient can stand up alone and without great trouble.Because the patient is standing strait this leads to the well known effects

- on the circulatory system in the sence of orthostatic regulation,
- on the skeleton by improving the inactivity-osteoporosis
- on the muscle by decreasing the atrophy and
- on the urinary system by increasing the flow

There is also a very important effect on the structure of motivation and on the self-confidence of the patient. The patient has to learn how to "get along" with his body by learning new schemas of motion, whereby the patient has to gain a new relationship to his body. Not without reason one sais "He is an upright person".

Methods

Motion is not to be seen as an unidirectional system.When we look at the voluntomotoricity as a regulation mechanism, healthy people have a control-system - by unlimited energy supply - where the prognostic movement is compared with actual movement, wich underlies different influences.In this case the closed loop characteristic over the gamma system determines the dynamic response.
If the flow of the planed movement is interrupted by a spinal cord lesion one can influence the system by electric stimulation of the nerve system.But when the gamma activities and thus the influence on the motoric is not interrupted, as is the case with spastic paraplegia, this activities lead to a change of the actual value of movement.A registration of this actual value has to control the

influence of the electric stimulation and this enables to form a koordinated movement.
To reach these goals we set different intermediated goals.
Basically we decided on a technology where the electrodes are implanted beside the nerve to have less fatigue and to reach a"round-about-stimulation". Also there were no problems with the skin as when using skin electrodes.

Results

After implantation, we left time for sufficient wound healing and we just looked whether a stimulation of the n.femoralis and the n.gluteus inferior on both sides had occured and how differnt combination of the electrodes worked.The same time different physio-therapeutical measures were taken to reach the same level of rehab-ilitation with the wheel chair as before the operation.

After that we began with an individual training programm to improve the muscle-strength and endurance. In spite of the spasticity, muscle atrophy occured during the years and the muscles were too weak to stand for more than a few minutes.
Because of the training the strength of the spasmens developed in a parallel way but this also lead to a better stability.

After the patients were able to stand up with personal assistance, the next goal was to stand up by themselves using a fixed point and a crutch with stimulation switch.
In the beginning there were balance-problems because patients had to learn to move their point of gravity.

Locomotion on a plain was the next intermediate goal.
This could be achieved by an intensive training programm in the Rehabilitation Centre Bad Häring.
First patients learned to walk in a stationary parallel bar, after that in a special built parallel bar with wheels.With that they could walk for about 10m in a room.The next step was to walk with a walker and after that with 2 cratches by a swing-through-gait. Thus the patients could leave their car without any help and walk for about 60m in swing-through gait. This gives greater possibilities to the patients that they have in a wheel chair, because of less trouble.

Locomotion in uneven surroundings is the highest goal, especially for climbing stairs by 4-point-gait.

This already means a great challenge to coordination and depends also on the level of the lesion because of the nerve supply of the latissimus dorsi muscle. One patient could take one step by holding on to a bare with one hand and a crutch in the other.A very small and powerful electric system is of great importance because it can slip more easily by going up a stair.

Discussion

All this could only be achieved with an equivalent motivation of the patients. The entire rehabilitation team with the patients formed a control system, in wich one could learn from each other and motivate each other.
The next goals are to improve the skills and to use them in daily life.Only at this point one can estimate the success whereby each patient has to be juged individually.
I would like to end with a quotation from the diary of one patient from May 1983:"My goal is to achieve more security and endurance. Maybe one day not too far away I can go somewhere, though the wheel chair will always remain the more secure and more comfortable way of locomotion."
Some steps foreward in this direction could be done already.

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MUSCLE TRAINING OF PARAPLEGIC PATIENTS BY FES DEVICE

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SUMMARY

In October 1982 two 8-channel devices for functional electric stimulation (FES) were implanted in two paraplegic patients at the Second Surgical Clinic, University Vienna.

The patients should learn to control the stimulation devices with two fingers of one hand by using electrical contacts located in one crutch.

The final aim of rehabilitation is to enable paraplegic patients to coordinate the active and electrically induced muscle activities resulting in standing up and "walking" over short distances.

After nine months of training with a special program muscle force in the stimulated muscles increased to approximately 400%, and the muscle-endurance was about 30 times higher.

After one year of training one patient is able to stand up actively, to do the four-point gait over short distances and began to climb up the first stairs in the parallel bars; the other patient is able to rise actively, to do the four-point gait and the "through-swing walking" without any help.

METHODS

Muscle training period

After a healing period of eight weeks (one patient spent four weeks on holidays in America) we examined the patients (Fig.1). Muscle and joint functions were specified and training plans for the next weeks were set up.

	OP	HEALING PERIOD	MUSCLE TRAINING	START RISING	REHAB. CENTER	START WALKING	TWO CRUTCHES	RESULTS
MUSCLE TESTS			*	*	*	*	*	
MONTHS			2	4	5	6	9	1 YEAR

Fig.1: ONE YEAR FUNCTIONAL ELECTRIC STIMULATION

In sitting position with 90° bent knee-joint we measured the isometric muscle force in the M.quadriceps using a strain-gauged load cell.

We noticed that the muscle force depends on the switching mode of the electrodes' combinations. The results of combinations can be avaluated only seperately; the use of a total mean may not be as informative.

Desireable combinations are those for which only a minimal stimulation current is necessary to result in a strong muscle contraction.

To strengthen the atrophied and weakened muscles we offer a special training program to the patients.
The most important point was: they should stimulate five seconds M.quadriceps and M.gluteus maximus on both sides, with all sixteen possible combinations, two series, four times daily.

During the exercises weights were applied at both ankles depending on the measured muscle-forces (1.2 - 3 kg).

Motions in the stimulated muscles are initiated by manual use of a special steering device.

The success of this muscle-strengthening phase was controlled after seven weeks. We measured an increase of muscle-force averaged 85% (range 50-150%, depending on electrode combinations) compared to the first examination.

Start rising period

The successes in increasing muscle-force led to the first attempts of standing in the parallel bars.
In this phase the patients started the coordination-training program including standing-up, standing in hyperlordosis and balance-exercises in the standing position with as little use of the arms as possible. They got special "stance-parallel-bars" for training at home.

The following training-plan was offered to the patients:

1) M.quadriceps, sitting and lying position:
   80% repetition maximum, five seconds/10 seconds rest, two series, once daily, "round-about stimulation" (once a week reoetition maximum).
2) M.quadriceps and M.gluteus maximus, alternating on both sides, five seconds stimulation/fifteen seconds rest, two times sixteen combinations, two times daily; sitting position.
3) Standing up in the stance-parallel-bars, six-eight times, one-three series daily (one serie instead of one serie 1)or 2)).

These exercises were designed to prepare optimal physical conditions to start the intensiv-training period at the rehabilitation center.

Intensiv-training in the rehabilitation center Bad Häring

Thanks to the support of the AUVA a four-weeks' training was possible in the rehabilitation center Bad Häring (director: Prim.Dr.E.Rainer).

The main goal was - additionally to increas of muscle-force, endurance, coordination and balance - to start walking. This could be done only by an intensive individual care through two physio-therapists as well as the infrastructure of such a special rehabilitation center.

Intermediately we used different aids: stance-parallel-bars, rolling-parallel-bars, parallel-bars-row, walker, parallel-bars amd one crutch, at last two crutches.

At the end of this third training phase muscle force was increased 70-100%.

The one patient with less physical activities at the beginning was able to perform four-point-walking over a short distance in the rolling-parallel-bars.
The second patient was able to get out of her car and to walk for sixty meters with "through-swing-gait".

We planned together further exercises which were to be done at home because both patients are in occupation.

RESULTS AND DISCUSSION

Finally I want to show up the successes of our patients and our experiences in one year FES:

First patient:

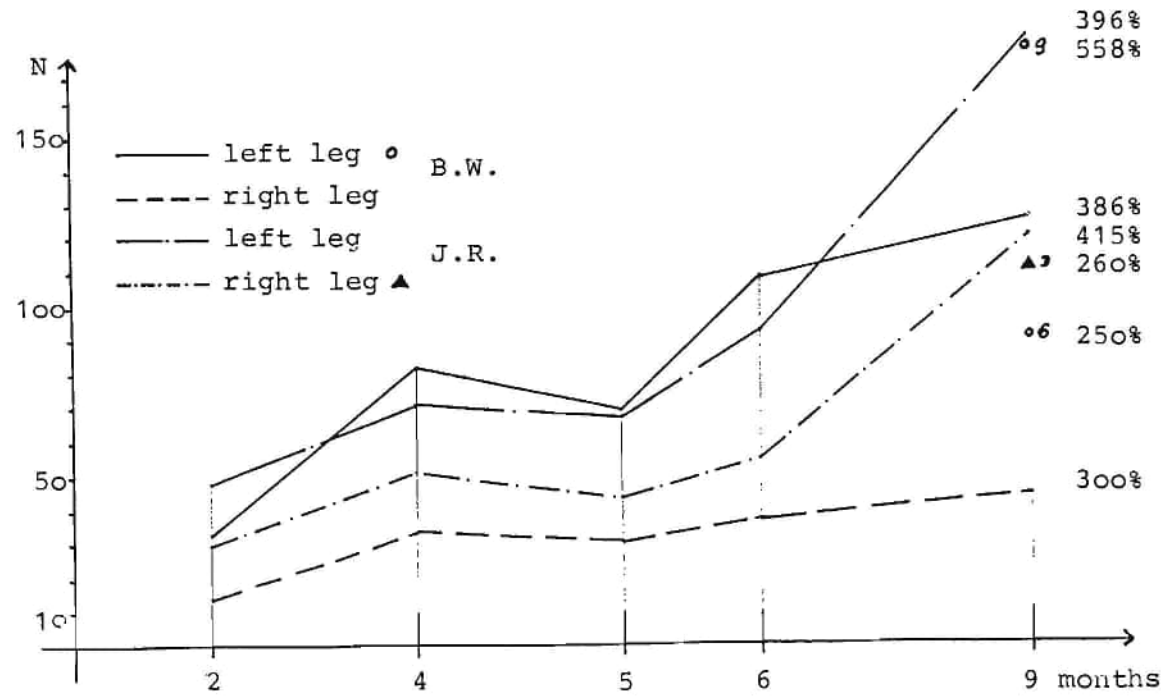
- Walking in the four-point-gait with two crutches over short distances without any help;
- the first steps only stimulated with FES were mastered in the parallel-bars in June 1983.
- Aims for the future: climbing upstairs, bicycle-riding.

Second patient:

- Security in the through-swing-gait with two crutches nearly perfect.
- Four-point-walking without any help, but short steps caused by less pelvic side tilting.
- Aims for the future: climbing upstairs.

▲3 705%

Fig.2: MUSCLE-FORCE DEVELOPMENT



Our results:

By means of FES both patients could do the through-swing-gait and the four-point-gait within ten months.

For postoperative rehabilitation with FES the combination of home-training and intensiv-training courses in special rehabilitation centers should be possible.

Individual care for a period of approximately two years after operation is necessary.

Muscle-force in M.quadriceps of both patients has been quadrupled, endurance increased to fifteen minutes (standing and walking) instead of thirty-fourtyfive seconds at the beginning. (Fig.2)

The phase of pure muscle-strenghtening should be shortened by praeoperative medium-frequency stimulation with surface electrodes. Additionally this praeoperative exercises could help to select compliant patients.

FES has exceeded expectations, but today it cannot be uncritically offered to all paraplegic patients.

Patient B.W. after one year FES:

> FES is the best walking appliance
> existing for a paraplegic patient today,
> and is superior to all other methods.

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INTRAFASCICULAR NERVE STIMULATION TO RESTORE LOCOMOTION IN PARAPLEGICS

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SUMMARY

The INSERM U 103 laboratory is working on F.E.S. problems for about 15 years. Anatomicals and electrophysiological preliminary researches carried out on a bipolar intrafascicular electrode device, which allowes unidirectionnal stimulation. After investigations on F.E.S. joint control, problems gait analysis and transducers technologies, we are developping a microprocessor control system with two sets of 4 closed looped stimulation units . In collaboration with the PROPARA Center, an evaluation of sublesional muscular function is performed. The use of walking machine constitutes a stage in reeducation and a preparation for an intraneural implantation.

MATERIAL AND METHODS

Our preliminary anatomical research on the quantification of nerve fibers in the peripheral nerves demonstrated the existence of fascicles whose configuration is variable. As of 1969, we surgically inserted microelectrodes 25 u in diameter made of Karma wire into the fascicles of peripheral nerves in order to stimulate the nerves' central extremity and accelerate the process of regeneration after nerve section. Work carried out with Professor Vilain of Paris and Professor Allieu of Montpellier, as well as Doctor Piglowski, demonstrated the feasibility of using this technique as a way of stimulating both sensory fibers and motor fibers in order to obtain proportional movements. Following our research carried out on the walking machine and its use in reeducating paraplegics to walk, a program of functional electrostimulation applied to locomotion was undertaken. In 1975, a contract with the Veterans Administration permitted us, in collaboration with a team from the Faculté des Sciences in Montpellier, to define the algorithms for controlling the position and force of an articulation with 1 degree of freedom using electrostimulation of agonist and antagonist muscles.(1) A study of different parameters revealed that the modulation of width is clearly the stimulation mode which avoids the maximum of fatigue phenomena.

Subsequently, in 1981 and 1982, using animals, we reproduced the experiments initially developed by McNeal and Mortimer. (2)-(3) We were able to modify the experimental procedure by using a bipolar nerve electrode with an intrafascicular microcathode and a large perineural anode. This carbon anode permits unidirectional stimulation because of its asymmetric radial field. A maximum muscle stimulation response was obtained with a stimulation voltage of between 120 and 220mV, with signal widths ranging from 100 to 500 microseconds. Special attention was given to research on the cathode, which was composed of a series of thin metallized wires approximately 3 u in diameter, microsurgically inserted into the fascicles. At the same time, another team developed the microprocessor-control for two sets of 4 stimulation units arranged in closed loops, using articulated sensors and sensors with ground contact. This was to allow the patients to have easy control, with a certain servo-control in the articulations. (4)-(5)-(6).

We had also resumed an analysis of the use of different muscles for a program of functional restoration of locomotion and it appeared that certain muscles, including the psoas and the gluteus medius, were not easily accessible for intrafascicular stimulation. Consequently, a technique of percutaneous implantation of electrodes in the intervertebral foramen was tried. This showed that radicular responses could be used and could be integrated perfectly well into the program for restoring locomotion. However, in this case it was impossible to implant an electrode with reversible inhibition of the sensory response. Because of this, we are currently working on the possibility of using epidural electrodes to stimulate the motor root near the intervertebral foramen, possibly with an electrode on the posterior funiculi to inhibit the induced spastic reactions. A combined use of the walking machine in the master-slave mode and in the individual mode constitutes, in our opinion, a stage in reeducation and a preparation for intraneural implantation. (7) Using this technique, it is possible to test the patients' reactions and also to prepare the control system in the crutches in order to make it ergonomically usable. Finally, we must stress the necessity of an extremely precise examination as a preliminary step before any attempt at electrode implantation. Not all patients are capable of benefiting from electrostimulation. This depends essentially on the level and the extent of the lesion, as well as the condition of the sub-lesional muscles. The examination performed in the Propara Center comprises an evaluation of th sub-lesional muscular function with electromyography, a measurement of the force and power of different muscular groups, mathematical and computerized evaluation of spasticity, as well as use of the CAT scan for an estimation of muscular densities in order to relate the morphological appearance of the muscles to their physiological value. Transcutaneous stimulation also permits us to test and develop muscular groups

The evolution of our present research program makes it possible for us to consider implantation in a patient before the end of 1983.

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DIAPHRAGMATIC PACING IN INFANTS AND CHILDREN: A NEW MODALITY FOR VENTILATORY SUPPORT

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SUMMARY

Percutaneous phrenic nerve stimulation by radiofrequency transmission of a programmed train of electrical impulses (diaphragmatic pacing) has been employed successfully in pediatric patients for the management of chronic ventilatory insufficiency caused by congenital or acquired diseases /1/,/2/. It has proven useful as an alternative method for prolonged ventilory assistance because it overcomes several of the drawbacks of positive-pressure respiration.

This report reviews our experience with diaphragmatic pacing to outline the principles, the indications, and the techniques that are specifically applicable to the use of this therapeutic modality in infants and children; it also emphasizes the modifications that are necessary to affect optimal outcome in this age group.

MATERIALS AND METHODS

Fourteen patients with inadequate spontaneous breathing were referred for evaluation between January 1975 and December 1982. Ten patients with central hypoventilation, primary in six and secondary in four, constitute the material for this report (TABLE 1). In all, awake and asleep respiration and ventilatory responses to hypercarbia and hypoxia were evaluated using previously reported methods./3/ Six patients had bilateral percutaneous phrenic nerve stimulation studies, as outlined in an earlier publication /4/, to evaluate the integrity of the phrenic nerves and diaphragms.

TABLE 1 - SURVEY OF CLINICAL EXPERIENCE WITH PHRENIC NERVE PACEMAKERS

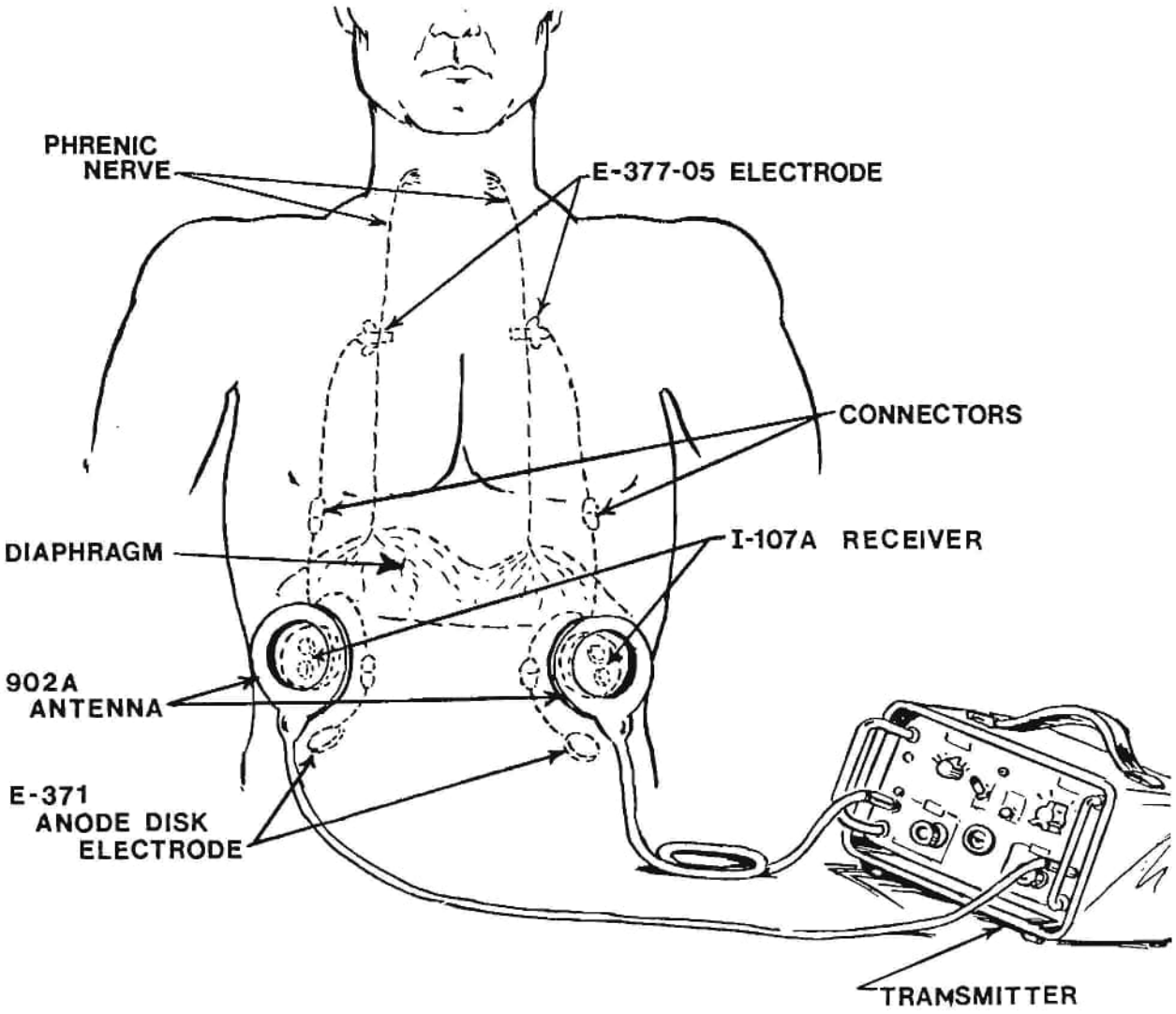
Patient	Age at start of pacing years	Follow-up years	Outcome
1. Congenital hypoventilation			
CN	0.5	1.0	Home. Bilateral pacing asleep, developed awake hypoventilation.
JKO	0.7	5.4	Home. Normal awake ventilation. Alternate pacing asleep.
RA	0.4	1.6	Home. Normal awake ventilation. Bilateral pacing asleep.
BB	0.2	0.5	Home. Normal awake ventilation. Bilateral pacing asleep.
JS	1.3	4.5	Home. Cor pulmonale. Awake bilateral pacing ventilation asleep.
DH	0.5	1.3	Home. Normal awake ventilation. Bilateral pacing asleep.
2. Secondary hypoventilation			
CB	1.0	2.0	Home. Unilateral pacing awake. Ventilation asleep. Hypothalmic dysfunction.
BR	1.2	2.5	Hospital. Posterior fossa tumor. Psychological problems preclude use of pacers.
HS	0.7	1.9	Home. Awake pacing. Ventilation asleep.
JJ	1.5	1.7	Home. Myelomeningocele. Awake pacing. Ventilation asleep.

The pacing system used consists of four components: an external radiofrequency transmitter that generates electromagnatic waves, an external transmitting antenna that carries the waves, an implanted receiver which converts the radiofrequency signals to a programmed train of electrical impulses, and a stimulating electrode that carries the current to the phrenic nerve./2/ (Figure 1)

The surgical technique used to implant the device has been described /5/. It utilizes a single thoracotomy incision for insertion of the electrode around the nerve and placement of the receiver in a subcutaneous pocket at the flank. Early in our experience a bipolar electrodes was used (7 pts). More recently, however, a unipolar electrode inserted as proximal as possible on the intrathoracic phrenic nerve has been used.

Stimulation of the phrenic nerve is initiated 10-14 days postoperatively. The first stimulating pulse within an inspiration (the threshold) is adjusted to stimulate just a few phrenic motor neurons. The stimulating current on subsequent pulses (tidal volume) is adjusted to use as little a current as possible to produce a near maximal diaphragmatic contraction. Adequacy of pacing is assessed by monitoring the end tidal P CO_2, transcutaneous PO_2 and tidal volume measurements./6/

FIGURE 1 - DIAPHRAGM PACING SYSTEM
(SUPPLIED BY AVERY LABORATORIES, INC. FARMINGDALE, N.Y.)



RESULTS

Six patients with congenital central hypoventilation manifested progressive hypercarbia and hypoxemia during sleep without any arousal from sleep, or increase in respiratory rate or tidal volume. However, awake ventilation was adequate in all of them initially. In contrast, the four patients with secondary hypoventilation had inadequate ventilation during awake and sleep states and were respirator-dependent.

Bilateral pacing was necessary in all patients up to five years of age. Subsequently, alternate unilateral pacing could provide satisfactory respiratory support. All patients required tracheostomy to bypass upper airway obstruction during pacing.

Follow-up is available on all patients 3 months to 5.4 years postoperatively. Nine patients were discharged home on diaphragmatic pacing. In six, no other ventilatory support is needed. In the other three, phrenic nerve stimulation is performed during the day to allow mobility, but the patients remain respirator dependent during the night. The tenth patient is still hospitalized and, for psychological reasons, refuses to use the diaphragmatic pacers. Two pacemaker receivers have failed 1.3 and 4.8 years after initial placement, and were replaced. There has been no apparent phrenic nerve injury. Nerve conduction time and diaphragmatic potentials remain normal up to 5.2 years of pacing.

DISCUSSION

In spite of the limited applicability of phrenic nerve pacing in pediatric patients, it has provided a good alternate for ventilatory support of patients who otherwise would have been respirator dependent and has contributed to their mobility and rehabilitation. Our experience, with diaphragmatic pacing in this group of patients has been encouraging and has been associated with good long term results and minimal complications. As in adult patients, the most important factor in establishing successful diaphragmatic pacing in infants and children, is viability of the phrenic nerves and diaphragms. However, there are a few factors that specifically affect the outcome of pacing in this age group.

First among these factors is the prevention of progressive nerve damage. Avoidance of surgical trauma to the nerve, the use of unipolar electrode and limiting the nerve stimulation to 12 continuous hours at one time and the total of 16-18 hours per day, resulted in maintaining normal nerve function in our patients./7/ Long term follow-up of conduction time of diaphragmatic action potentials, confirms the absence of any secondary deterioration due to pacing./4/

Another factor is pacing-related upper airway obstruction caused by failure to activate laryngeal and upper airway muscles during pacing./8/ Although a similar phenomenon is observed in adults, the larger airway in older patients allows sufficient air entry and does not produce clinically significant obstruction. Thus, tracheostomy is needed in all pediatric patients using phrenic nerve stimulation.

A third factor is the inability of diaphragmatic pacing to sustain adequate ventilation with unilateral stimulation before five years of age. This limitation is probably related to the mobile mediastinum in young children and is similar pathophysiologically to the poor tolerance of unilateral diaphragmatic paralysis in children./9/ In patients with congenital central hypoventilation who have adequate awake repsiratory drive, diaphragmatic pacing can correct sleep related hypoventilation making them ideal candidates. However, in patients who are totally respirator dependent, as those with awake and sleep hypoventilation, pacing can be used for 12 hours during the day, allowing for mobility, but positive pressure ventilatory support is needed during the night. In this group of patients, the

respirator and the pacer compliment each other functionally and contribute to effective rehabilitation. Obviously, when the child is old enough to tolerate unilateral pacing, alternating nerve stimulation for 12 hours on each side will completely relieve these patients from their dependance on the respirator.

In conclusion, phrenic nerve pacing is currently an appropriate and successful mode of therapy in infants and children who only need ventilatory support during sleep or in whom awake pacing will be used as an adjunct to ventilatory support during sleep.

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ELECTROPHRENIC STIMULATION IN CHILDREN: REPORT OF TWO CASES

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SUMMARY

External bilateral phrenic nerve pacing was used for treatment of two infants (age 5 and 21 months) with congenital central hypoventilation (ONDINE´s syndrome). Stimulation electrodes were implanted on both phrenic nerves in the thorax and electrical stimuli applied transcutaneously using a radiofrequency transmitter. Both patients could be weaned off the respirator. The method is effective now for more than three years, respectively 6 months. The problems of a long intensive care period and conditioning of the phrenic nerve-diaphragm system are discussed.

INTRODUCTION

Long term respiratory insufficiency can be of acquired and more rarely congenital origin. Treatment consists of intermittent or permanent mechanical ventilator therapy, very often combined with tracheostomy and permanent institutional care. In infancy, respiratory insufficiency can be due to congenital failure of automatic ventilation. Such children, when awake, behave perfectly normal; when falling asleep severe hypoxia and hypercapnia develop making immediate mechanical ventilator therapy necessary. Thus pulmonary vasoconstriction and pulmonary hypertension develop leading to right heart failure and early death /1/. This phenomenon of chronic central hypoventilation or "forgotten breathing" is also called "ONDINE´s curse" or "ONDINE´s syndrome" /2, 3/. Pharmacological treatment for effective stimulation of the central chemoreceptors does not exist /4/. An alternative and effective method of treatment presents bilateral phrenic nerve pacing.

MATERIAL AND METHODS

Our experience with transcutaneous phrenic nerve pacing is based upon two patients with congenital form of central hypoventilation syndrome. In both cases artificial ventilation was mandatory since birth. The presence of sleep apnea was analyzed in detail by evaluating lung function during daytime or overnight, measuring blood gases and airway resistance. The applicability of a phrenic pacemaker depends on the positive proof of the viability of the phrenic nerve and its conduction time /5, 6/. The diaphragm pacemaker * consists of a signal generator situated outside the body, a radiofrequency receiver with nerve electrodes implanted under the skin for each phrenic nerve. The electrode contains one (unipolar) or two (bipolar) platinum bands embedded in a silicon rubber cuff. In children these electrodes are implanted on the thoracic portion of the phrenic nerve, using a thoracotomy /7/. Utmost care has to be taken during the implantation to avoid any mechanical lesion to the nerve. The cables lead to a receiver (weight 30.5 g) implanted in a subcutaneous pocket e.g. in the abdominal area. The receiver is energized through the skin via a coiled antenna. The output signal of the external radio generator consists of repetitive series of duration-modulated pulse trains of a carrier frequency of 2.05 MHz. The

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respiratory rate is adjusted by the time interval between each series of pulses; the depth of inspiration is determined by the current amplitude which is depending on the width of each radiofrequency pulse train. Diaphragm excursions are produced by gradually increasing the energy of the pulse train in order to stimulate slowly more and more nerve fibres. Synchronization of both diaphragms is achieved by a bilateral transmitter with individual controls (see figure 1).



Figure 1

X-ray, pat. J.K.
5 months after implantation of bilateral phrenic nerve pacer.

After implantation of the unit a healing period of about 10-12 days should be expected. Then pacing can be initiated by determining the threshold current using fluoroscopy. Starting with very short stimulation periods (5-15 min/h) and slow increase of stimulating time several hours of effective diaphragm respiration will be reached after a couple of weeks. This process of conditioning is of utmost importance and requires careful adjustment of variables /7/.

RESULTS

Two male infants were treated because of symptoms of central alveolar hypoventilation when falling asleep. The first infant was 5 months old and on nasotracheal intubation, when a phrenic nerve pacing unit with bipolar electrodes was implanted, first on the right side and then on the left side via thoracotomy (February-March 1980). Initiating then stepwise stimulation of the phrenic nerves after 3 months normal blood gas values could be obtained. During the following 7 months intermittent intubation and mechanical respiratory support were necessary because of infectious bronchitis and upper airway obstruction. Then finally a tracheostomy was performed almost one year after pacemaker implantation and the symptoms of upper airway obstruction ceased. It took another year until the child could be discharged at home. Now 3 1/2 years after pacemaker implantation the child is normally developed, the pacemaker is functioning during sleep providing normal blood gas values. The rate of stimulation is 17.5/min, there is no increase of stimulation threshold or phrenic nerve conduction time over this period.

The second child was on the respirator with tracheostoma for 21 months since birth until bilateral phrenic nerve pacing units with unipolar electrodes were implanted (February-March 1983). Preoperative cardiac catheterisation showed elevated pulmonary vascular resistance (5.1 E/m^2) and undersaturation of the blood in the left atrium (86% oxygen). Postoperatively, weaning off the respirator was delayed because of multiple episodes of infectious bronchitis. After 5 months of intensive care treatment finally the patient was off the respirator. In this case, a different nerve conduction time and threshold existed between left and right phrenic nerve, making snychronized pacing quite difficult. This patient could leave the hospital 5 months after bilateral pacemaker implantation with a well functioning unit.

DISSCUSSION

Phrenic nerve pacing is applied successfully in certain forms of acquired chronic respiratory insuffiency e.g. poliomyelitis, encephalitis, tumors, and especially trauma. The biggest experience ist presented by GLENN and his group /8/. According to their experience phrenic nerve stimulations could be useful in about 40% of patients with quadriplegia and respiratory paralysis. Similar results are reported by OAKES /9/ and TALONEN /10/. Experience with treatment of congenital central alveolar hypoventilation snydrome in infants is sparse. RADECKI reports 5 1/2 months of effective phrenic pacing in an infant, who died of bronchopneumonia /11/. The largest series is presented by ILBAWI and HUNT /12, 13/ describing 6 infants and satisfactory ventilation by pacing, 3 died several months afterwords. They also emphasize the necessity of a meticulous operating technique on electrode implantation in order to avoid mechanical damage to the nerve. They recommend the application of a pericardial flap in order not to dissect the nerve. Besides injury to the nerve during surgery it may also be produced by continous pacing /14/. In our patients this has not occured, since we limit our duration of continuous pacing to a maximum of 10 hours. Even though histological changes of phrenic nerves have been seen at autopsies after a stimulation time of 2 months to 4 years, the cause of such damage is unclear. Our unchanged threshold values after 6 months respectively 3 1/2 years reveal the suggestion that intraoperative nerve damage is of more importance than damage due to electrical stimulation /15/. It is generally agreed that the problem of upper airway obstruction requires a tracheostomy. In none of the children it was possible to obtain an acceptable tidal volume by unilateral pacing only as it is possible in certain adult patients. Even though this method most often requires long term intensive care treatment, it presents the treatment of choice for infants with congenital central hypoventilation syndrome.

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INTRAMUSCULAR ELECTRICAL ACTIVATION OF THE DIAPHRAGM USING AN UPPER AIRWAY TRIGGER

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Supported by a Veterans Administration Merit Review and the American Lung Association.

SUMMARY

The limited clinical application of diaphragm pacing, has been in part a consequence of the need for surgical exploration of the phrenic nerve. In addition, fixed rate pacing may result in asynchronous contraction of the diaphragm and other respiratory muscles which may limit the tidal volume achieved. We approached these problems experimentally in dogs by studying the efficacy of diaphragm stimulation achieved via intramuscular monopolar electrodes (IM) placed in each hemidiaphragm. Average maximal tidal volumes (VT) and transdiaphragmatic pressures (PDI) produced with IM were similar to that achieved with directly applied nerve electrodes. Synchronization of diaphragm and accessory muscle activity by triggering the diaphragm from the alae nasi muscle EMG, resulted in an augmentation of VT and a reduction or elimination of the paradoxical inward motion of the upper rib cage observed when stimulating the diaphragm out of phase with other inspiratory muscles. A more easily applicable and physiologic system for electrically activating the diaphragm could significantly enhance the clinical relevance of this field.

MATERIALS AND METHODS

Anesthetized intubated dogs were studied in the supine position. Tidal Volume (Vt) was recorded by electrical integration of the flow signal from a pneumotachograph (Fleisch No. 1). Blood pressure was monitored continuously with a catheter placed in the femoral artery and arterial blood gases were constantly monitored with a blood gas analyzer (Corning, Medford, MA). Transdiaphragmatic pressure (PDI) was measured by balloons in the stomach and esophagus connected to separate pressure transducers. Rib cage and abdominal surface motion were monitored with inductive plethysmography (Respitrace) bands which were calibrated so as to have equall gains. Multi strand helical electrodes formed from Teflon insulated wire were used and inserted directly into the diaphragm via a small midline incision. The electrodes were led directly through the skin to the stimulator (Applied Neural Control Laboratory, CWRU) which delivers a balanced charge biphasic stimulus and provides a pulse width modulated impulse ranging from 0-100 msec with a variable time constant under operator control. The stimulus frequency was adjustable from 10-40 Hz and the current amplitude variable between 0 and 20 mA. Stimulation of single hemi-diaphragm electrodes were compared to stimulation of ipsilateral phrenic nerve electrodes placed around the cervical phrenic nerve (C 5, 6, 7). Comparison was also made during stimulation with supra-maximal 40 Hz trains against an occluded airway at functional residual capacity, to control for pre-contraction length. In these studies of diaphragm contractility, stimulation was performed following hyperventilation of the animal to apnea with a mechanical ventilator.

Tidal volume and rib cage and abdominal surface motion were compared during fixed rate (open loop) stimulation in apneic animals and during stimulation of the diaphragm triggered from the phasic respiratory electrical activity recorded from the ala naesi EMG muscle. The signal was recorded with bipolar electrodes inserted in either ala naesi muscle. The EMG signal was high pass filtered to retain only frequency components above 17 Hz prior to rectification and integration. A leaky integrator with an adjustable time constant between 50 and 400 msec allowed variable low pass filtering of the rectified signal. The integrator output caused a trigger pulse when it exceeded a integrator output caused a trigger pulse when it exceeded a threshold level. The pulse could be delayed by an adjustable time period before it triggered the diaphragm pacer and a lockout circuit was included, which prevented the stimulator from being retriggered for a set time period, following a trigger pulse. Triggering was performed with both intact and sectioned phrenic nerves.

RESULTS

Efficacy of stimulation with intra-muscular electrodes

During these studies there were no episodes of arrythmias or unexplained hypotension which might have been related to the electrical stimulus being transmitted to the

intra-muscular electrodes in relatively close proximity to the heart. This was despite the use of 40 Hz, supramaximal current stimuli. In animals stimulated following hyperventilation to apnea maximal tidal volume achieved with unilateral and bilateral stimulation of single hemi-diaphragm electrodes was equall to that achieved with conventional phrenic nerve electrodes. Mean tidal volume (liters) for unilateral muscle electrodes was 0.27±SE .04 and 0.26±SE .03 for the ipsilateral nerve electrodes. For bilateral stimulation maximal tidal volumes achieved with both electrode systems were also indistinguishable. During stimulation against an occluded airway over a range of 10-40 Hz with a supramaximal current stimulus, PDI generated by a single hemi-diaphragm electrode or an ipsilateral nerve electrode were the same.

Effect of diaphragm stimulation triggered from the ala naesi EMG on tidal volume generation and ribcage movement.

Triggering of the diaphragm stimulus from the ala naesi EMG resulted in an augmentation of tidal volume in the intact, spontaneously breathing animal.

In animals with sectioned phrenic nerves, activation of the diaphragm with the fixed rate system during apnea (in the absence of ribcage muscle tone), or out of phase with spontaneous inspiration, resulted in paradoxical inward motion of the ribcage. Activation of the diaphragm via the ala naesi trigger with the same stimulus intensity resulted in a reduction or elimination of the ribcage paradox and the generation of a larger tidal volume.

DISCUSSION

Intramuscular diaphragm electrodes appropriately placed in proximity to the entrance of the trifurcations of the phrenic trunks into the hemidiaphragms, can ellicit effective ventilatory function of the diaphragm (1). In the studies described, single monopolar electrodes in each hemidiaphragm produced similar trans-diaphragmatic pressures and tidal volumes as ipsilateral nerve electrodes. This was true for both unilateral and bilateral stimulation and the pattern of relative ribcage and abdominal motion produced was also similar. Despite the proximity of the electrodes to the heart (particularly on the left side), no arrythmias or unexplained episodes of hypotension were observed. Given the 40 Hz supramaximal current stimulus used in parts of the experiment the technique does not appear to pose a risk under these circumstances.

We have also demonstrated the ability to augment spontaneous tidal volume in an intact spontaneously breathing animal by triggering a stimulus to the diaphragm during spontaneous breathing. In addition we were able to demonstrate that for a given stimulus to the diaphragm, synchronization of the stimulus with spontaneous activity of the accessory muscles resulted in a larger tidal volume and an elimination or reduction of upper ribcage paradox during inspiration.

Phrenic nerve stimulation has been used to a limited extent in clinical medicine for the management of high quadriplegics and central hypoventilation syndromes (2,3). More general application of the concept to a wider patient population of hypoventilators is severely limited by the potential risk of damaging the phrenic nerve at the time of electrode implantation. The feasibility of effectively activating the diaphragm via intramuscular electrodes which do not risk damage to the phrenic nerve may allow for evaluation of diaphragm pacing in a larger population of non-paralyzed patients, such as those with chronic obstructive lung disease (3).

Fixed rate stimulation of the diaphragm does not take advantage of any inherent respiratory activity and thus may not achieve the greatest degree of ventilatory effort available. This phenomenon may also result in diaphragm contraction during upper airway closure which results in the need for a permanent tracheostomy (2,4). The studies described related to tidal volume generation as it pertains to ribcage muscle activity (intercostals, sternocleidomastoids). These experiments were performed in

intubated animals to eliminate any upper airway considerations. The ala naesi EMG used as the trigger signal fires phasically with spontaneous respiratory activity and generally precedes phrenic electrical activity by 75-150 msec (5). This early firing of the signal allows for the generation of a signal of appropriate magnitude before the stimulus to the diaphragm has to be triggered. Other efforts have been made experimentally to develop closed loop systems for diaphragm pacing. End-tidal CO_2, change in inspiratory and expiratory air temperature and sternocleidomastoid EMG have been used as central triggers (3) but they have not proven to be appropriate techniques for clinical evaluation. The respiratory function of the ala naesi muscle may make it suitable for further study in this regard.

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FURTHER EXPERIENCES WITH ELEKTROPHRENIC RESPIRATION

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SUMMARY

Effective diaphragm pacing as a method of long term artificial respiration in patients suffering from central alveolar hypoventilation or respiratory paralysis due to cervical spinal injury is possible. Electrically induced fatique at the level of the neuromuscular junction can be prevented by a new method of nerve stimulation simulating the natural "rotation of activity". We use now a system with transcutaneous transmission of the stimulating impulses to a receiver implanted in the subcutaneous tissue. The electrodes are placed around the nerve either by a cervical or a thoracic approach (partial sternum splitting incision).

INTRODUCTION

Electric stimulation of one or both phrenic nerves (Electrophrenic respiration-EPR) to achieve diaphragm contractions sufficient for adequate ventilation of the lungs is an alternative to intermittent positive pressure ventilation (IPPV) in selected patients requiring artificial ventilation.
Advantages of EPR include the absence of decreased venous return to the heart and the lack of an increase in pulmonary vascular resistance as caused by IPPV, thus avoiding a reduction in cardiac output (2,3). In addition we can achieve a better ventilation of the basal regions of the lung and a reduced risk of infections. There is no ventilation/perfusion imbalance during EPR like in IPPV (1). EPR per se does not require intubation or a tracheostomy. Diaphragm pacing requires a normal function of phrenic nerves, lungs and diaphragms and absence of upper airway obstruction. Indications for diaphragm pacing are therefore indicated in cases of central alveolar hypoventilation or respiratory paralysis due to high cervical spinal injuries.
Continous electric stimulation of the phrenic nerve with conventional bipolar electrodes showes progressively diminished contractions of the diaphragm due to interference with the transmission of impulses across the neuromuscular junction (5).
To overcome this, we have developed a new method of nerve stimulation (called "Karusselstimulation"), which simulates the natural rotation of activity with the aid of a changing electrical field around the nerve (3,6)

METHODS

TECHNICAL DETAILS

To obtain the wanted effect, the following requirements have to be met: Stimulation current has to be low enough to prevent the stimulation of the whole nerve and high enough to stimulate a sufficient number of fibres. The electrical field must be inhomogene.

If the stimulating electrodes are positioned closer to the nerve, the inhomogenity of the electric field increases (Fig. 1)

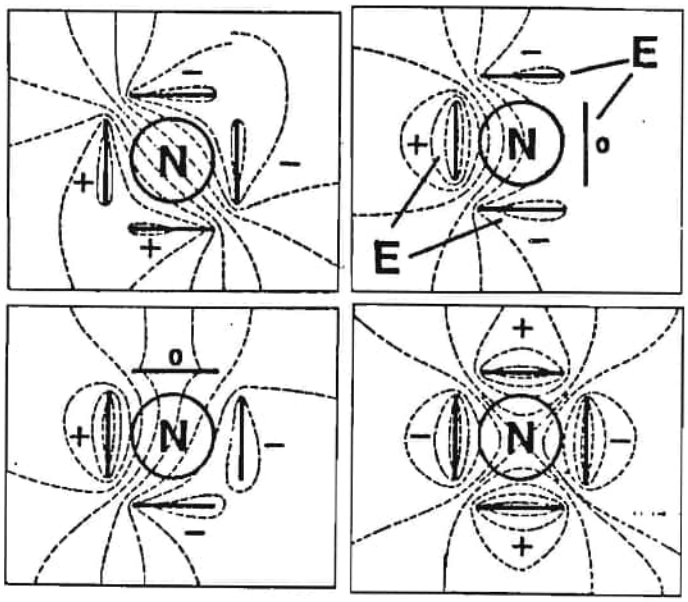
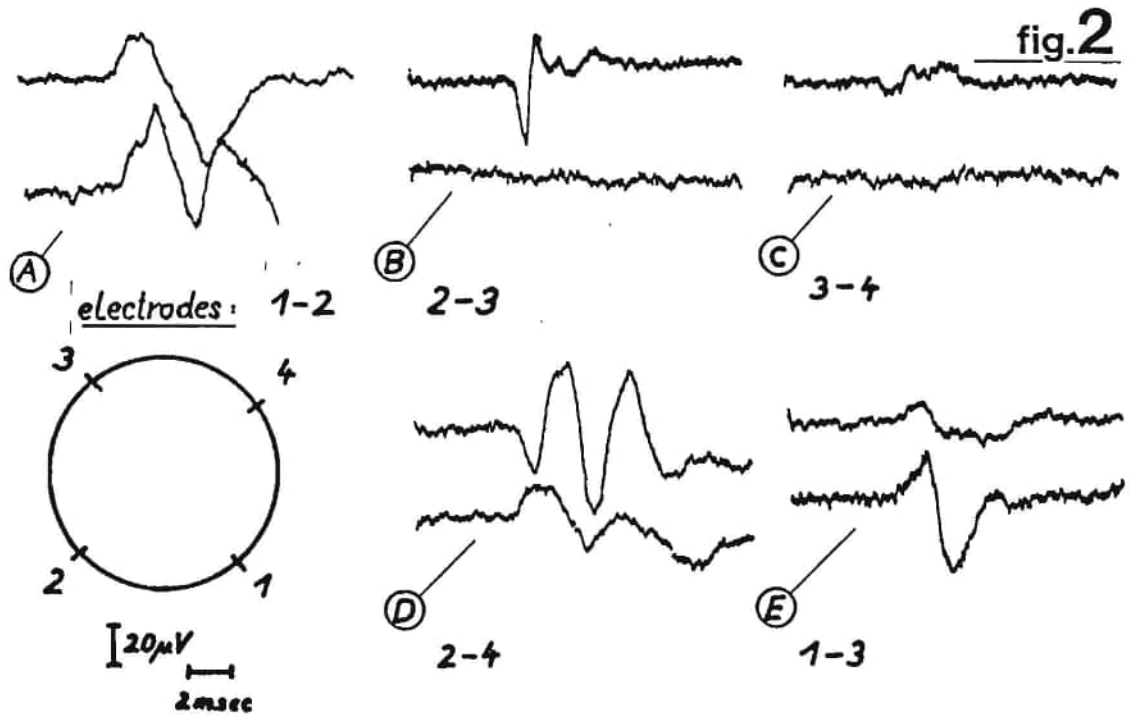


fig.1

N... NERVE E... ELECTRODES

When - for example - four electrodes are placed around the nerve one can achieve a variation of intensity of the local electric field by different polarizing of the electrodes. An automatic switching logic causes a rotating electric field in the nerve cross section -"Karusselstimulation". Animal experiments proved the positive effect of this method (Fig. 2): Four electrodes were positioned around the right phrenic nerve. Muscle actions of the diaphragm were measured by means of needle electrodes. Two myograms were registered simultanously. The switching mode of the electrodes influences the diaphragm muscle reactions measured at two different point.



SURGICAL APPROACH

After extensive testing of our system in animal experiments we implanted electrodes in 3 patients using a cervical approach. The nerve is exposed on the surface of the anterior scalene muscle. 1 patient suffered from a central alveolar hypoventilation and two from high cervical spinal injuries In two additional patients with quadriplegia we used a thoracic approach via a partial sternum splitting incision. Both pleural cavities were opened and electrodes (4 each) were placed close around the phrenic nerves in the upper mediastinum. Microsurgical techniques were used to secure the electrodes in proper positions.

RESULTES

Although unilateral stimulation can result in sufficient ventilation we prefer bilateral simultanous stimulation. In 3 patients with electrodes implanted in the neck EPR was used continuously for up to 160 days. No fatique of the nerve-muscle-system was noted during the whole period.
Since patients with cervical implanted electrodes complain very often of troublesome discomfort or pain related to stimulation, we now implant electrodes via a partial sternum splitting incision and fix them to the phrenic nerves within the upper mediastinum. We have done this now in two patients, wich respond excellent to electrophrenic stimulation. Tidal volumes of up to more than 600 ml are achievable with submaximal stimulation.

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PARASPINAL MUSCLE STIMULATION FOR SCOLIOSIS IN CHILDREN, SURFACE STIMULATION.

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SUMMARY

The treatment of progressive scoliosis in children has seen major changes in the last ten years. Initially, the treatment of curves less than 40 degrees was only by the use of Milwaukee bracing (1,2). However, problems with patient acceptance led to the search for alternative methods. Work by the author and W.P. Bobechko led to the development of a technique of using electrical stimulation to treat scoliosis (3,4). Animal experimentation was used to test the hypothesis that unilateral electrical stimulation of the paraspinal muscles could be used to alter the direction of growth of the spine, and thus would hold promise as a treatment modality (5,6). The implantable stimulation system known as Electro-spinal Instrumentation (ESI) developed out of this work, and is in use in centres throughout the world.

Approximately nine years age, an effort was made to assess whether the electrical stimulation could be delivered through the use of surface electrodes placed on the skin. The initial clinical work in this area was carried out by Dr. N. McCollough III of the University of Miami, Florida (7). While the results of these preliminary experiments were equivocal, experience since then has shown that this is a viable alternative to bracing. The work presented in this report is a summary of the results of a clinical study involving 21 orthopedic surgeons.

MATERIALS AND METHODS

Clinical Material: Scoliosis patients were accepted for treatment using surface electrical treatment if they were skeletally immature, had either a single or double curve measuring 30 degrees or more, or a curve of 20 to 29 degrees with a documented progression of 5 degrees or more.

Equipment: Treatment was carried out using ISOMOD model 3100 or 3100-2 systems manufactured by Medtronic, Inc. of Minneapolis, Minnesota. The model 3100 was a single channel only unit, with output current adjustable from 0 to 50 ma. It was set to cycle on 5 sec, off 25 sec, with a ramp on of 0.5 sec. The pulse train consisted of 425 usec pulses at 50 pulses per second. The model 3100-2 had two channels cycling together, and could be used as either a single or dual channel unit. The output was adjustable from 0 to 100 ma. and it was set to cycle on for 6 sec, off 25 sec, with a ramp on time of 1.5 sec. The pulse train was set at 225 usec width at a rate of 35 pulses per sec. It also had a current meter for monitoring usage. The stimulation was applied to the skin through a connecting cord and carbon filled silicone rubber electrodes (5 cm. x 3.5 cm.). Contact with the skin was through a conducting gel or karaya pads.

Protocol: Patients to be treated using stimulation were instructed thoroughly in the equipment, and its usage. Initial documentation of the scoliosis by X-ray was carried out. The patients and their parents were shown the proper electrode positions and how to attach the electrodes.

Treatment was carried out at night only while the patient was asleep. The electrodes were applied at bedtime and the unit turned on. Upon awakening in the morning, the patient turned off the transmitter, and removed the electrodes. There were no restrictions on the patient's daily activity, no braces were worn and no supplemental exercises given.

Two electrodes were used for each channel of stimulation, with the electrodes placed above and below the apex of the curve on the convex side. Electrodes were placed either adjacent to the spine (paraspinal position), on the axillary line (lateral position), or midway between the two (medial position). Dual channel devices (model 3100-2) used four electrodes (2 per channel) to treat double curves. Both channels cycled simultaneously, although the amplitudes were independently adjustable. Electrode placement was the same as though two single devices were being used with one pair placed on the convex side of each curve.

Patient progress was assessed through regular followups at three month intervals. AP standing radiographs were taken, and the curves measured by the Cobb technique. Comparison was made to the last standing radiograph taken before the start of treatment.

RESULTS

A total of 236 patients were reported in this study, but 28 do not have followup at this time. A further 49 patients are not included since their curves do not fit the protocol. The 159 remaining patients consist of 71 with curves between 20 and 29 deg with documented progression, 55 with curves between 30 and 40 deg, and 33 with curves between 20 and 29 deg, but inadequate documentation of their progression. Table 1 lists the basic data on this group.

Table 1: Basic Patient Data for Protocol Patients

protocol patients: 121			female/male ratio = 5.3/1
mean curve: 28 deg			range: 20 to 40 deg
age distribution:			
2% (1-5 yr)	14% (6-10 yr)	77% (11-15 yr)	7% (16-20 yr)
curve location:			
thoracic (73%)	thoraco-lumbar (18%)	lumbar (9%)	
time in treatment:			
0 - 12mo (44%)	12 - 24mo (36%)	25 - 36mo (16%)	36 - up (4%)
Risser sign at start:			
Risser 0 (65%)	Risser 1 (10%)	Risser 2 (20%)	Risser 3+ (6%)

Results of Treatment: If the curve changed by 4 deg or less, it was

classified as Unchanged, while 5 deg or more of improvement was rated as Improved and a 5 deg loss was Progressed. In the study, there were 28% of the patients classed as Progressed, 54% as Unchanged, and a further 18% with significant improvement in their curves. Table 2 lists the results of treatment stratified according to various starting criteria.

Table 2: Results of Treatment of Protocol Group.

	Improved	Unchanged	Progressed
males	5 %	60 %	35 %
females	21	52	27
Risser 0	19	49	32
Risser 1	20	60	20
Risser 2	5	70	25
Risser 3+	17	63	0
20 - 29 deg	20	56	24
30 - 40 deg	16	51	23
Thoracic	13	56	31
Thoraco-lumbar	26	48	26
Lumbar	36	55	9
Paraspinal	29	42	29
Medial	11	66	23
Lateral	14	56	30
Treated up to 1 yr	21	52	27
Treated 1 to 2 yr	11	60	29
Treated over 2 yr	24	48	28

Complications: Problems arising from the use of surface stimulation are almost non-existent. The major problem is skin irritation, which is usually of a minor nature, and can be kept under control by changing to different conductive pastes. Approximately 15 - 25% of the patients are troubled by some skin irritation, although the actual number who have to be discontinued for this problem, is very small. Hypersensitvity of the skin has been reported in a couple of cases. The only major concern is the need to educate the parents and patient to place the electrodes in the correct position, since inappropriate positioning of the pads can leave the curve untreated, or even worsen a second curve.

DISCUSSION

Electrical stimulation of the paraspinal muscles to treat scoliosis in growing children is now an accepted alternative to bracing programs. The use of the Isomod system of surface stimulation has yielded excellent results in the treatment of this disease. Nighttime treatment has been well received by the patients because it does not interfere with their life, and there are no peer problems as with bracing (8).

In most centres, the success rate of stimulation is as good as for bracing, with minimal compliance problems.

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Treatment of Scoliosis with LEOS

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Since 1981 we do electrical neuromuscular stimulation of progressive scoliosis, using one channel. The stimulation is applied through electrodes.
Until this time we treated 23 patients between $7\frac{4}{12}$ and 15 years.
In 5 patients the treatment is finished. In 3 patients we were successfull in reversing the progression of scoliosis in 2 patients in arresting the deformity.
In 3 patients we had to change to brace, because severe progression of deformity appeared. 2 patients of them meanwhile underwent Harrington rod instrumentation. In 2 cases we stopped treatment after several weeks because of intolerance.
Two patients refused Scolitron and brace after one year although they showed good results.
Follow up results of the 11 patients are demonstrated and difficulties during the treatment are described.

CENTRO DI RECUPERO FUNZIONALE - FONDAZIONE PRO JUVENTUTE
Don GNOCCHI FIRENZE, Italia

Prof. G. Frontino- Dr. A. Corigliano

RESULTS OF THE LATERAL ELECTRIC SURFACE STIMULATION OBTAINED AS OF END OF JULY 1983.

One of the newest and most promising system to treat conservatively: the juvenile idiopathic progressive scoliosis is the Lateral Electric Surface Stimulation. (L.E.S.S.)
We started investigating this method in March 1979, after having joined the International Investigation Protocol launched by the Rancho los Amigos Rehabilitation Centre of Los Angeles.
The program was started utilizing the "Scolitron" muscle stimulator Based upon our experience that is so far exceeding 500 cases, our opinion is that a single channel unit is not flexible enough, and furthermore cannot treat effectively double major curves, much fixed single curves, very long curves (as in some thoraco-lumbar patterns)
This very fine programme has been seriously compromised in the 1980 by the financial distress of the original sponsor. Only this year the new sponsor NEUROMEDICS has introduced a dual channel stimulator.
In view of the broader indications for a two-channels system we have developped since 1980 the stimulator that we are now utilizing in our centre. It features: two synchronous operating channels, with independant adjustable amplitutde, constant current, and remote digital control to check the stimulations parameters.
As a coupling media of the electrodes to the skin we use only some special karaya based pads,developped by our Centre, in orderd to manage better the skin rash problems we had to face at the beginning.
The placement of electrodes normally utilized is as recommended by the Authors:Brown and Axelgaard, with some slight modificatiions in some instances:
A slight transverse positioning in absence of hyperlordosis, seems to be more feective over lumbar curves.In presence of double thoracic curves we utilize a bilateral placement, with the upper cuople of electrodes in a paraspinal placement, as soon as we notice that the hump relavant to the upper thoracic curve trends to increase. In presence of thoracic curves particularly fixed

we obtain a much better acute reduction with two pairs of electrodes placed on the same side.

As far as the selection of patients is concerned, we use the Rancho's protocol scheme, however when one or more criterias are violated but progression seems eminent, the patients are admitted as "non protocol" ones.

Results from protocol and non protocol patients are processed separately.

We have utilized 65 Scolitron and 438 Spinelectrons follow up of the 503 patients shows a rate of stabilization of all the curves of about 76% (July 1983).

The worsening of the curves (>5°) forcing the discontinuation of such treatment is so far a small percent of the total drop outs : 8,5%.

In fact the second and third major reason for dropouts are the non tholerance (5,7%) and personal decision (with no sign of progression) : 6,1%

The use of special karaya pads has limited the non manageable skin problems to a low 1,7%.

Occasional skin rash that we have been able to manage so far is in the range of 25% of cases, with peak of over 30% in the warm season.

The "A" group (protocol high risk patients) has been stratified in:

56 Thoracic Curves

51 Thoraco-lumbar curves

52 Lumbar curves

53 Double Major curves

The "B" group (post puberty) has been stratified in:

40 Thoracic curves

54 Thoraco-Lumbar curves

16 Lumbar Curves

54 Double Major Curves

These two groups of patients (375) are the ones still in treatment, and with a follow-up of at least 6 months.

It is our practice to call the patients on monthly controls. In that occasion we control the proper electrodes placement, proper functioning of the stimulator, skin care, and most important we measure the humps to have an early warning, should the system fail to arrest curve progression.

The following diagrams are showing the behaviour of curves and humps, of both "A" & "C" groups, and based upon the results our preliminary conclusions are:

So far the use of LESS has provided an effective stabilization of the treated curves, stabilization that can be much compared to the best bracing treatments.

The little invasiveness of this methodology may lead in a near future to decide for an earlier than it is now treatment, thus permitting us to achieve even better results! We feel in fact that we should treat scoliosis as a whole deformity and not simply as an independent parameter tied to the Cobb angle.

Early treament that will allow us to greatly limit the cosmetic appearance damages caused by curves often well below 20°

We are fully aware that such approach will raise any perplexities, even if are due to the fact that so far we do not dispose of a viable prognostic method.

FUNCTIONAL STIMULATION FOR THE TREATMENT OF JUVENILE SCOLIOSIS - COURSE CONTROL

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SUMMARY

Four scoliosis patients with spinal deformations varying from 12 to 25 degrees received conservative treatment for a period of six months. The course of therapy was marked by X-rays at the beginning and end of the observation period as well as by periodic interference-pattern analysis from electromyograms of the paravertebral back musculature. Changes could be observed in the X-rays as well as in the pattern - analysis. This would indicate a direct connection between changes in the bone structures and their related muscles, whereby stress-free myopotential analysis would seem to open new possibilities for regular therapy.

INTRODUCTION

The lateral bending of the spine which occurs during scoliosis always carries with it a rotation of the vertebrae. Once an imbalance has occured, any further deterioration leads to progressive deformation which, once it has reached 50 to 60 degrees according to Cobb, can only be corrected by surgery. All conservative treatment methods, including functional stimulation, aim to stop this deterioration. The earlier the treatment begins, the better the chances for success. Treatment must take place at regular intervals and be continued until the end of a person's growth period, since deformations of less than 50 degrees can only be considered fully and finally arrested when all growth has stopped. This means a treatment span of up to 8 years entailing rather severe modifications of normal life style.

Functional Electrostimulation

At first implantable stimulators were used. Today, these have been largely replaced by surface stimulators to avoid surgery. In most cases, stimulators are positioned at the level of the rear axillary line of the convex spinal musculature and activated during sleep. It is hoped that severe contraction of the back muscles will result in a straightening of the spine. Long lasting improvement after such treatment is rare, but in 80 to 90 % of all cases further deterioration can be avoided. It is unclear precisely how long a oeriod of treatment is necessary, since different experts indicate varying frequency and duration of stimulation.

Patients

Four patients ages 9 to 14 with scoliosis ranging from 12 to 25 degrees. Where one leg was shorter than the other, a pad was placed in the heel of one shoe. Two of the patients received only physical therapy, while the other two also received stimulation of the convex

musculature. Both physical therapy and stimulation took place twice for half an hour daily.

METHOD

Main interest focused on the progression of the deformation. To judge the success of this therapy we have only two indicators : the less than totally reliable Moiré topography on the one hand and a complete standing X-ray profile on the other. Because of the damage done by X-rays, these could only be taken every six months. For this reason - and since all changes in bone structure presuppose other changes as well - more attention was paid to the muscles. Regulation of muscle force occurs through the firing rate of individual muscle fibers as well as through the sheer number of activated muscle fibers. Individual muscle contraction yields a characteristic interference pattern which can be seen in the myogram derived from a reading of the muscle surface.

Myograms demonstrate rather large variability, even physiologically, so that a direct comparison between two people is practically impossible. It makes far more sense to compare contra-lateral muscles or to compare measurements taken under the same conditions at different time periods. In cases of neuropathologies or myopathologies, there are even more striking changes.

Changes in the interference pattern follow from clearly defined experimental conditions: the patient stands upright and holds a 0.5 kg weight in his horizontally outstretched arms. Surface electrodes have been attached to the paravertebral muscles on both sides of the spinal column. The use of surface electrodes results in more accurate reproduction values as well as in reduced stress for the patient, which is of prime importance for the quality of the analysis. That is to say, better results stem from reduced stress and anxiety in the patient.

Through amplification and digitization by microprocessor the myogram is divided into individual oscillations and their overlaid oscillations and the corresponding amplitude and frequency value of each half period measured. The processor assigns each oscillation to one of 16 frequency domains and gives the incidence for each of the frequency-amplitude domains. Through these measurements as well as through their corresponding relationships the myogram can be precisely described. Thus one can represent changes in the interference pattern which are not visually discernible.

RESULTS

Let us look at two cases to show the usefulness of these interference patterns. In the future we will still not be able to by-pass X-ray examination, but the stress-free interference analysis method makes possible more frequent measurement - and thereby more accurate control - of the chosen course of therapy.

Case 1

This patient demonstrated a right convex thoracic scoliosis of 25 degrees before treatment, which was limited to a course of physical therapy as well as orthopedic shoe correction to level the pelvic imbalance. After six month of treatment the deformation was reduced to 15 degrees.

After six months of physical therapy a originally concave oreponde-

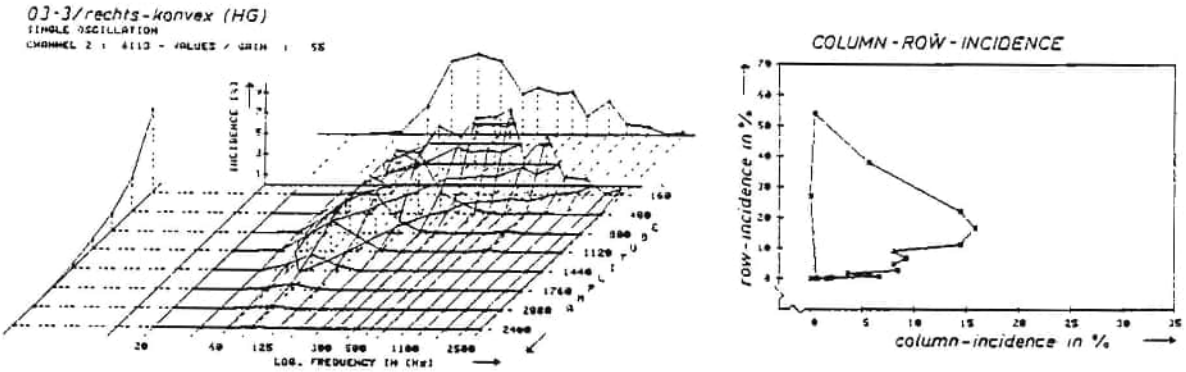


Fig.1 : Amplitude-frequency distribution for single oscillations right, konvex side before treatment.

rance goes over into a predominantly convex one. During the first three months both sides showed lower signal amplitudes, although after six months circumstances are similar to those at the beginning.

The high frequent portions on both sides of the spinal column diminish in similar ways and stabilize in a frequency range of 180 to 250 Hz.

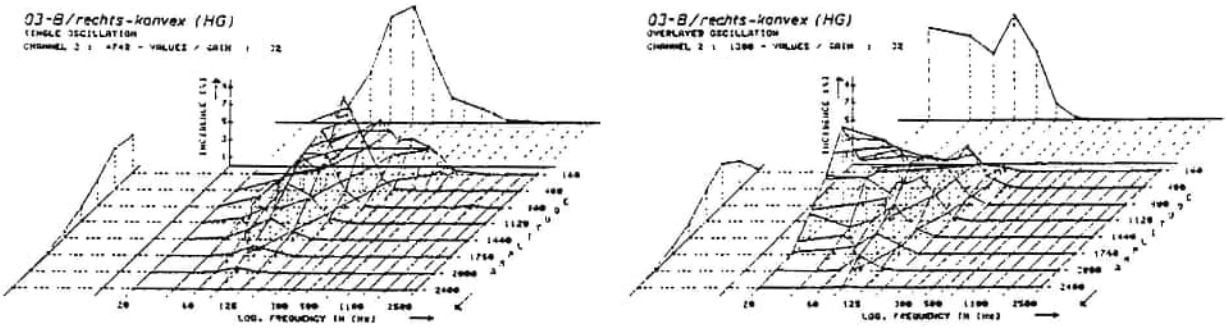


Fig.2 : Amplitude-frequency distribution for single oscillations right, konvex side after 6 months of physical therapy

Case 2

Before beginning treatment this patient demonstrated a left convex

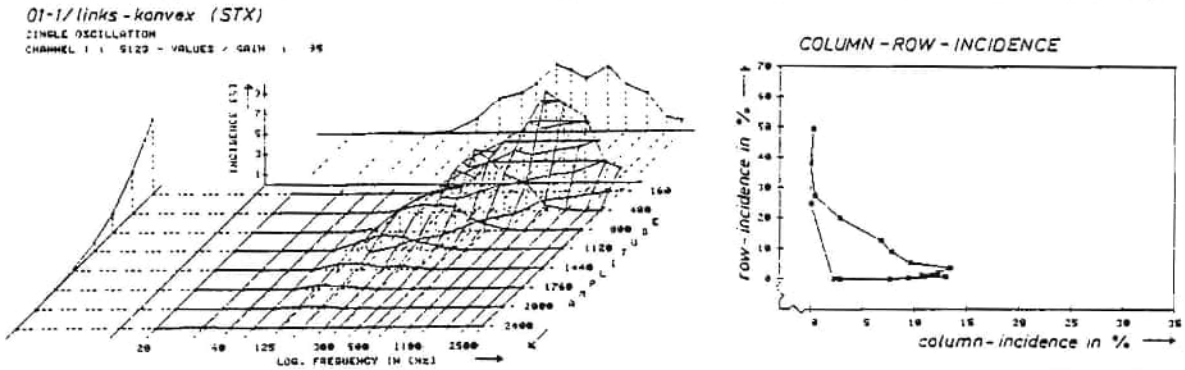


Fig.3 : Amplitude-frequency distribution for single oscillations left, konvex side before treatment.

thoracic scoliosis of 14 degrees. During the course of the six months treatment his condition imoroved and now the spine shows absolutely no deformation. The patient was treated with physical therapy as well as with convex-side functional stimulation.

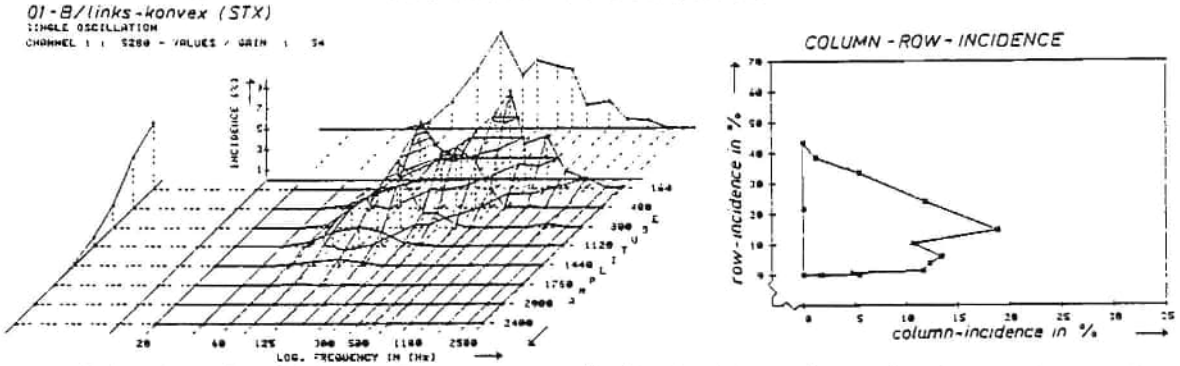


Fig.4 : Amplitude-frequency distribution for single and overlayed oscillations, left, konvex side after 6 months treatment.

During the first three month of treatment the originally concave configuration became more pronounced; however, after six months this switched over into markedly convex activity.

Before beginning treatment high frequent portions are found on the convex side. These become reduced during the course of treatment. The frequency distributions on both sides thus approach each other more and more. On both sides the maximum of incidence is around 200 Hz. The same decrease seen in the single oscillations, can also be seen in the overlaid ones.

DISCUSSION

Out of the four examined patients, two were treated only by physical therapy. The other two were treated with physical therapy as well as with convex-side functional stimulation. Only one patient without functional stimulation showed the same degree of deformation after six months of therapy. The other three showed evident correction of the spine deformation.

Especially in the case of the demonstrated patient with functional stimulation the correction could be influenced by three possible facts - physical therapy, functional stimulation and orthopedic shoe-correction. Up to now it is unclear, which one is the main-influence.

Important however is that the x-ray controlled correction of spine deformation leds to a altered frequency-amplitude distribution of the analysed electromyogram of the paravertebral back muscles.

These changes however can be seen by way of suggestion just after a few days of therapy. Therefore it is possible to control nearly stress free the influence of different therapies after short periods.

Before you can generalize the results the measurements must be done with more patients, divided in groups with only one kind of therapy to seperate the influence of each treatment.

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DAILY SHORT-TERM-STIMULATION IN THE EARLY TREATMENT OF THE IDIOPATHIC SCOLIOSIS

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SUMMARY

Physical therapy for conservative treatment of idiopathic scoliosis includes many excercises often heavy to learn for the young patients, so that regular control by a physical-therapist is necessary. Brace-wearing for treatment of heavey deformities is always a psychological problem for the adolescent patients. Therefore the present state of conservative treatment in idiopathic scoliosis can not be satisfying.

In the last years some electrostimulation methods are propagated for the early treatment of idiopathic scoliosis. But these methods also includes many problems, because they are long-term-stimulation methods performed during the night.

Therefore we developed a new stimulation method, which allows early treatment by short-term-daily-stimulation by the application of a strong current strength to reach all muscles being able to correct the scoliotic deformity.

With our method of muscle stimulation we were able to stop the curve progression in 94,0 % of sufficient treated patients. In addition we saw an electromyographically measurable training-effect on stimulated muscles.

MATERIAL AND METHODS

Treated patients and scoliotic curves

We treated at all 40 patients (6 males, 34 females) between 7 and 18 years old. The mean age was 13,7 years. The mean scoliotic angle at the beginning of treatment was 26,5°. 36 cases showed a right convex thoracal scoliosis, 4 cases whowed s-shaped scoliosis with thoracal convexity to the right. All patients showed a Risser-stage as following: Risser-sign 0 = 20%, Risser-sign 1 = 25%, Risser-sign 2 = 48%, Risser-sign 3 = 78%.

Stimulation method:

Electrostimulation of the intercostal muscles was performed with a pulse-generator, that produced rect-angular pulses of 1 msec. duration at a fixed frequency of 100 pulses/sec. The maximum current strength reached 80 mA. We stimulated with skin-electrodes (electrode area: 39,2 cm^2).

The electrode localisation was in the paravertebral region on the convex side at the apex of the scoliotic curve, 2 - 3 cm laterally from spinous process.

The strength of stimulation current was strong enough that strong contractions as well of paravertebral muscles as especially of intercostal muscles could be felt by the palpating finger.

The duration of one stimulation period was 20 minutes per day. We stimulated in the mean at three days a week.

Method of evaluation

To control the immediate stimulation effect on the scoliotic curvature we performed X-rays during stimulation, measuring as well the correction of scoliotic angles (LIPPMANN-COBB-Method) as rotation correction (NASH and MOE's Method).

We controlled the stimulation effect on stimulated paravertebral muscles by a comparatively quantitative measurement with skin electrodes during body-lifting. The examination was taken four, twelve and forty weeks after the beginning of treatment.

Mean duration of stimulation was 2,5 years. Long-term results could be taken in the mean two years after the end of treatment.

RESULTS

On this way we could observe 31 patients. 7 cases could not be evaluated because of irregular stimulation treatment and insufficient stimulation-time. In 2 cases the applicable current was not strong enough.

The mean correction of curves during stimulation was better at slight curvatures beyond 35° than those above this limit. It was on the average 39 %. Whereas the angle above 35° showed only a slight reduction of 9,2 %. The correctability of scoliotic angles was better in those curves with a short history and only slight structural changes. The mean correction of rotation-deformity beyond 35° was from 1 to 1,5. Above 35° we didn't reach a significant rotation-correction.

The long-term-observation of the treated curves showed an increase of curvature on average of 31 % before the beginning of treatment. The long-term result of one year stimulation was a decrease of 26,5 % from the beginning value. In the following period we saw no further decrease. On the average 44 % of all patients showed a reduction of scoliotic angles of more than 5°. 50 % were unchanged; 6 % worsened. The long-term-observation two years after the end of treatment (25 patients) showed no significant changes of mean scoliotic angles (fig. 1).

The stimulation effect on stimulated muscles consisted in significant decrease of activity after the beginning of treatment (fig. 2).

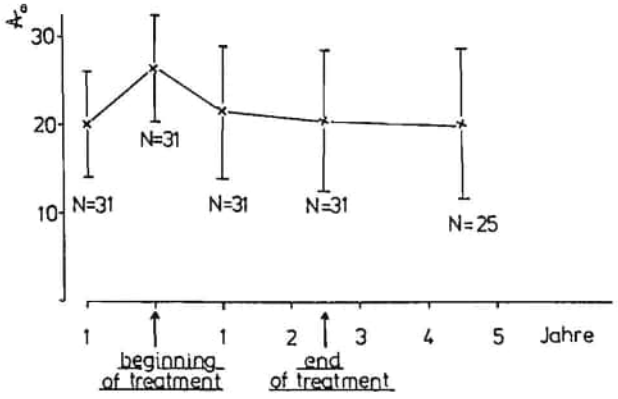


fig. 1

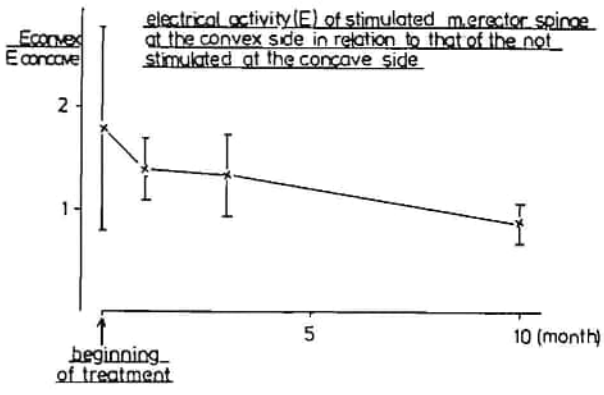


fig. 2

DISCUSSION

Earlier investigations have shown, that the paravertebral muscles, superficial trunk muscles and especially the intercostal muscles with their rib levers at the convexity of the scoliotic angle are able to stop the increase of scoliotic deformity (SCHMITT, 1981). The electrical stimulation as an early treatment of idiopathic scoliosis therefore must include all these muscle groups in order to have the best redresion-effect.

Over this electrostimulation it is also possible to make a muscle fibre hypertrophy (GOLISCH et al., 1970; PETTE et al., 1973). This muscle training effect can only be observed after strong muscle contractions (HETTINGER, 1983).

With our method we can stimulate all correcting muscles simultaniously by maximal stimulation strength. This is only possible by daily stimulation. Our investigations have shown, that by daily short-term-stimulation (20 min. a day) we could reach as well good clinical as especially an electromyographic measurable training effect on stimulated muscles.

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ELECTRO-SPINAL INSTRUMENTATION: REPORT OF A MULTI-CENTRE TRIAL IN EUROPE

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SUMMARY

To evaluate the management of progressive Idiopathic Scoliosis by electro-spinal instrumentation, a multi-centre trial was set up in Europe in 1980. 160 patients with 199 curves have been treated by this method.

The overall results to date show that progression has been arrested in 77% of all cases of progressive Idiopathic Scoliosis.

The results so far suggest that electro-spinal instrumentation does have a part to play in the treatment of progressive Scoliosis. In this respect it rivals the Milwaukee brace as a method of treatment with all the advantages of allowing a child to lead a completely normal life by day having treatment at night only.

MATERIAL AND METHODS

Using electrical stimulation, it has been shown that both in the experimental animal and in the child with Scoliosis, electrical stimulation of the paraspinal muscles on the convex side of Scoliosis canpreduce correction in a progressive curve.

The present system, which has been developed in conjunction with Medtronic Inc., utilizes an implantable radio receiver linked with three electrodes, an external antenna and transmitter device. The electrodes are placed on the convex side of the spinal curvature deep in the paraspinal muscles. The receiver is energised by a signal from the transmitter via the antenna, the transmitter being pre-programmed to provide the desired stimulation pulses. The signals are superimposed on a radio frequency carrier wave transmitted through the skin by induction coupling, picked up and modulated by the receiver, and transmitted through the electrodes as electrical energy. This causes muscle contraction.

RESULTS

160 patients with 199 curves have been treated by this method following strict patient selection criteria.

The diagnosis of progressive Idiopathic Scoliosis had to be made in all cases by exclusion following routine investigation. Curve progression had to be documented on at least two serial successive radiographs. Bone age was determined by the Tanner and Whitehouse method and all patients were required to have at least two years growth potential remaining. The curve limits were set at 20-40^{o} with at least 50% correction on side bending. In certain circumstances the upper curve limit was raised to 45^{o}, either because of remarkable flexibility in side bending films or where the second curve of a double major curve slightly exceeded 40^{o} the other curve being slightly under 40^{o}.

The age range of patients was from 3.6 to 16.3 years with a mean age of 12.8 years. 90% were females and 10% were males. The mean bone age at time of implantation was 12.4 years.

The mean curve size treated was 29.3° with a range from 20–45°.

There was a mean length of follow-up of 14.9 months.

During the trial period of 3½ years, treatment has been discontinued in 17 curves. Bone maturity has occurred in 8 curves in 7 patients. Unacceptable curve progression has occurred in 7 patients and 2 patients have been lost to follow-up.

The overall results to date show that 34% of all curves have been improved. In 43%, progression has been arrested and in 23% the curve has worsened.

A more detailed analysis of the results relating length of stimulation to curve correction, shows only 17% of curves worsening in the first year of treatment. Thereafter the proportion of good results drops from 83% at 12 months to 77% at 30 months.

After three years of treatment there appears to be a modest improvement in good results but so far only 10 curves have been treated for this length of time.

If the initial curve size is correlated to treatment it appears that the best results are obtained in the two groups of curves measuring 25–29° and 35–40°. No firm explanation can be given for this apparent paradox although it is possible that a larger proportion of smaller curves occur in the younger age group. Such results are seen not only at one year following treatment but also at the two year follow-up period.

Curve location does not appear to modify the response to treatment. Both at one and two years post treatment there is no significant difference between the response of thoracic and thoraco lumbar/lumbar curves.

The relationship between the chronological age of the patient and the response to treatment shows a significantly larger proportion of poor results in the group starting treatment under the age of 11 years. This is evident at one year follow-up.

At two year follow-up it is also evident that not only in the under 11 year old group but also in the 11–13 year old group, the results have been poor although the numbers are to date small.

An attempt has been made to compare the group of patients whose curves have been improved or arrested during treatment, with those whose curvatures have worsened.

Parameters studied included initial curve size and location, chronological and bone age, sex, number of curves treated and the size of initial correction obtained.

Such analysis shows that the patients whose curves were improved at one and two years post treatment had a mean age of 13.4 years and there were a larger proportion of thoracic curves. Due to the small numbers reaching two year follow-up a statistical comparison cannot be made. It is also evident that patients demonstrating improvement of a continuous nature at 1, 2 and $2\frac{1}{2}$ years could not be distinguished from those patients whose curves progressed.

DISCUSSION

Although the results are encouraging at the present time, it is accepted that the follow-up period of three years is comparatively short and in consequence a small number of patients reaching maturity do not allow for adequate statistical analysis. Likewise parameters do not exist which would enable a selection to be made of those curves which are likely to progress, although initial indication suggest that the bulk of poor results are in the younger age group. Nonetheless it is diffucult to understand why some of the smaller curves especially in the $20-25^{\circ}$ range do poorly even in the older child.

If the average curve measurement is taken for the group as a whole, the pattern of response to treatment is seen to show a typical early correction over the first year with maintenance of this correction over the ensuing one to one and a half years.

By curve location a very similar graph is demonstrated showing no difference between thoracic and thoraco lumbar/lumbar curve response.

If curve sizes are plotted taking a division point at 30° it can be shown that the average curve response is similar in both groups.

The results so far suggest that electro-spinal instrumentation does have an important part to play in the treatment of progressive Idiopathic Scoliosis. However, in view of the short follow-up period, further clinical experience is necessary before long-term conclusions can be drawn with statistical accuracy.

ELECTRO-SPINAL INSTRUMENTATION IN THE TREATMENT OF SPINAL DEFORMITY

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SUMMARY

In spite of considerable research, especially in the last twenty years, the precise aetiology of Idiopathic Scoliosis still remains a mystery.

As James (1) has said "Our knowledge of the aetiology of Idiopathic Scoliosis is negligible probably less is known of it than any other disease so common or so visually evident." Sixteen years later this statement still remains valid.

At the present time most orthopaedic surgeons when faced with the problem of progressive idiopathic scoliosis measuring less than 40^{0}, utilize spinal bracing as the treatment of choice.

Bracing has obvious drawbacks; the patient is restricted in terms of physical activity and the bulky nature of some devices make concealment difficult from the rest of the peer group. Patient compliance with treatment over a long-term period can be seriously reduced (2). Bracing is however a reliable and effective method of controlling curve progression (3).

In the search for alternative treatment a method is needed which will be at least as effective as bracing, but which increases patient compliance and intrudes less on normal daily living.

Using the principle of electrical stimulation, Bobechko (4) conducted a series of experiments using the rabbit and later the pig as animal models to study the effect of paraspinal muscle stimulation on the development and correction of lateral spinal curvatures.

He was able to show that a Scoliosis could be induced in animals with straight spines by unilateral electrical stimulation and that the Scoliosis could be corrected by subsequent contralateral stimulation.

Following further technological refinement and research Bobechko, in conjunction with Medtronic Inc. developed a radio frequency coupled system for the treatment of Scoliosis in the human.

This radio frequency device has been used to treat progressive Idiopathic Scoliosis and the results so far suggest that electro-spinal instrumentation have an important part to play in the treatment of progressive Idiopathic Scoliosis. In this respect it would rival the Milwaukee brace as a method of treatment with all the advantages of allowing a child to lead a completely normal life by day having treatment at night only.

MATERIAL AND METHODS

FUNCTIONAL ELECTRO-STIMULATION

For many years clinical observers have noted the frequent occurrence of Scoliosis in neuromuscular disease and radiologically, these curves are indistinguishable from those in progressive Idiopathic Scoliosis in the early stages of the disorder.

It is possible that in neuromuscular disease a muscle imbalance between the paraspinal muscles on the two sides of the spine might result in the development of a Scoliosis. Therefore an induced muscle imbalance might be used to alter the direction of growth of the spine and hence treat a pre-existing spinal deformity. Such an imbalance can be created by unilateral electrical stimulation which is known to produce muscle hypertrophy and muscle fibre-type change.

The system utilizes an implantable radio receiver linked with three electrodes an external antenna and transmitter device. The electrodes are placed on the convex side of the spinal curvature deep in the paraspinal muscles. The receiver is energised by a signal from the transmitter via the antenna, the transmitter being pre-programmed to provide the desired stimulation pulses. The signals are superimposed on a radio frequency carrier wave transmitted through the skin by induction coupling, picked up and modulated by the receiver, and transmitted through the electrodes as electrical energy. This causes muscle contraction.

The stimulator is adjusted to cause muscle contraction lasting one second with a rest period of nine seconds between contractions. This sequence prevents muscle fatigue. The stimulation over one second is not a single pulse but a burst of pulses lasting 220 microseconds repeating every 33 milliseconds. The pulse bursts are carried by a low frequency (450 KHZ) carrier wave for transmission through the skin. The receiver filters out the carrier signal and conducts the burst through the leads to stimulate the muscle. The output amplitude is adjustable to a maximum of 15 volts. The system is powered by a nine volt battery in the transmitter.

The surgical insertion of the receiver is simple and straight forward. The patient is anaesthetised and intubated without the use of muscle relaxants and positioned on an operating frame similar to that used in routine spinal operations. A mid line incision is utilized, and with reflection of skin and subcutaneous tissues on the convex side only, the paravertebral muscles are exposed.

The incision extends three vertebral levels cephalad and two vertebral levels caudal to the apex of the curve. Through the same approach a small subcutaneous pouch is made just below the 12th rib to accommodate the receiver.

Optimal sites of muscle contraction are verified by the use of trial concentric needle electrodes. Maximum contractions of the muscle and correction of the curve are most often seen with electrodes placed corresponding to three and one vertebral levels above the apex and one level below the apex of the curve. The site is usually 2.5 - 3cm from the appropriate spinous processes. Once optimal positions of electrodes are found the trial electrodes are replaced by the corkscrew electrodes connected to the receiver. The entire process is carried out under x-ray control.

Latterly it has been possible to use a dual channel system in which two major curves can be treated. This system is essentially two single channel devices operating on different carrier frequencies but contained within the same implantable receiver.

Wound closure is carried out after strict haemostasis using a subcuticular stitch or metal skin clips.

The patient is kept in bed for 24 hours to discourage post-operative haematoma formation. Thereafter the patient is allowed out of bed and discharged from hospital on the third post-operative day.

Clips if present are removed on the 12th post-operative day and an in-patient programme of stimulation begins lasting three days. During this period the patient and parents are familiarised with the equipment and the stimulation strength is gradually increased.

Over the first three months the patient attends hospital at monthly intervals, the transmitter controls being adjusted each time towards an optimum voltage for maximum stimulation. Following this the child then attends at four monthly intervals throughout the rest of the stimulation programme, progress being assessed by routine radiography.

Treatment is undertaken during the night. The patient during the day is allowed to lead an entirely normal life including the participation in all sporting and recreational activities. The antenna is connected to the transmitter and then placed over the receiver using an appropriate adhesive disc. The battery is tested and the transmitter switched on. The receiver is usually kept in a small pocket on the night attire, may be clipped to the blankets of the bed or left on a bedside table.

Radiological estimates are made of bone growth and maturation. When growth is deemed to have ceased, treatment continues for a further four months.

At this stage treatment is stopped and the implant left in situ for a further four months. If there has been no deterioration the implant is then removed.

Assessment of the efficacy of treatment is undertaken in standard antero-posterior radiographs of the spine. These x-rays are taken at least six hours after the cessation of the previous night's stimulation. The Cobb technique is used for measurement. Assessment is made by comparison with the last pre-operative film taken before the implantation. If the curve has changed 4° or less (either plus or minus from the pre-operative value) the curve is classified as unchanged. If the curve shows 5° or more correction it is classified as improved; 5° or more deterioration is classified as progressed.

To study and evaluate this form of treatment in progressive Idiopathic Scoliosis strict patient criteria were chosen.

The diagnosis of progressive Idiopathic Scoliosis was made in all cases by exclusion, following routine investigation. Curve progression was documented on at least two serial successive radiographs. Bone age was determined by the Tanner and Whitehouse method and all patients were required to have at least two years growth potential remaining. The curve limits were set at $20-40^{\circ}$ with at least 50% correction on side bending. In certain circumstances the upper curve limit was raised to 45°.

Using these criteria 17 patients with 19 curves have been treated. The mean age at treatment was 12.9 years with a range of 9.6 - 15.5 years. 8% of the children were under the age of 11 years with 44% occurring in the 11-13 year old age group. There was only one male patient in the series. The mean length of follow-up was 20 months.

The average curve size was 36.3° with a range of $25-45^{\circ}$.

17% of the curves fell in the range $25-29^{\circ}$, 22% in the range $30-34^{\circ}$, 44% were in the range $35-40^{\circ}$ and 17% were greater than 40°.

In 78% of the patients the curves were in the thoracic region, 11% were classified as thoraco lumbar and 11% were in the lumbar spine.

At one year follow-up improvement in the curve has been noted in 46% and progress has been arrested in 54% of the curves. At 18 months follow-up 72% of all curves have been improved or progress has been arrested and progression has been noted in 28% of cases.

At 24 months 67% of all curves have been stablised but progression has occurred in 33%.

Four curves have been successfully managed to maturity, but three curves have shown unacceptable progression and have thereafter been subjected to routine Harrington instrumentation and spinal fusion.

A comparison between the U.K. results and the European study group as a whole suggest that the average curve size treated is higher in the U.K. series and that there is a higher percentage of children under the age of 13 selected for treatment. The two groups cannot however be strictly compared statistically, because of the relatively small numbers involved in the U.K. series alone. It is however of interest to note that when taking the European results as a whole, the poorer results are seen in the younger age group. There does not however appear to be any correlation between curve correction and curve size in a linear fashion across the range of 20–45°.

Due to the short follow-up period further clinical experience is necessary, although the initial results are extremely encouraging. It is felt that this method of treatment offers a rational and alternative method of dealing with progressive Idiopathic Scoliosis. Compliance rate has been 100%, and all children have led a perfectly normal uninterrupted daily lives.

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PARASPINAL MUSCLE STIMULATION FOR SCOLIOSIS IN CHILDREN. IMPLANTABLE STIMULATION (ESI)

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SUMMARY

Scoliosis (lateral curvature of the spine) is a common disease of unknown etiology. In North America, up to 15% of the school age population are reported to have scoliosis (1). In 0.3% of the children, it is highly progressive (3 to 5 deg/mo) and requires aggressive treatment (2). The age of the patient and the degree of curvature (0 degrees is a straight spine) determines the treatment selected. In adults, curves of more than 40 deg are probably biomechanically unstable and progress relentlessly. In these patients it is necessary to fuse the spine to stabilize it and prevent its continuing collapse. Lesser curves are rarely progressive, and no treatment is indicated.

The rate of curve progression parallels the rate of growth in children, slowing or stopping at skeletal maturity. In children whose curves have progressed beyond the 40-50 degree range, the only effective treatment is spinal fusion, since these curves will be unstable during adulthood. For children whose curves measure less than 40 deg, treatment is usually by bracing, or more recently, by electrical stimulation. The majority of bracing programs use the Milwaukee brace (3). The brace surrounds the body with a tight fitting pelvic bucket and three vertical steel rods that join in a neck ring. Pads attached to the bars exert three point bending forces on the spine. The patient does exercises in conjunction with brace wearing. Bracing is carried out for 22 hours per day. Since the majority of patients who require brace treatment are adolescent females, this is a very difficult time for the patients, and the need to wear the brace continuously can lead to significant psychological problems; brace programs have a large number of non-compliant patients (4). Because of these problems, many centres have concentrated on the design of new braces that are easier to hide under clothes.

Many years ago, we began investigating the use of electrical stimulation to control scoliosis in children (5,6). The goal of the work was to establish a treatment based on the concept of electrical stimulation of the paraspinal (back) muscles at night while the child slept. There would be no requirement for bracing or exercise programs.

The animal work showed that nighttime unilateral stimulation of the paraspinal muscles could alter the direction of growth of the spine, with the spine curving towards the stimulation. This meant that if the stimulation were applied about the apex of the curve on the convex side, it would produce a force countering the increasing scoliosis. Other studies were directed to understanding the effect of long term

intermittent stimulation on skeletal muscles (7).

MATERIALS AND METHODS

Equipment: The radio frequency coupled stimulator (ESI) was developed in conjunction with Medtronic, Inc. (Minneapolis). The system consists of an implantable receiver-lead unit with an external transmitter and antenna. The stimulation pulses are transmitted from the transmitter (via the antenna) noninvasively through the skin to the receiver.

The batteryless receiver is tuned to receive only the signals from the transmitter, modify them, and then conduct them through the leads into the appropriate muscles to produce stimulation. The receiver components are embedded in an epoxy disc (4 cm. diameter, 1 cm. thick) coated with silicone rubber for tissue compatibility. The receiver is attached to three leads of platinum-iridium wire terminating in platinum corkscrew electrodes. The electrodes are placed into the appropriate paraspinal muscles at the time of surgery. The three electrodes are placed above, at and below the apex of the curve on the convex side in a negative-positive-negative configuration. This arrangement reduces the current spread to other areas of the muscle, helping to localize the contraction to the desired area.

The external transmitter has adjustments for the stimulation parameters (usually only amplitude is adjusted). The antenna is a flat silicone rubber covered disc, which is taped on the skin over the subcutaneously placed receiver with a disposable, double sided adhesive patch. There is a 6 foot extension cord between the receiver and antenna, allowing the patient to move around in bed at night.

Stimulation Parameters: The stimulator is adjusted to provide a muscle contraction lasting 1.5 sec. followed by a rest period of 9 sec. The actual stimulation is a 1.5 sec. train of 220 usec. wide, AC coupled pulses at 30 p.p.s. The paraspinal muscle contraction follows the timing of the train envelope (on 1.5 sec. off 9 sec.).

The pulse bursts are transmitted on a 450 kHz. carrier wave through the skin to the receiver. In dual channel devices (for double curves), the second channel carrier is 185 kHz. For both channels, the pulse trains are cycled at the same time, but the amplitudes are independently adjustable. The receiver integrates the carrier signal to provide the stimulation energy. Amplitude is adjustable to a maximum of 15 volts and the transmitter is powered by a 9 volt battery.

Surgical Insertion of the Receiver: The receiver is inserted under general anesthetic using a midline skin incision. The receiver is placed in a subcutaneous pouch inferior to the twelfth rib. Disposable needle electrodes are used to test various stimulating positions located about the apex of the curve. Trial stimulation is carried out under x-ray and visual control to locate the electrode positions producing maximal muscle contraction and correction of the curve. Once the optimal electrode positions are found, the needles

are replaced by the corkscrew electrodes, using specially designed instruments. The skin is closed and the patient discharged from hospital within 2 days. Treatment is started 10 days later.

Patient Selection: Patients are suitable for treatment by stimulation if they have a single or double curve between 25 and 40 deg. and are skeletally immature. After implantation the stimulation levels are set, and then the children are followed as outpatients at 9 month intervals. On the day of the return visit, they turn off the stimulator in the morning and then are seen in the afternoon clinic. A standing 3-foot AP radiograph is taken (no stimulation) and the measurement compared to the last prestimulation x-ray. If the changes are less than 5 deg (either increased or decreased), the patient is classified as Progression Arrested, while improvements of 5 deg or more are IMProved and increases in the curve of more than 5 deg are PROGressed. Patients as young as 3 1/2 yr have been implanted.

RESULTS

Clinical Results: The results in Table 1 are for 134 patients with 184 curves under treatment (50 double curves). All the curves were greater than 25 deg, except where the patient had a double curve with one greater and one less than 25 deg. Seventy-five per cent of the curves were greater than 30 deg. Nearly 50% of the patients had at least 2 yr of followup, with the average being 2yr 4 mo.

TABLE 1: ESI RESULTS

Curve(deg)	No.	Prog.	P.A.	Imp.
10-19	3	0%	67%	33%
20-29	39	15	54	31
30-39	99	19	51	29
40-49	39	44	28	28
50-59	4	50	50	0

From the table, it is seen that the success rate (the sum of the P.A. and Imp. columns) ranges from 80% down to 100% for curves less than 40 deg. As the curve increases, the success starts to fall and is down to 50% for curves over 50 deg. Fig.1 shows the results of treatment with one patient.

The average change with stimulation in the improved group is 8 degrees, with the best result being one male who after 3 years of treatment had his curve reduced from 32 degrees to 7 degrees. At this time he is skeletally mature, and we have stopped his treatment. In the unchanged group the average change is 0 degrees. The failure rate of treatment, as determined by the need to carry out a spinal fusion, is approximately 12%. In these children, stimulation has failed to stop or slow the curve progression adequately. This number is less than the Progressed column values, since the latter results include many children who have shown 5 degrees (or more) of progression, but whose curves are kept under adequate control, and fusion is not required. Despite being classed as Progressed, they are clinical successes.



FIG 1: Results of treatment on a 14 1/2 yr male after nearly 2 yr of ESI treatment.

Twenty-eight curves have been followed for an average of 18 mo. after skeletal maturity. At that time 86% of them were improved or arrested, when compared to the start of their treatment. No changes in the patient's naturally occurring kyphosis or lordosis was measured (lateral x-rays are taken every 18 mo). While lead lifetime was a problem at the start of the program, recent improvements in the lead design has produced a lead whose reliability is currently 100%. No other serious complications have arisen.

DISCUSSION

The use of electrical stimulation (ESI) to treat scoliosis in growing children is an excellent alternative to bracing. It is highly successful in arresting curve progression and in a large number of patients, there is significant improvement in the curve. Most importantly, patient compliance has been 100%.

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PARASPINAL ELECTROSTIMULATION
EXPERIMENTAL STUDY IN SHEEP

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Unsatisfying brace-treatment of idiopatic scoliosis lead to the research of alternativ treatment with paravertebral electrostimulation of the muscles.
Three types of stimulation units were developed. An eight-channel-unit (1), a miniature stimulation unit supplied by an extracorporal driving unit (2) and a completely implantable and programmable battery-powered stimulation unit (3).
Additionally new screw electrodes with a central needle were developed.
Animal experiments were performed in sheep, 4 sheep type 1, 2 sheep type 2, 2 sheep type 3.
Observation time was up to one year.
Long time direct muscle-stimulation was realizable in all cases. The degree in the gained scoliosis was decreasing with the duration of experiment and at the end only muscle contractures but not bending of the spine was documented. The reason for this observation could not be objectivated.
Scalatal growth and maturity combined with increasing rigidity on the other hand and decrease of muscular bending force seam to be the most influencing factors.

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MULTIPOLAR NON INVASIVE ELECTRODE FOR PARTIAL, DIRECT CYCLIC SKELETAL MUSCLE NERVE STIMULATION

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SUMMARY

The stimulation of a skeletal muscle in order to obtain energy to drive an artificial heart pump is considered. To avoid steady state fatigue problems, it is necessary to stimulate the muscle by means of partial, cyclic involvement of its fibers. This may be obtained by a partial stimulation of the muscle motor nerve. A theory based on the calculation of an induced electrical field inside a nerve section is developed, resulting into the design of a non-invasive electrode capable to generate particular electric fields inside a nerve section by means of electrode spots placed on the nerve surface.

MATERIALS AND METHODS

Introduction

Skeletal muscle electrical stimulation is usually carried on for experimental purpose, by means of either motor nerve or muscle-inserted electrode stimulation. Various patterns of stimulation may include a steady continuous one, but quite rarely this is prolonged for very long (years) periods of time. The described stimulation theory, together with its relevant electrode, has been originally thought for the stimulation of a skeletal muscle to obtain energy to drive a total Artificial Heart pump. It may be nevertheless applied to different purposes, as example for rehabilitation and when mechanical energy is required from a skeletal muscle. This paper will refer to the Artificial Heart application.

Description of the system

Current state of the art in Artificial Heart technology includes power sources external to the body, but very likely the ultimate solutions will be totally internal ones (Total Artificial Heart, TAH). One of the possible internal TAH power sources is the skeletal muscle one: mechanical work is generated by a suitable skeletal muscle, disconnected at one of its ends and reconnected to a fluid pump hydraulically linked to the artificial atria + ventricles system [1].

The electrical stimulation necessary to drive such a system must follow the muscle requirements which are, for the special purpose of the application, the control of the following muscle outputs:

(a) - Total power (about 3÷4 W onto the blood, ab. 10 W gross).
(b) - Contraction rate, about 70/60 Hz, possibly tunable from ab. 50/60 up to 120/60 Hz.
(c) - Power control, via a feed back system rated on the body requests.

Also the fatigue problem, to avoid muscle fatigue phenomena, is a very serious danger for the application, and the achievement of its control, in conjunction with feature (c), will mean a significant improvement towards the ultimate solution.

Description of the method

As known, when a quantity of mechanical work must be produced from a skeletal muscle, only a quantity of its fibers necessary to produce that work is recruited. To prolong the output, these may be relieved by other ones in a kind of rotating switch.

The control of this behaviour is mainly carried on by the nervous system and allows both for power control and fatigue control (up to, of course, the muscle physiological

limits).

An intervention on this system would therefore allow for the control of feature (c) and fatigue, as above.

The recruitment and relief of the muscle fibers is fired through the muscle motor nerve, namely from the single axons which compose it, each of which is directly connected with a number of muscle fibers. A signal therefore runs longitudinally through the nerve axons and on each ideal nerve cross section there will be, at the stimulus time, a number of stimulated and not stimulated axons, described by their electric potential value , with respect to the body-ground reference value. The excited axons potential treshold is about V_c= -30mV with respect to the body ground: below (as absolute value) this, the axons remain passive; above this value, they get excited and a signal starts running along (its intensity irrespective of how much the potential exceeds V_c) to the relevant muscle fibers. The V_c value inside a nerve cross section can be therefore regarded as a border between the not-stimulated and the stimulated quantity of axons, or section areas.

An Artificial stimulation method may be therefore based on the artificial generation of an electric field around the perimeter and thereforeinside a motor nerve cross section: where the field-resulting electric potential value exceeds V_c, the axons in the area will be excited and their corresponding muscle fibers will be stimulated, generating mechanical work. If the so-described electric field is suitably varied, different areas of the nerve section may be involved, and therefore different muscle sections - in location and quantity - will be involved generating a controllable power. The muscle fibers location variation accounts for muscle fatigue control, while the quantity variations accounts for power control.

Description of the electrode

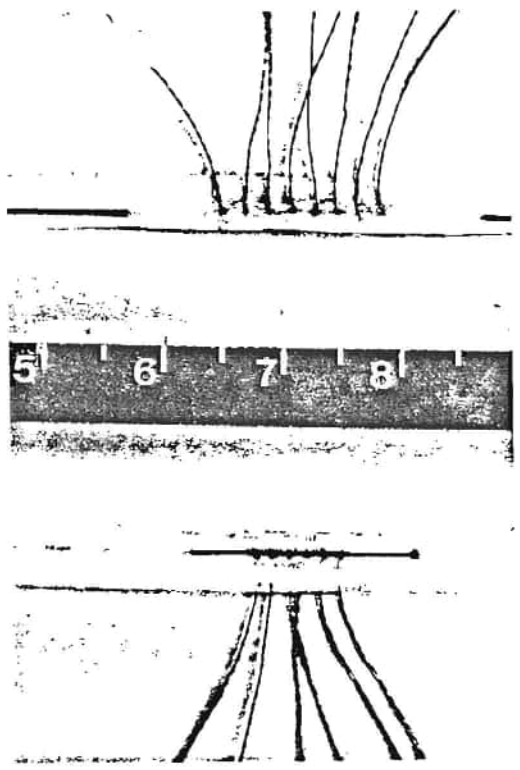


Fig. 1 - Photo of tested multipolar electrodes.

A permanent implantation requires a non-invasive electrode, and the described theory aims to the motor nerve as where the stimulation will be applied. As explained, a nerve cross section must be interested and a radial-ring electrode has been therefore choosen. This is made of a rectangular, long dacron (or other suitable flexible material) support on which a number of poles is fitted, normally sewed in the support fabric. The poles are made of conductive material, electrically insulated through an enamel, but for thier connection and where they will touch the nerve surface (Fig. 1). When fit, it is helically (at very low pitch) winded around the nerve, and sewn in place at its ends (Fig. 2). This way, a number of poles remains fit and pushed onto a nerve quasi-cross sectional perimeter, as shown in Fig. 2 (detail). The quantity of poles is chosen according with the stimulation theory described below.

Electrode theory

The complete theoretical description

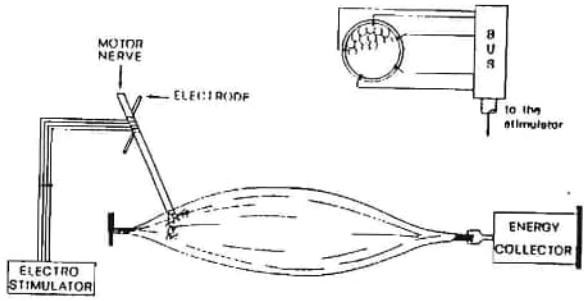


Fig. 2 - Complete system with implanted electrode.
Detail of motor nerve cross section.

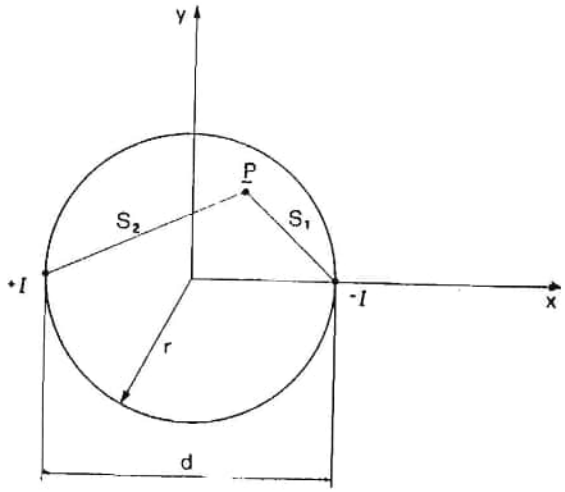


Fig. 3 - Motor nerve cross section. Theoretical model of a two poles stimulation.

of a system as per Fig. 2, if several poles are involved, may be quite complicated due to the boundary conditions, and will be discussed in full in a future paper. The feasability of the described system may more easily be quickly evaluated considering at first two poles only, of equal, opposed charge density placed at the ends of a section diameter. The theoretical model becomes then as shown in Fig. 3.

The following hypotheses must be firstly formulated, and may be accepted given the conditions [3], [4]:

(a) The medium (nerve section) is assumed to be linear, homogeneous and isotropic;
(b) anytime, the potential field satisfies the Laplace equations ($\nabla^2 V=0$);
(c) the boundary conditions are those which would exist if the source conditions were stationary;
(d) the two electrode poles may be considered as point sources (they are small with respect to their mutual distance).

The electric field intensity $\underline{E}$ equation may be written as

$$\underline{E} = \ell\, \underline{J} \qquad (1)$$

where:

ℓ is the medium resistivity

$\underline{J}$ is the current density

The potential being

$$\underline{E} = -\nabla V \qquad (2)$$

Therefore:

$$V = -\int_{\infty}^{S} \underline{E} ds = -\int_{\infty}^{S} \ell \underline{J} ds \qquad (3)$$

The potential V at any point P inside the nerve section, at a distance s from the point source, according to the geometry shown in Fig. 3, may be obtained superimposing the potential V_1 generated in P by pole 1 to the potential V_2 generated in P by pole 2. Being:

$$V_1(s_1) = -\int_{\infty}^{s_1} \frac{\ell I}{4\pi s_1^2} ds = +\frac{\ell I}{4\pi s_1} \qquad V_2(s_2) = -\int_{\infty}^{s} \frac{\ell I}{4\pi s_2^2} ds = -\frac{\ell I}{4\pi s_2}$$

Thus:

$$V(P) = V_1 + V_2 = \frac{\ell I}{4\pi}\left(\frac{1}{s_1} - \frac{1}{s_2}\right) \qquad (4)$$

$$V(P) = \frac{\ell I}{4\pi}\left[\frac{1}{\sqrt{(r-x)^2+y^2}} - \frac{1}{\sqrt{(r+x)^2+y^2}}\right] \qquad (5)$$

where I is the source current.

The equation (5) allows to calculate the value of the potential V at any point P (x,y) inside the nerve section. Or, on the other hand, inserting the treshold potential value V_c at which the axons are excited into eq. (5), the shape of the border curve inside the nerve section (dividing it into the stimulus and non-stimulus areas) may be obtained for the given point sources configuration.

RESULTS

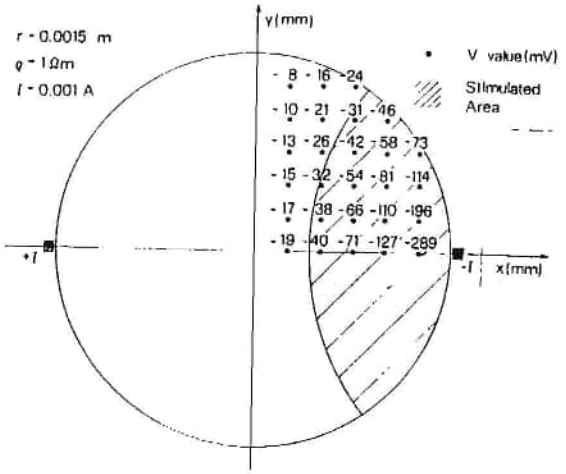


Fig. 4 - Motor nerve cross section. Map of sample two-poles stimulation potential V computation.

Fig. 4 shows a sample calculation on a 3 mm diameter nerve section, assuming a two poles stimulation like in Fig. 3, with equal current value of + 1mA and - 1mA. Given a medium resistivity $\rho = 1\Omega \cdot m$ [5], a map has been plotted showing the potential V value at several points. A clear - 30mV borderline is found, confirming the theoretical validity.

According to the above theory, some electrodes, different in shape and size, have been manufactured and testedin various experiments finalized to the TAH energy source research [2].

The experimental results have been encouraging and the mechanical output clearly showed a selected fibers involvment, so calling for further, more electrode-oriented experimental study.

DISCUSSION

The proposed method of stimulation and related theory show that an electrode manufactured as proposed may stimulate a muscle mass to contract selectively, allowing in future for implantable controlled stimulation systems for power generation or rehabilitation application. On this basis, a number of experiments is already scheduled starting with 4÷6 poles electrodes in order to check the entire system behaviour and measure in each case the resulting muscle mechanical energy response.

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FIRST EXPERIMENTAL RESULTS ON ELECTROSTIMULATED MUSCLE ENERGY OUTPUT FOR TOTAL ARTIFICIAL HEART

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SUMMARY

Total Artificial Heart pumps may be driven by either external or internal power sources. The latter are the obvious ideal long term solution, and among various alternatives mechanical power may be collected at the disconnected end of a permanently electrostimulated skeletal muscle. A suitable multipolar electrode provides a peculiar voltage stimulation which only recruits selected muscle fibers. At a muscle end, a strain gauge load cell allows for isometric contraction force measurement, comparable with a short isotonic contraction and therefore to an equivalent biologic work production. The experimental chain is presented. Results confirm the validity of the proposed electrode, the existance of tresholds defining a range in which multipolar stimulation would be feasible, and show some first mechanical output values. The behaviour of the various chain components with respect to the overall results is discussed.

MATERIALS AND METHODS

The design of an Artificial Heart must allow for a minimum system duration of ab. 6/8 years. Its engineering is therefore affected by the type of power source capable to supply the requested 3÷4 W onto the blood (10÷40 W gross depending from the system overall efficiency) reliably all along that duration. In principle these sources may be external or internal to the body. First ones allow for smaller, lighter internal engineering methods (magnetic coupling or cross-skin wire connection, both carrying to rapid skin deterioration); the latter, to be considered the ultimate solution, may be chemical or electrochemical (with size and output control problems), or nuclear (with heat disposal problems).

To avoid these last problems, the feasibility to generate mechanical work via the electrostimulation of a suitable skeletal muscle disconnected at one end has been considered [1]. Such a system has the advantages of a direct mechanical energy output, consequent high efficiency in transferring it onto the blood (only 9 W, $\eta = 0.35$, necessary to drive a complete chain) mechanical simplicity and direct energy production from the methabolic processes. An internally implanted Total Artificial Heart (TAH) system may be therefore designed around this energy source. As part of the complete research, an experimental chain has been prepared as below to verify the correspondance between theoretical and experimental results. It must be pointed out that, up to now, literature about the capabilities of skeletal muscles to supply collectable work looks short: electrostimulated muscles behaviour is mainly studied from their structure changes point of view, or behaviour to tetanic stimulation, here useless as it generates no work (tension only) [2-6]. The present work is related to a TAH application, but further ones obviously result from this operating principle.

The experimental chain

Fig. 1 shows the scheme of the experimental chain: a specially designed electrode [7] is winded around the motor nerve and driven by a suitable stimulator allowing for recruitment of selected muscle fibers, so controlling both energy output and fatigue. The muscle, disconnected at one end, is re-connected to a load cell to measure its isometric tension under stimulation: in the first 10% muscle length shortening, isometric and isotonic forces can be regarded as equal from a mechanical point of view. A myographic recorder is connected to the muscle surface to monitor the contracting zones. All the system are connected to an oscilloscope and the actual signals recorded. Fig. 2 shows the electronic control units. The load cell is made of a strain

gauge fixed on one side of a column support, vertically fixed into the operating table and bending when loaded: this system allows for a much greater load measurement accuracy with respect to a tensile working one, but cannot be practically implanted. For future in vivo tests piezoelectric, tensile working load cells will be used and reconnected to the bone the muscle end was disconnected from.

Experiments were carried onto landrace type minipigs, female, age 3÷4 months, weight 20÷25 kg, totally anesthetised. The sural triceps muscle was selected in the first phase, due to its suitable position for the external load cell connection. Results may be reported to specific muscle weight and size values.

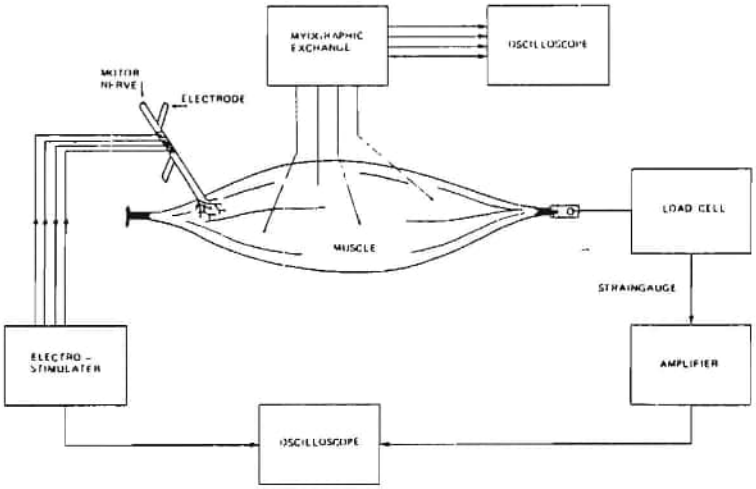


Fig. 1 - The measuring chain.

Stimulation was in voltage for practical purpose (0.5÷6 V), the pulse rectangular, symmetric, at zero average value to avoid polarization, pulse duration 2 ms, frequency 1÷2 Hz. The latter was fixed at cardiac typical frequencies, assuming an isofrequency link between muscle and heart pump: missing this feature, an energy storage system would become necessary between the two, what should be preferably avoided for engineering reasons.

The first experimental phase aimed to the following targets: a) optimise all the stimulation parameters and set up their working range; b) check the correct electrode behaviour; c) elapse force-stimulus amplitude graphs, fixed the other parameters, to confirm the feasibility of a cyclic stimulation; d) evaluate the mechanical output results and their possible decay on long term. The stimulation was applied to fixed electrode poles (i.e. not cyclically) in the first phase. Fig. 3 shows a typical oscilloscope trace obtained during these probes.

RESULTS

First results showed the following:

- correct electrode behaviour;
- an experimental relationship between the applied stimulus and the resulting force: fig. 4 shows the resulting extrapolated graph; this allows for a future cyclic stimulation feasibility;
- acceptable specific energy output for the purpose (strength ab. 500 N/dm^3 ; power ab. 12 W/dm^3 at 2 Hz).

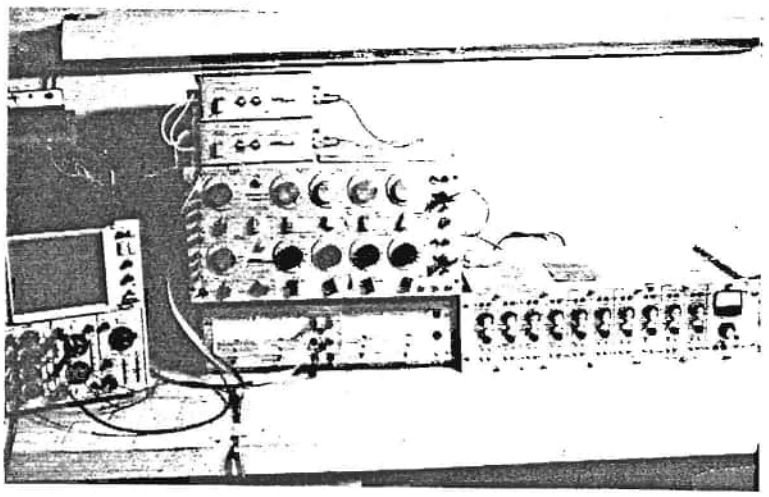


Fig. 2 - Instruments for electronic controls.

DISCUSSION

First experimental results pointed out the desirability to further investigate the following:

A - The electrode was very sensitive with respect to the implantation, expecially to winding tightness. It had to be re-engineered (maintaining the operating principle) and further results show a definite improvement.

B - The electrode signal, as read on the oscilloscope trace, showed a capacitive effect. This may be due to electrochemical reactions on the pole surface, or system structural behaviour; in both cases, it will require further investigation.

C - A major decrease of the mechanical output was found after several minutes of stimulation, and could be initially restored by a stimulus amplitude increase up to a certain time, after which an output fall down occurred. A change in the poles choice showed that other parts of the muscle could still work properly, as well as the original ones after a suitable rest. This facts point out the importance of a cyclic stimulation to control fatigue, but attention must be paid to possible chemical reactions (due to the flowing current) which could affect the long term correct behaviour of the poles; calling for further studies in this direction, and for current stimulation in future.

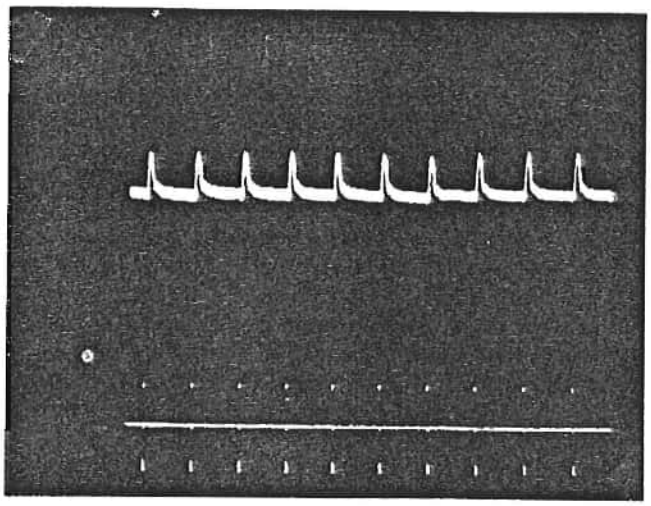


Fig. 3 - Oscilloscope trace (up: muscle tensile output; down: stimulation input).

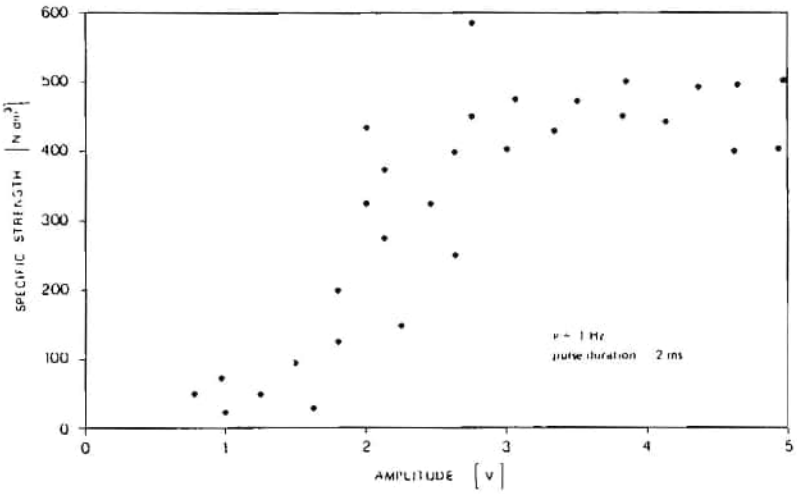


Fig. 4 - Stimulus amplitude muscle response.

D - To increase the specific mechanical output of the fibers, so allowing for longer resting times in the cyclic stimulation, an input at the same rates but with stimulus wave trains could be scheduled in future.

E - A very rigid connection between animal and operating table must be secured to avoid cynetic energy waste and subsequent apparent output decrease.

Future planning aims to obtain graph relationships between the various parameters in different conditions and, if results will be encouraging, to install a totally internal load cell for long term energy generation control and recording during normal animal life.

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THE CHRONICALLY STIMULATED PSOAS MUSCLE AS AN ENERGY SOURCE FOR ARTIFICIAL ORGANS - AN EXPERIMENTAL STUDY IN SHEEP *)

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SUMMARY

In a first series (5 adult sheep) the psoas muscle of one side had been stimulated by electric stimulation of the muscle nerves with an implantable stimulation unit for 5 weeks without any interuption. At the final experiments the isometric tension of the stimulated muscles was reduced to 50-70% of the contralateral normal muscle. The use of only 15 Hz as stimulation frequency led to a transformation of the originally fast contracting muscle into a slow muscle with more resistance to fatigue.
In a second series (5 sheep) the effect of the steel electrode sutured to the nerve was tested without electric stimulation. The results showed that the muscle function was not reduced and that the functional loss in the former series was caused by the long-term stimulation.
A third series (6 sheep) was to show the effects of prolongation of the chronic stimulation of the psoas muscle up to 12 weeks. There was no further reduction of the functional condition. In this group maximal tetanic tension was 66(±10)% of the non-stimulated control side.

INTRODUCTION

An energy supply for implantable artificial organs independent from external energy sources would be the solution of the main problem left unsolved especially in the field of the "Artificial Heart" (3, 5, 7). Chronic electric stimulation of striated muscles as an internal generator seems to be the ideal concept for achieving independence from external energy sources. As we found in former investigations (2), the psoas muscle fulfils the necessary presuppositions to a great extent. A first experimental series was performed to show the effects of continous electric stimulation of the psoas muscle in sheep for 5 weeks. The isolated effect of the steel electrode on the muscle nerve without electric stimulation was tested in a further series. In a third series the long-term stimulation was prolonged up to 12 weeks.
The morphology of the treated muscle and its nerve as well as the functional capacity were compared with those of the non-treated side.

MATERIAL AND METHODS

Stimulation unit: For testing optimal stimulation parameters, an implantable and programable stimulation unit was developed. The generator is battery powered and designed to function up to 12 weeks. We used a stimulation frequency of 15 Hz in order to transform the

*) Supported by the Austrian Research Foundation and the Hochschul - jubiläumsfond der Stadt Wien

originally fast psoas muscle into a slow muscle with more resistance to fatigue (1, 4). The impulse duration was adjusted to 0.6 ms, the action time to 500 ms and the ratio action/idle to 1:2. Polarity of pulses changed automatically with each impulse. Pulses of constant voltage were delivered, and a decoupling capacitor prevented constant currents, which was necessary for the durability of the electrodes and the nerves. The overall dimensions of the unit were 65x25x50 mm. Sealing was done with Hysol.

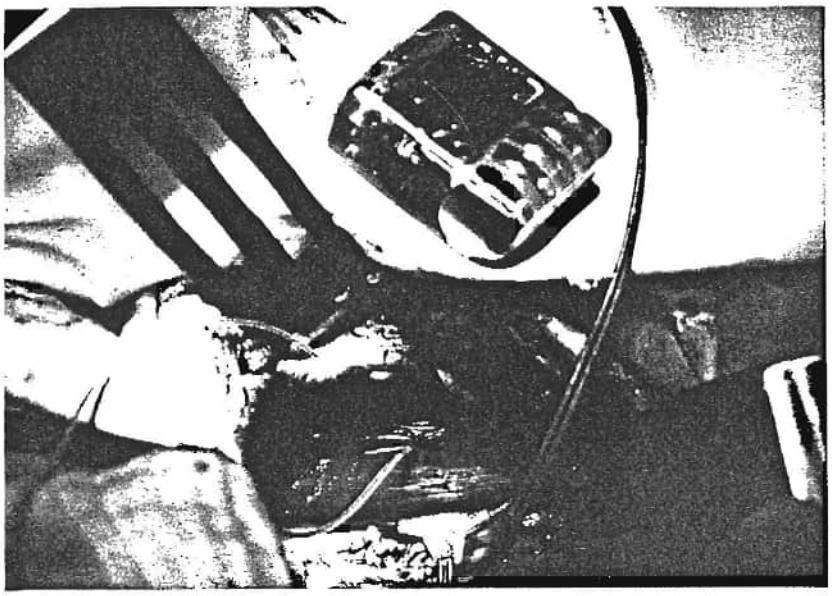


fig. 1: Operative situs: Stimulation unit, psoas muscle exposed, steel electrode (sutured to the muscle nerves)

Operative procedures: In the first series including 5 adult sheep (body weight 36-57 kg, anaesthesia with Halothan/O_2/N_2O-gas mixture) the psoas muscle was exposed on the left side by a flank incision under sterile conditions. One small electrode was fixed to the epineurium of each of the two plexiform muscle nerves by atraumatic 6-0 nylon sutures. The electrode line was brought through the muscle layer of the abdominal wall, and a pocket was formed subcutaneously where the stimulator was put in (fig.1). Two additional small electrodes were implanted into the muscle belly to register EMGs through a plug in the skin. The stimulators were switched on one week after the operation. Afterwards the function of the stimulation unit was checked by watching the cyclic movements of the left hind limb and by recording EMGs. When necessary, the amplitude of the stimulation pulses was increased according to the clinical effect of muscle contraction. In the second series including 6 sheep the same procedures were performed.
In a third series of 5 sheep the influence of the long lasting contact of the electrode with the muscle nerve was tested by electrode implantation in the same way as in series 1 and 2. The ends of the electrode lines were not connected to a stimulator, but were positioned with a plug in the subcutaneous layer.
Final experiments: The final experiments were performed after 5 weeks of continous stimulation in the first series, after 12 weeks in the second series. The animals were anaesthesized again with Halothan/O_2/N_2O. The stimulation unit and the psoas muscle of both sides were exposed. The effect of non-stimulating electrodes was assessed after 24 weeks.
Force measurements: After dissection the insertion of the psoas muscle was connected to a force transducer (Hottinger-Baldwin cantilever beam type Z6). After isometric force measurements under different stimulation parameters (2 mA/15 Hz, 2 mA/30 Hz, 5 mA/15 Hz, 5 mA/30 Hz), the excursions of isotonic contractions were measured.
After completion of force measurements on the treated and non-treated

sides, all muscles were used for histological, histochemical and biochemical investigations.

RESULTS

During the first two weeks it was necessary to raise the stimulation amplitude in all sheep of the two series with implanted stimulators. At the beginning of the stimulation, voltages of 1.5 -5 V were sufficient, but after two weeks twice the voltage was necessary. For the following weeks an almost constant voltage (4 - 9.5 V) resulted in a visible moving effect at the hind limb.

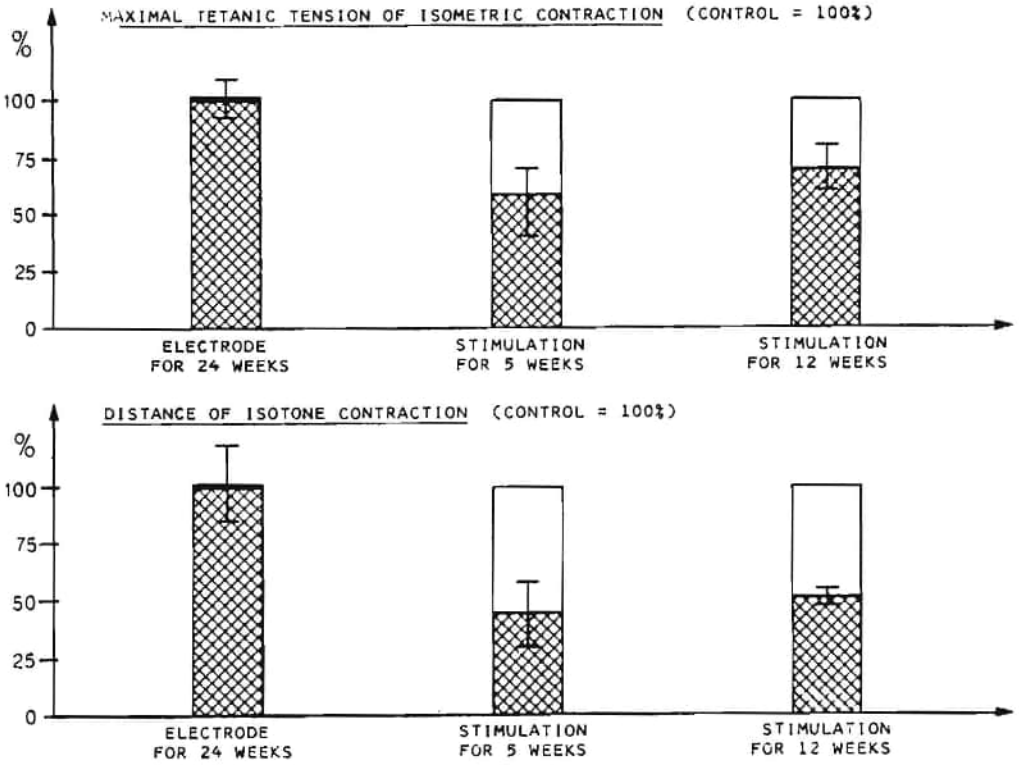


Fig. 2: Maximal tetanic tension of isometric contraction and distance of isotone contraction as percentage of the non-treated control side

As seen in fig.2, on the average maximal tetanic tension was 50 (±11)% of that of the contralateral side after stimulation for 5 weeks, and 68 (±10)% after stimulation for 12 weeks.
The low stimulation frequency of 15 Hz caused a transformation of the muscle from a fast to a slow muscle. As a consequence 15 Hz means fusion frequency and a tetanic contraction in the chronically stimulated muscle. In the healthy muscle this low frequency leads to clonic contraction (fig. 3).
The measurements of the excursion of contraction under isotonic conditions showed results parallel to the isometric measurements. After long-term stimulation the excursion of the contraction was reduced to about 50% of that of the control.
Application of the steel electrode to the nerve without stimulation for 24 weeks had no effect on muscle function (fig. 2).

DISCUSSION

In the final experiments all stimulation units were still in function. Thus we can assume that the capacity of the used batteries was sufficient for this long-term use. The extraordinary mechanical load was sustained by using a winding electrode with different thickness of the surrounding isolating material according to the zomes of mechanical load.
The variance of the necessary stimulating amplitude (1.5-5V) at the beginning of the experiment can be explained by the individual local conditions for the application of the electrode at the nerve, for instance, the different distances between the two nerves supplying the psoas muscle. In former investigations we found that the reaction at the nerve electrode contact is at a maximum during the first two weeks and afterwards decreases (6). In these series it was necessary to increase the stimulating amplitude to double values (4-9.5V). An augmentation of the connective tissues at the nerve electrode contact may have caused an increase of the rheostat. After two weeks the stimulation amplitudes remained stable until the final experiments.

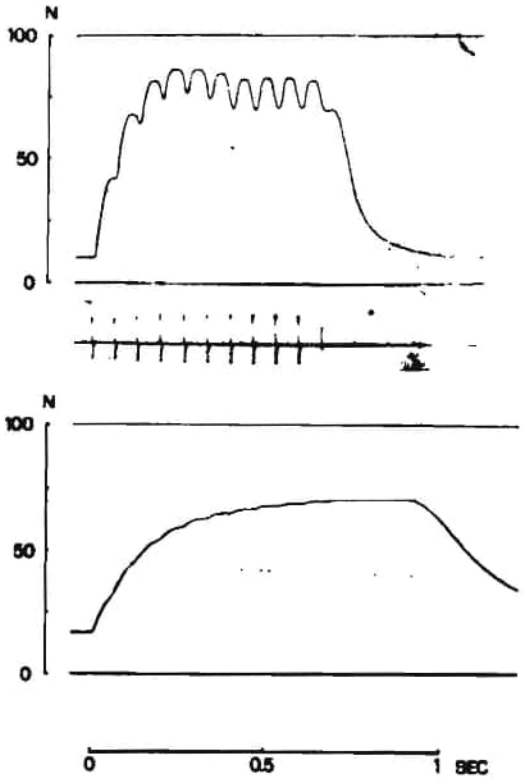


Fig.3: Upper curve: Isometr. Contraction of normal psoas muscle (15 Hz/5 mA); Lower curve: Tetanic answer of the stimulated psoas muscle (5 weeks).

PETTE et al.(4) described the possibility of transforming a fast contracting muscle into a slow muscle by long-term electric stimulation with low frequencies. The slow muscle is more resistant to fatigue. Therefore, this transformation is our aim, when we intend to use the stimulated muscle as an energy source for driving an artificial organ. Reducing the stimulation frequency to 15 Hz transformed the psoas muscle into a slowly contracting muscle with typical isometric contraction curves. 15 Hz became the fusion frequency and caused tetanic contraction. In the normal muscle the fusion frequency is about 30 Hz. Stimulation reduced the maximal tetanic tension to 50-70%. It was intersting to note that the psoas muscles stimulated for the longer period (12 weeks) had somewhat better functional results. This phenomenon could be caused by an initial period of fibre transformation with a decrease of muscle force, followed by a period of restitution and hyperzrophy with an increase of force. On the other hand a training effect by the chronic stimulation could be discussed. The reduction of the functional capacity as well in the 5 week stimulation series as in the 12 weeks series is caused by the stimulation and not by the foreign body effect of the steel electrode, because there is no decrease of the functional parameters in this series.
In view of the results of these experimental series, it may be feasible to use long-term electric stimulation of sceletal muscles as an energy source for driving an artificial organ.

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ANIMAL EXPERIMENTS ON EFFECTS OF ELECTRICAL STIMULATION ON THE AUDITORY NERVE x)

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SUMMARY

To evaluate single- and multichannel hearing prostheses investigations of the discharge pattern of primary auditory nerve fibres are necessary. Sound evoked impulse patterns were compared to those evoked by electrical stimulation (ES) of the round window of intact and destroyed cat cochleae. The main difference was the stronger synchronization of nerve action potentials (APs) to the ES in the destroyed cochlea. With ES in the intact cochlea no significant effects of fibre place of origin within the cochlea (determined by the Characteristic Frequency (CF) of the fibre) on threshold were found.

MATERIAL AND METHODS

25 cats were prepared for single nerve fibre recordings /1/. 0.8 mm diameter Ag-AgCl stimulus electrodes were placed in the round window niche of the cochleae. The indifferent electrode was inside the bulla or in the contralateral pinna muscle. The stimuli from the isolated current source were sinusoidal 50 Hz - 2 kHz and short biphasic pulses (0.2 m s each phase). In intact cochleae the CF of a fibre was determined by acoustic stimulation. Cochleae were mechanically destroyed by rupturing the basilar membrane and refilling the scalae with glutaraldehyde. The nerve responses were recorded by a PDP11-Computer which calculated Period Histograms (PH), Post-Stimulus-Time-Histograms (PSTH) and Interval Histograms (IH). For sinusoidal electrical and acoustical stimulation the synchronization index (SI) was calculated from the PH /2/. SI is 1 if there is a complete jitterfree phaselock of the APs to the stimulus and 0 if there is no synchronization.

RESULTS

Sinusoidal ES of intact cochleae with a frequency of 100 Hz led first to a synchronization of the spontaneous evoked APs to the negative phase of the current (round window cathode) (Fig. 1) and than to an increase of the discharge rate. Phaselocking thresholds (SI >0.1) were between 4 and 68 µArms and impulse rate thresholds (20 APs >spontaneous rate) between 6 and 97 µArms. With stronger currents the PHs showed sharper peaks with shorter latencies and up to 2 - 3 APs/period (10 ms).

In contrast, acoustically evoked discharge patterns showed weak modulation of the spontaneous activity. With high sound pressure levels (SPLs) a second AP/period could sometimes be recorded from low CF neurones (Fig. 2)
The discharge of nerve fibres from destroyed cochleae showed no spontaneous activity and strong phaselocking with currents just above rate thresholds (Fig. 2). With sinusoidal stimulation the PHs were similar to those from intact cochleae. Because of the absence of spontaneous activity the SI was >0.9 (see also Fig. 3).
Electrical pulse stimulation of the intact cochlea showed 3 types of responses.
First: APs were directly evoked by the shock with latencies from 0.5 to 1.2 ms (Fig.1)
Second: PSTHs showed multiple peaks with latencies >1.5 ms and inter-peak latencies of 1/CF like acoustically evoked click-PSTHs (Fig. 2). Third: With high current amplitudes a slow frequency 'ringing' response with latencies >10. ms could be measured.
With electrical pulse stimulation of the destroyed cochlea only the first response

x) Supported by the Deutsche Forschungsgemeinschaft (SFB 45)

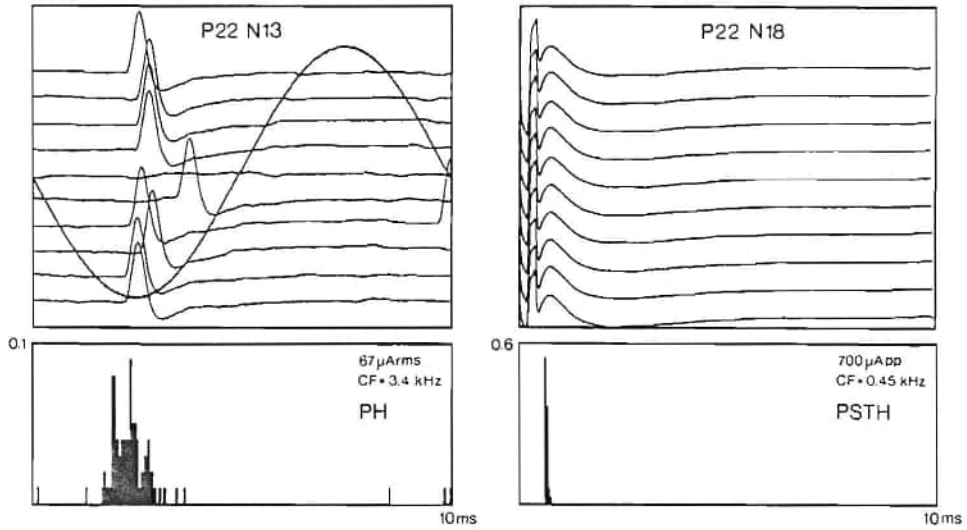


Fig. 1: Original recordings (top) and PHs (bottom) with sinusoidal (left) and pulse (right) stimulation. Top: 10 sweeps with current signal superimposed (100 Hz); 10 sweeps shown the remaining pulse artifact followed by an evoked action potential (AP) (33 Hz). Bottom: PHs: 256 bins, 100 APs left and 200 APs right.

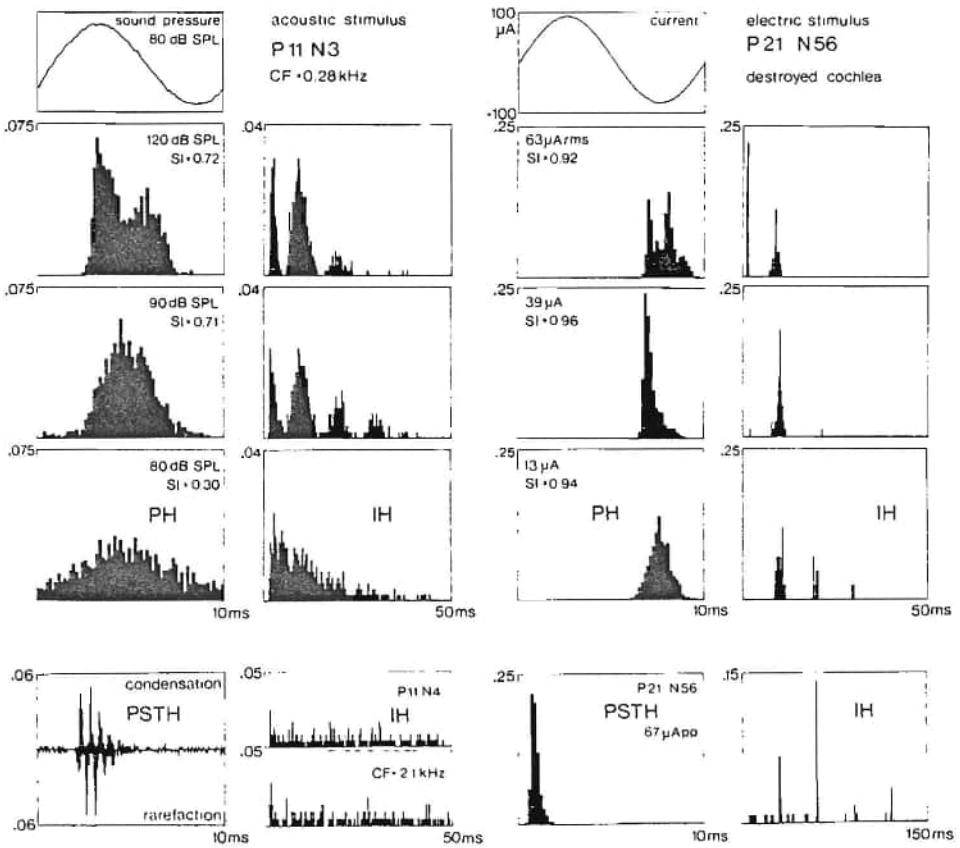


Fig. 2: Activity evoked by acoustical (left) and electrical (right) stimulation of two different animals. Left: 100 Hz acoustical stimulation with increasing SPLs (top) and click stimulation (bottom) of two units from the same intact cochlea. Right: 100 Hz sinusoidal electrical stimulation with different currents (top) and 33 Hz pulse stimulation (bottom) of a unit in a mechanically destroyed cochlea. Ordinate scaling: APs (intervals) per bin / total number of APs (intervals). Sinusoidal stimulation:PHs: 64 bins, 1000 APs; IHs: 320 bins. Click and pulse stimulation: PSTH left: 400 bins, 350 APs; PSTH right: 64 bins, 500 APs; IH left: 320 bins; IH right: 960 bins.

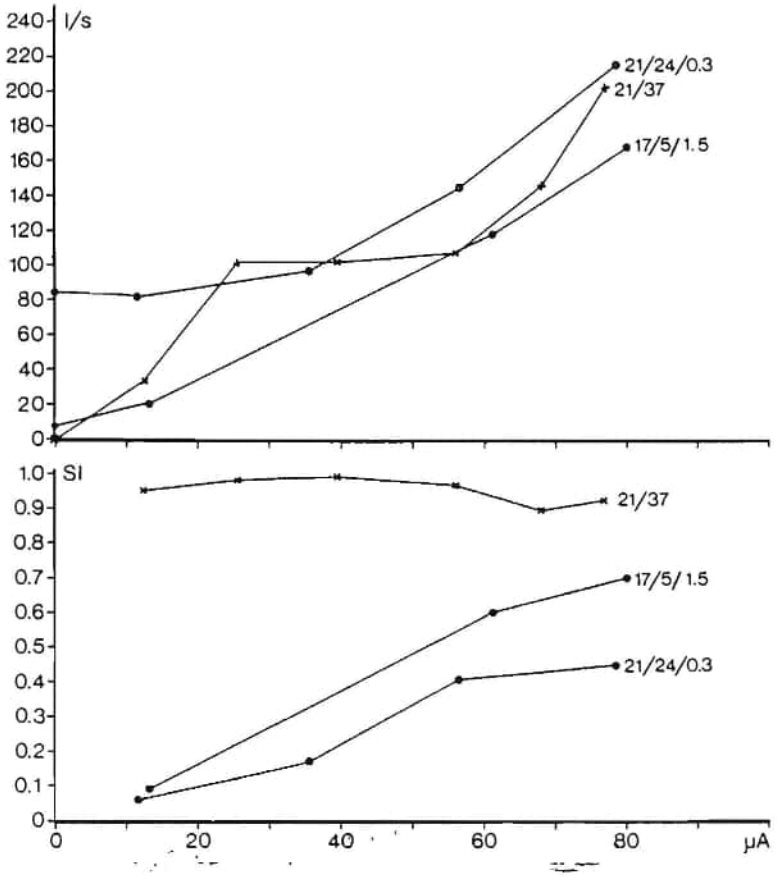


Fig. 3: Typical neuronal responses to 100 Hz sinusoidal electrical stimulation of intact and destroyed cochleae. Mean discharge rate (top) and SI (bottom) as a function of stimulus current. In this and subsequent figures, the numbers beside each curve are animal number/ unit number/ CF in kHz.

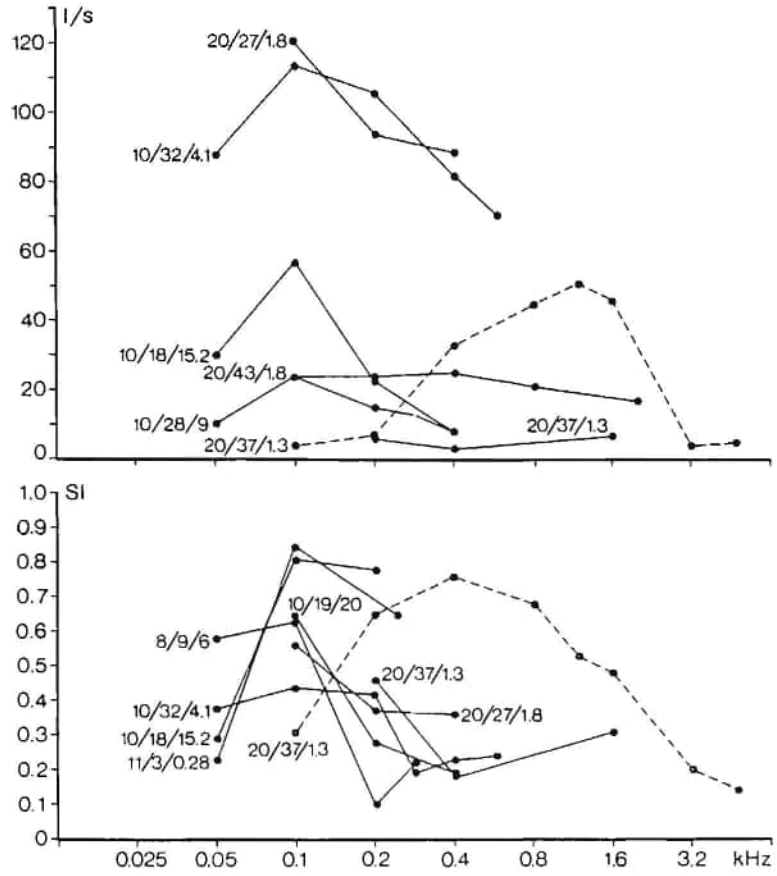


Fig. 4: Neuronal responses to sinusoidal electrical stimulation (●——●, 50 µArms) from intact cochleae compared with sinusoidal acoustical stimulation (o- - -o, 120 dB SPL). Mean discharge rate (top) and SI (bottom) as a function of stimulus frequency.

type with short latencies 0.5 to 1.2 ms could be evoked and the PSTHs were very different to those evoked by acoustic click stimulation (Fig. 2). Neuronal impulse rates evoked by sinusoidal ES of the destroyed cochlea were different to those seen in intact cochleae. Neurones in destroyed cochleae often followed the stimulation frequency or a multiple of it over a wide intensity range. Fig. 3 shows a comparison of typical intensity functions of a low and a high spontaneous fibre from an intact cochlea and a non-spontaneous one from a destroyed cochlea. The SI increased continuously for the spontaneous fibres in contrast to the SI of the fibre from the destroyed cochlea. The impulse rate and the SI showed a maximum in the frequency range about 100 Hz (Fig. 4) for both intact and destroyed cochlea. Additionally, in low CF fibres from intact cochleae impulse rate maxima could be evoked by ES in the CF range (this was probably an electromechanical effect). An example of an acoustically evoked impulse rate and SI from a fibre with 1.3 kHz CF is given in Fig. 4 (dashed lines).

DISCUSSION

With round window stimulation of the intact cochlea activation thresholds were independent from nerve fibre CF (origin within the cochlea). That means for single-channel prostheses with extra cochlear electrodes /3/, that all information of speech signals could only be coded by the time structure ('periodicity pitch'). A 'place pitch' sensation, which could be achieved with intracochlear multichannel devices /4/ is unlikely. The effective current range (4 to 120 µArms) is in good agreement with patients' data /3/.
The artificially strong phaselock of nerve discharges with ES and the absence of spontaneous activity in the deaf cat provided a good reproduction of signal time structure. However, this differs considerably from the normal acoustically evoked response pattern.

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MODELS FOR THE ELECTROSTIMULATION OF THE NERVUS ACUSTICUS

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SUMMARY

Electrostimulation of the nervus acusticus has been successfully used to achieve speech understanding. Two models for nerve excitation were computed on an Hybrid Computer and the introduction of a stochastic term showed accordance with the empiric results at single acoustic mammalian fibers observed by J. E. Rose et al.

INTRODUCTION

This paper is motivated by the pioneering work of I.J.Hochmair-Desoyer et al. on cochlear protheses which have been used with remarkable success in cases of severe damage to the inner ear structures which has made the transformation of the incoming sound into neuronal activity impossible.

The protheses consist of implants comprising electrodes, receiver, stimulator circuitry and an external sound processor/transmitter coupled to the implant. This will be described in another paper at the conference and has been reported on in /1/,/2/. The important result from the point of view of this paper is the fact that a high degree of speech understanding has been achieved with this device using a single stimulating dipole electrode situated either in the scala tympani or else by an electrode outside the scala tympani in the form of a wire. This rules out any kind of tonotopy mediated by resonant membranes possible in the normal ear. The sound processor produces an analog signal and the question arises how the frequency and amplitude information is conveyed by the acoustic nerve still present in the patient´s ear. This paper is concerned with this question. Physiological models of nerve action are studied which might provide a theoretical explanation of the clinical success achieved.

DISCUSSION OF MODELS

The fluid surrounding the implanted electrodes is an electrolytic conductor in which unmyelinated nerve membranes and dendrites are embedded. Voltages applied between electrode terminals establish an alternating current distribution with membrane normals forming various angles with the streamlines. The component of current normal to the membrane must excite typical action potentials, although this method of excitation was not used in the classical physiological experiments leading to the Hodgkin-Huxley equations. They were empirically derived, using thin capillaries filled with conducting liquid inserted into the membrane. We shall use a model based on these equations for the relation between membrane voltage and current. They lead to a model described by five coupled nonlinear equations which can be solved numerically. This was done with the help of the Hybrid computer of the

Technical University,Vienna. In a previous paper /3/ an instructive model, the Bonhoeffer, Van-der-Pol, Fitzhugh model (BVP-model) was used which restricts the number of equations to two by projecting the parameter space of Hodgkin-Huxley (HH) equations onto a two-dimensional one. This BVP-model /4/ has been found to account qualitatively for a wide variety of nerve behaviour and it has the advantage that the mathematical analysis provides a clear insight into the underlying phenomena.The advantage of the HH-model is that it is based on physiologically vouchsafed behaviour and is more likely to lead to quantitatively correct results.

The previous paper also tried to account for the results of basic animal experiments carried out by Rose et al /5/. These authors were able to observe the signals at the output of a single mammalian nerve fiber when a sinusoidal acoustic signal was offered to the animal. It turned out that the nerve-fiber-transmitted action potentials of standard amplitude are phase locked with the acoustic signal. On the other hand, the relation between fiber output and signal is of a stochastic nature. Not every maximum of the sinusoidal signals causes an action potential (spike) but only a random sample of the maxima leads to spikes. A spike is most often followed by the next one after an interval of one signal period, less often after two intervals, still less often after three intervals etc. This behaviour may be illustrated by the histograms of fig. 1 showing the probability of time-difference between two spikes.

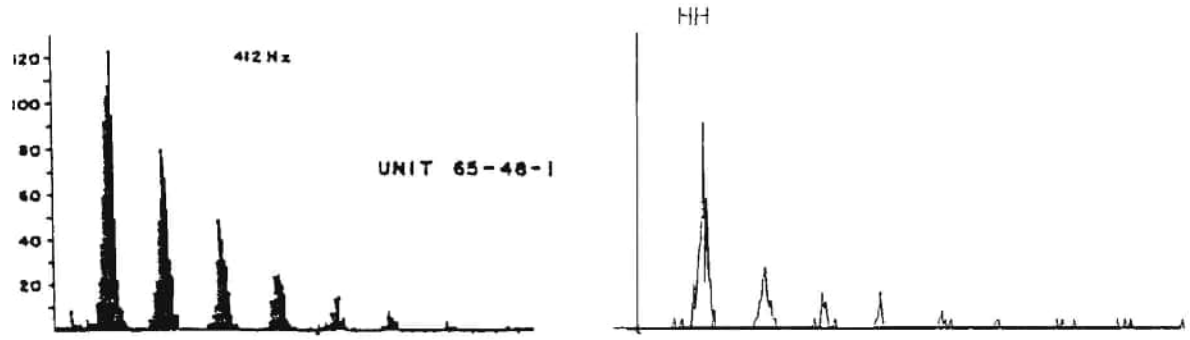


Fig 1: Interspikeintervals for a single auditory neuron, observed at a squirrel monkey in response to 1 sec tones at 80 dB left and computation of the HH-model (with shorter duration) right.

Our basic assumption is that the stochastic behaviour comes about by a combination of a noise-like electrical activity of the nerve which exists before a signal is applied. Such activity certainly exists and is witnessed by the fact that spikes are spontaneously produced by subthreshold activity in absence of a signal. A subthreshold signal may then lead to a spike when a noise amplitude is added to it and in this way a whole range of amplitudes may lead to spikes. Large amplitude noise pulses are less frequent and therefore weaker signals lead less frequently to action potentials. This was mathematically studied in /3/ by means of the BVP model and histograms of the type of fig 1 were found for each amplitude level of the signal, but more spikes are concentrated in the first peak of the histogram when signal level rises. Thus while the intervals between spikes are integral multiples of the period and may be said to code the frequency, the amplitude is coded by the interval statistics. It seems idle to speculate at this time how the brain would decode the information, but it is interesting to note that noise increases the information content. This is not as paradoxical as it seems at first sight.

THE HODGKIN-HUXLEY MODEL

According to the HH-model the current I is given by

$$I = C.\dot{V} + I_i + S$$

where S represents the acoustic signal (f.e. S=a.sinωt), I is the total current through membrane, C the membrane capacity, V the voltage and I_i the ionic current which in turn is given by

$$I_i = g_{Na} m_1^3 . m_2 . (V-V_{Na}) + g_K . m_3^4 . (V-V_K) + g_L . (V-V_L)$$

the m_i (i=1,2,3) obey equations

$$\dot{m}_i = \alpha_i(V) . (1-m_i) - \beta_i(V) . m_i + ma_i . noi$$

g_{Na}, g_K, g_L are sodium, potassium and leakage conductances, V_{Na}, V_K, V_L the corresponding Nernst potentials and the m_i are probabilities for the opening and closing of ion channels where α_i and β_i are functions of V of exponential behaviour. The three stochastic variables ma_i.noi (noi means white noise) allow the necessary fluctuation in the response V for a given acoustic signal.

The frequency behavior of the nerve response obtained by our computations is shown in fig 2 where amplitude is plotted against frequency. The lower curve shows the amplitude needed for the onset of spikes, the upper curve shows the amplitude which is necessary to produce permanent repetitive firing, while a sample of intermittent firing is given in fig 3.

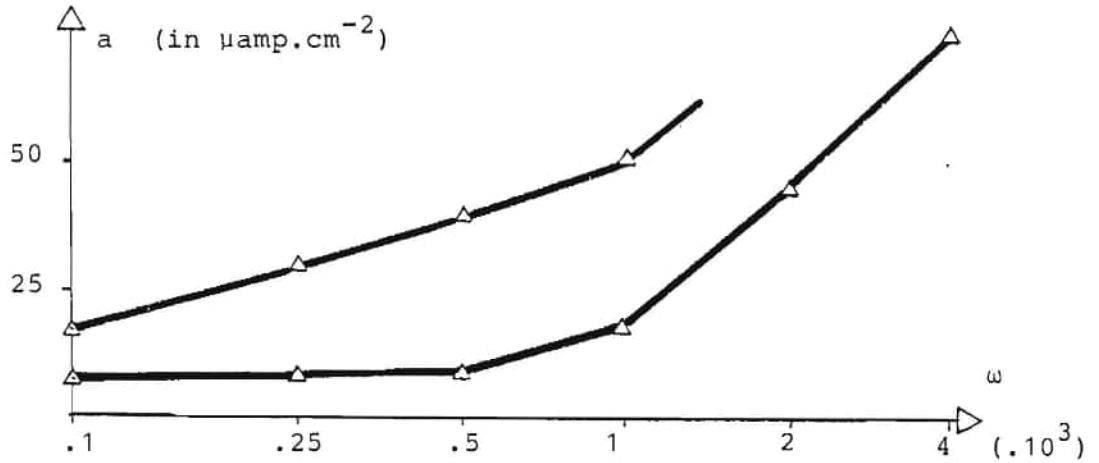


Fig 2: Minimum and maximum amplitudes of sinoidal signals to get relevant responses from HH-model as function of frequency.

CONLUSIONS

It is seen from fig 2 that the signal necessary to produce action potentials rises with frequency and this is in accordance with the clinical findings. A range of about 2-3 kHz is attainable and this again is clinically found. We have taken nerve data obtained by Hodgkin and Huxley from squid nerve but results are not very sensitive to details of data. An amplitude range up to a factor 5 is obtained with the HH-model which is an improvment over the BVF-model. Altogether, results from the model can account for experimental facts.

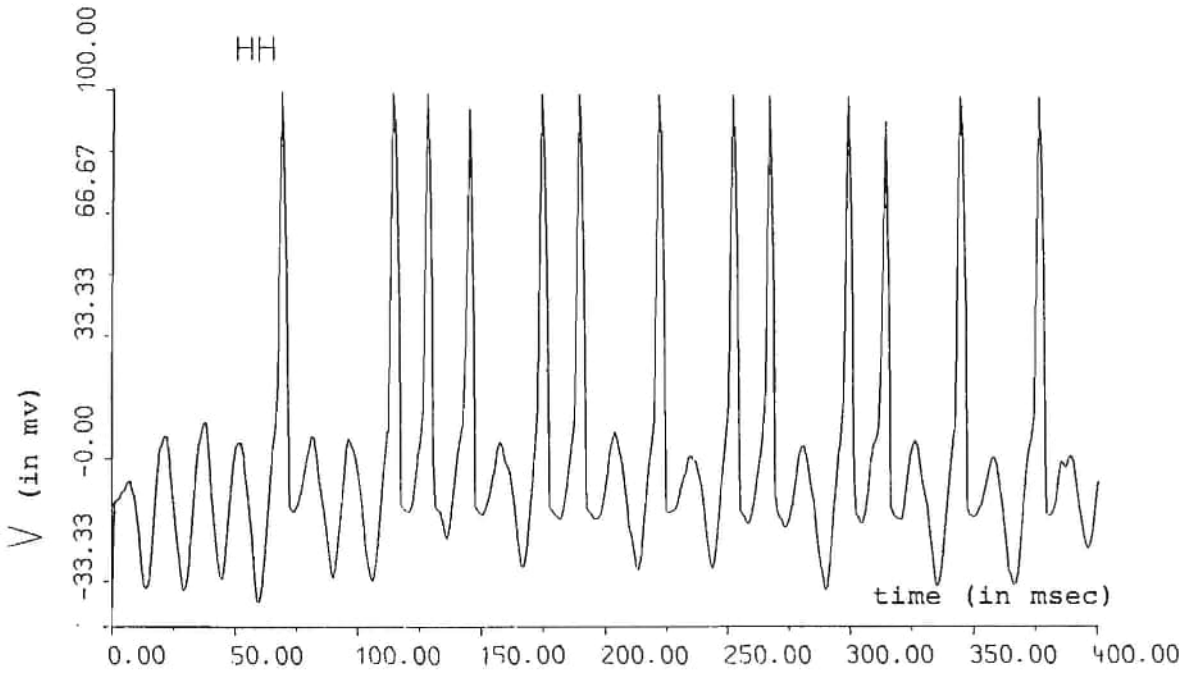


Fig 3: Voltage at membrane as a response to sinusoidal source computed from HH-model

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FIRST RESULTS OF CHRONIC ELECTRICAL STIMULATION WITH A ROUND WINDOW ELECTRODE IN TOTALLY DEAF PATIENTS.

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SUMMARY

A few patients become totally deaf when adult were chronically implanted with an electrode on the round window. Elicitable auditory sensations were limited but prooved beneficial enough so that a small portable stimulator was proposed for everyday use. Over a period of several months subjects were monitored several times for a few days at the laboratory and trained to better use their prosthesis. Such a device appears safe and patients have become attached to its use. One subject suffering from tinnitus was also given another stimulator delivering positive direct current which suppresses his tinnitus.

INTRODUCTION

Electrical stimulation of the ear can result in induction or suppression of hearing according to the direction of current flow. These two aspects were reported a long time ago (5,6). Its therapeutic uses therefore followed two orientations: artificial hearing and suppression of tinnitus. For hearing induction alternating currents can be used whereas for tinnitus suppression a direct current is necessary (4). it is well known that direct currents are dangerous and some animal experiments illustrated their damaging effects on the organ of Corti (1,2). Therefore the use of direct currents to suppress tinnitus can only be envisaged in the cases of total deafness. It is also in cases of total deafness, in order to induce hearing, that alternating currents are considered. Alternating currents warranting a zero net charge applied to the cochlea seem safe (3).

These two therapeutic possibilities, hearing induction and tinnitus suppression, were proposed to a few patients become totally deaf when adult. Pocket size stimulators were designed and built. The preliminary results after several months of experience are presented.

METHODS

Four adult male patients, who had normal hearing and speech but became totally deaf, were implanted. They all presented no reaction to sounds of 120 dB HL from 125 to 8000 Hz. Subject PB had a head trauma about five years before implantation, subjects JLD and HD presented a 3 and 2 months old sudden deafness and subject GM suffered from chronic bilateral otitis for several years, he became totally deaf 1 year before implantation. Patient HD also suffered from continuous tinnitus, becoming sometimes very annoying. They were all explained that the operation and the use of the electrical stimulator could give them some auditory sensations but certainly not a normal hearing. Subject HD was also informed that his tinnitus might be suppressed when a stimulation was applied.

The electrode was made from a platinum wire heated at one end to make a ball about the size of the round window niche. It was isolated along its length with a silastic catheter. At the other end it was soldered to one pin of a small two-pin electronic socket. To the other pin a 1.5 cm long bare platinum wire used for reference was soldered. For surgery a transmeatal approach was used. The skin of the meatus was detached from the bone along the posterior wall. The round window could be seen easily and the electrode was placed in the niche. A

small groove was made in the bone in which the wire was placed and glued with fibrin. The reference wire was introduced under the skin on the mastoid bone and the meatal and pinna skin put back in place. The wire with the connector remained behind the pinna.

A pocket-size electrical stimulator was designed and built in the laboratory. It was made of a microphone followed by a low pass filter with a cut off frequency of 1000 Hz. The signal was then passed through a very important amplitude compression followed by an adjustable ac coupled output amplifier. For tinnitus suppression a single dc voltage source was used with a limiter and a potentiometer to adjust the output level.

When the patients were sent back home with their own stimulator, they were suggested to train daily particularly in rather quiet conditions for discussing with one or a few other persons. In several occasions they were seen again at the laboratory, they were questionned about their routine use of the prosthesis, their sensitivities were checked and some evaluation and training were performed with a speech therapist.

RESULTS

A few days after operation, the patients were first tested using synthetized sinusoidal stimuli, in all four cases auditory sensations could be evoked. Receptive fields showed that only low frequencies up to around 1000 Hz were usable, discriminations of about 10% were observed for all subjects. The available dynamic range varied greatly from 6 to 20 dB between patients. Estimations of temporal resolution gave comparable results in the different cases, a delay of about 4 ms induced a first perceptible change in loudness and around 20 ms were necessary for the perception of two separate stimuli. It must be emphasized that all evoked auditory sensations varied from a hushing or buzzing noise for low and middle frequencies towards some hissing noise or whistling for the highest frequencies. Increases in stimulus intensity were clearly and selectively associated with growth in loudness, whereas changes in frequency induced pitch variations very often mixed with loudness changes certainly related to the uneven frequency sensitivity.

The first impression of the patients was always a keen pleasure to perceive again auditory sensations. It was generally followed by disappointment when they progressively realized the poorness of sensations actually induced.

The first functional use of the prosthesis in a normal acoustic environment appeared to be that of a warning system. After some experience several familiar noises became readily identifiable. A series of noises such as walking steps, telephone ringing, horns and car traffic, were recorded on tape and served regularly for training and tests. Successes varied greatly between subjects but noises mentionned earlier could be most of the time recognized. The patients reported that when wearing their prosthesis at home it could also be used as a warning system.

The help eventually brought in oral communication was assessed in collaboration with a speech therapist just after the operation and on several occasions during the following months. In a first stage the ability to perceive prosodic features was tested with the following stimuli pronounced by the therapist : large pitch rises or falls on a sustained vowel, important stress on one in a few successive short sounds, and various series of mixed brief and long sounds. All the patients always clearly identified these important pitch, loudness or temporal variations (table 1). For these tests the patient could look at the speech therapist who avoided to produce non acoustic clues, when the stimulator was disconnected the recognitions were impossible. Then sentences, written on a paper presented to the patient, were pronounced randomly as either a question or a statement. The patients were asked to indicate whether it was a question or a statement. The locutor was visible to the patients but without electrical stimulation they reported the judgement to be impossible. The prosthesis helped the subjects who then proposed a judgment, success rates of 64 to 81 per cent were obtained (table 1). Related experiments were also performed

to assess the perception of melodies. A series of five well known melodies was used, their title was written on a paper showed to the patients, they were then sung randomly. The patients reported they were unable to recognize them and even after some training their guesses were unsuccessful.

In a second stage phoneme recognition was tested. No phoneme could readily be recognized ; the evoked auditory sensations bore little resemblance with what was heard before. However some perceptions evoked with electrical stimulation alone varied enough so that good discriminations could be obtained in the very short term after selective training on pairs of phonemes. When distinctions and recognitions between several were tried they all became confused. Even after several sessions of training and practice no reliable and durable identification can be performed by the patients. When used in combination with lip reading an appreciable improvement in intelligibility was observed (table 1). This improvement comes mainly from the distinction between voiced versus voiceless oppositions undetected with lip reading alone but clearly indicated with electrical stimulation. Lists of dissylable words from classical speech audiometry were used. Groups of ten words readable by the patient were tested with lip reading alone or in combination with electrical stimulation. Electrical stimulation improved intelligibility scores by 8 to 27 percent.

Electrical stimulation helped the elocution of the different patients. A text, often a tale for children, was given for loud reading with or without artificial stimulation and tape recordings were performed. The feed back from the prosthesis produced a somewhat slower elocution but with a notably more regular pace and some improvement in intonation.

The help of electrical stimulation for speech communication appeared very limited to the patients but it was sometimes perceived more strongly by close relatives. Indeed family members or friends reported they could understand the implantee more readily and were thus more enclined to develop discussions.

Subject HD suffered from continuous tinnitus which was some days difficult to support. A positive direct current was applied to his round window electrode. A tension of two volts started to diminish his tinnitus and five volts were necessary to suppress it totally. In a first period a dc stimulator with an output limited to three volts was given to him for use at will. After two months the patient was seen again at the laboratory and tested. He reported to have been using his stimulator almost every day for several minutes with some relief while stimulation was on. Since his sensitivity appeared unchanged the maximal output was adjusted to five volts and the patient went back home. He was seen again one month later and reported that he had tried several times the stimulation but quickly stopped it because it produced an unpleasant effect within his head.

CONCLUSION

These first results of chronic electrical stimulation of the ear in totally deaf patients are in good agreement with what could be expected from previous reports. Both hearing induction and some tinnitus relief might be very beneficial for the patients and are certainly worth proposing to them for trial.

Although very limited the possibilities of hearing induction can be actually of considerable interest for every day life as witnesses the attachment of the implantees for their prosthesis. The first important effect is the psychological impetus given by the break from total auditory isolation. The possibility of alarm with sometimes the recognition of familiar noises give back to the auditory system one of its most rudimentary role. Finally some improvement in speech communication, both in voice reception and production, can be observed. The experience of chronic tinnitus suppression, limited to one case, cannot be conclusive and needs further study.

The use of a unichannel extra cochlear electrical stimulation requires very simple and safe surgery. Long term chronic stimulation also seems to be safe and simple devices produce fruitful results. In these conditions the therapeutic

possibilities of hearing induction or tinnitus suppression can certainly be helpful for several cases of total deafness and deserve continued study. Technically several developments are under study concerning signal processing and transmission as well as convenience of use.

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TABLE I

Subjects	Tests of prosody				Dissyllables	
	Pitch	Loudness	Rhythm	Q/S	L.R.	L.R.+E.S.
P.B.	92	88	86	8I	77	88
J.L.D.	I00	I00	I00	65	68	95
H.D.	73	70	72	65	85	93
G.M.	I00	70	I00	64	60	79

Values are percentages of recognition

THE COCHLEAR IMPLANT: THE CODING OF AUDITORY INFORMATION

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Investigators have compared psychophysical behavior in electrially stimulated patients with that in normal hearing subjects. Using current auditory coding models, investigators have found significant differences between model predictions and psychophysical measures. Such differences may help us develop useful extensions to current models of the auditory system.

Phase-locking to electrical stimuli: perceptual consequences

Electrophysiological recordings /1/ indicate that electrical stimulation of the auditory nerve elicits phase-locked responses to sinusoidal stimuli at frequencies up to 3 KHz. However, post-lingually deaf subjects implanted with similar intracochlear stimulating electrodes do not perceive changes in pitch for stimulus frequencies significantly above 300-600 Hz /2,3/. Also, frequency discrimination is extremely poor at stimulus frequencies above 300-600 Hz /2,3,4/. These results indicate that a simple periodicity-extraction mechanism is probably not operating for stimulus frequencies above about 300-600 Hz in these subjects. These results are consistent over a wide range of stimulus sites and over a wide range of stimulus intensities. By "simple periodicity-extraction mechanism", we refer to a neuronal frequency-extraction mechanism that measures the interspike intervals of a single neuron or group of neurons to estimate the stimulus spectrum /5,6/.

There are several possible explanations for the relative insensitivity of the implant recipient to differences in stimulus frequency above 300-600 Hz:

First, the normal nervous system may simply not be sensitive to such fine grain temporal information. If this is the case, the "place" theory would account for all pitch discrimination in both normal and prosthetic hearing. The classical "place" theory holds that the stimulus is completely coded in the discharge rate vs. cochlear place profile. However, this explanation is contrary to a considerable body of evidence supporting the perceptual significance of fine-grain temporal information (up to 3-4 KHz) in auditory nerve firing patterns /7-12/. For example, Viemeister's /11/ study indicates that behavioral performance in an intensity discrimination task (ie. tone in notch filtered noise) is relatively better than would be expected at the higher stimulus intensities if only rate-vs-cochlear-place information were used by the nervous system. Neurophysiological data /7,13/ indicate that a large percentage of eighth nerve fibers saturate in firing rate (or are nearly saturated) at the higher stimulus intensities, causing a broad plateau in the rate vs place profile. As a consequence, less information is available to the CNS at the higher stimulus levels <u>if</u> only rate-vs-place information is used. Such saturation occurs at the higher stimulus levels for both narrow-band and wide-band stimuli. Dye and Hafter /10/ have drawn a similar conclusion from their frequency discrimination experiments in which a wide-band masking noise was used. At the higher stimulus-masker intensities, they expected a poorer performance in the frequency discrimination task than at the moderate stimulus-masker intensities <u>if</u> only rate-vs-place information was being used. Only at stimulus frequencies of 3 KHz and above did the frequency discrimination performance decrease with stimulus-masker intensity. As a consequence, they concluded that a temporal mechanism is likely operating at frequencies up to 2-3 KHz, since such temporal information is not lost when overall firing rate saturates /7,8/. Sachs and Young /7,8/ studied eighth-nerve discharge patterns in cat as a function of stimulus intensity. They used a steady-state vowel stimulus and found that the vowel's spectrum was well represented in the temporal firing patterns distributed along the cochlea, even at the higher stimulus intensities. In contrast, the vowel's spectrum, when represented by the discharge-rate-vs-place

profile, became severely distorted at the higher stimulus levels. The extreme distortion was primarily due to response rate saturation at the higher stimulus levels.

The second explanation for insensitivity to electrical stimulus frequency above 300-600 Hz is that these deaf subjects could have become insensitive to temporal features of eighth nerve excitation patterns as a result of prolonged auditory stimulus deprivation. Inotherwords, the CNS of these individuals may have changed as a result of such prolonged auditory stimulus deprivation.

Third, certain forms of auditory processing could be occurring which are not currently incorporated in classical "place" or "temporal" theories or in a more recent synchronization vs. place theory suggested by Sachs and Young /8/. The nervous system might be highly sensitive to the differences in discharge times between individual fibers. With electrical stimulation, it has not been possible to generate fine-grain interfiber discharge timing patterns corresponding to those generated by acoustic stimuli in the normal cochlea. In the normal cochlea, interfiber discharge timing is a function of the traveling-wave motion of the basilar membrane. Our data indicate that electrical excitation in the suprathreshold region around a scala tympani electrode is highly synchronous, with small latency increases in the liminal fringes. We expect that the "fringes of excitation" will extend more or less equally in all directions from the electrode site /14,15/. The implanted-subject's CNS might be able to make only limited use of the temporal-spatial information generated during electrical stimulation because it differs significantly from the temporal-spatial excitation patterns generated during acoustic stimulation. It may be that interfiber discharge timing sensitivities do exist in the nervous system and that they contribute significantly to spectral extraction mechanisms for both simple and complex stimuli /1/.

A more acceptable coding theory might be synthesized from Sach's and Young's periodicity-vs-place coding model and an inter-fiber timing model. Simple neural networks that perform a spatial-temporal cross-correlation across cochlear space might form a part of this extended model /1/.

An Improved Representation of Auditory Excitation: A Separate Excitation Pattern for each Spectral Band

After recording from a large population of eighth-nerve fibers, Young and Sachs used a "temporal synchronization index vs. cochlear place" function to generate a stable representation of the spectrum of their steady state vowel stimuli /16/. The authors refer to this synchronization index as the "average localized synchronization rate" or simply "ALSR". From each fiber's post-stimulus-time-histogram (PSTH), the magnitude of the fourier component at the fiber's characteristic frequency is calculated and displayed as a function of the fiber's cochlear origin. The fiber's characteristic frequency is that stimulus frequency at which the fiber is most sensitive. The "ALSR vs cochlear place" representation of auditory nerve activity has great appeal because the representation of the stimulus spectrum is relatively invariant across a wide range of stimulus intensities; whereas a "rate vs. cochlear place" representation of the spectrum severely degenerates at the higher stimulus intensities.

Although the ALSR representation of Sachs and Young is useful in preserving the stimulus spectrum, this representation fails to carry information pertaining to the absolute intensity of the stimulus (see Figure 12 of Young and Sachs /16/). In the ALSR representation, the synchronization index does not significantly change as the stimulus intensity of the steady-state vowel is increased. Perceptual measurements indicate that subjects are quite capable of utilizing absolute intensity information /17,18/. For example, a steady-state vowel presented at 40, 60, and 80 dB SPL will clearly be perceived as very different in loudness at each level. However, the ALSR representation of Sachs and Young would give little or no

information about absolute intensity for those stimuli. With complex vowel-like stimuli, pulsation threshold measurements indicate that masking significantly increases with stimulus intensity /17/. This supports the view that the "internal representation" of the acoustic stimulus contains absolute intensity information.

The auditory system could obtain absolute intensity information and accurate spectral information from the more complete spatial-temporal representations displayed in figures 3-5 of Young and Sachs /16/. In these displays, the fourier magnitude for each spectral component of the stimulus is plotted as a function of cochlear place. The information contained in eighth nerve firing patterns is represented across three dimensions: spectral magnitude of the PSTH is plotted as a function of both frequency and cochlear place. In this representation, the formant peaks are clearly represented at all tested stimulus intensity levels - just as they are clearly represented in the two-dimensional ALSR representation. In the three-dimensional representation, there is information useful in estimating the absolute intensity of the stimulus. As the intensity of the vowel-like stimulus is increased, the synchronization to the first formant (F1) spreads to fibers originating from more more basal regions of the cochlea. To a somewhat lesser extent, this is also true for synchronization to the second formant (F2). In this 3-dimensional excitation pattern model, each spectral component or "band" has its own representation across the cochlea - as though each spectral band had a separate excitation pattern associated with it. However, each excitation pattern is not entirely independent of "interference" from the other spectral components of the stimulus. The excitation patterns representing the weaker spectral components are most affected by the stronger spectral components. Suppression of synchronization and suppression of average firing rate generate such cross-couplings between the spectral components. In the pulsation-threshold experiment, the observer adjusts the probe level so as to obtain the closest match to that specific excitation pattern associated with the masker component at or near the probe's frequency.

Florentine and Buus's analysis /19/ indicates that a "multi-band or multi-region" representation more accurately models "intensity discrimination vs. stimulus level" functions for a wide range of intensity discrimination experiments using masked tones. This finding further supports the concept that the auditory system is capable of decomposing the auditory nerve's fine-grain temporal patterns into components which represent the stimulus spectrum. And more importantly, this evidence supports the concept that this decomposition of multiple spectral components occurs over a large region of the cochlea. In the ALSR representation, each spectral component is represented by only one restricted region of the cochlea. Such a representation is less likely to yield models that accurately mimick measured intensity discrimination behavior. However, if spectral components are resolved at multiple sectors along the cochlea, better agreement with psychophysical intensity discrimination measures is likely.

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EVALUATION OF A MULTIPLANAR COCHLEAR ELECTRODE ARRAY*

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SUMMARY

A sixteen channel microelectrode array has been developed for the purpose of electrical stimulation of the cochlea. Designed for implanation via the round window, the array is based upon photolithographic techniques which have been extended to produce multiplanar arrays. Based upon the buildup of single planes of electrodes, this technique increases the number of discrete electrode stimulation sites, while maintaining a narrow array profile and reliable feedline widths.

The use of silastic carriers with shape memory alloy inserts is also discussed, as an aid to the repeatable surgical implantation of these arrays.

MATERIALS AND METHODS

1. General Considerations

Several factors affected the choice of the materials and methods used for constructing the electrode array. Apart from the general conditions which all electrodes used for stimulation have to meet, namely, non-toxicity to tissue, reliability and longevity, there was the need to have a process that is adaptable to mass production of the electrode array with high precision.

The use of microelectronic fabrication methods was selected because it met both requirements for mass production and precision. Further, it had the flexibility of rapid alteration of the array configuration by a simple substitution of a photomask. Other advantages included the use of well-characterized techniques and the use of existing equipment, hence keeping down start-up costs.

The object of this exercise was to develop a flexible, non-toxic, reliable, mass produced and hence inexpensive electrode array which could be inserted into the Scala Tympani a distance of about 2.5 cm from the round window without causing excessive trauma to the organ.

The choice of how many single electrodes to have in the array had to be made on the basis of the minimum width of the conductors and the separation required between them, given the reliability constraints and the cross-sectional area of the Scala Tympani. On the basis that the electrode array should not be wider than 1 mm if it is to enter the Scala Tympani, a choice of nine discrete electrodes in the same plane was made. However, to demonstrate the versatility of the approach, a second layer of seven conductors was deposited on the first to increase the total number of electrodes to sixteen.

2. Choice of Materials

The choice of platinum as the conducting material was based on the well-documented

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performance of this material in electrostimulation applications. /1/

Several insulating materials were considered. These included teflon and mylar. the major problem encountered included the difficulty of producing a smooth surface clean enough to obtain good adhesion between insulator and conductor. Also, since the platinum was deposited by radio frequency sputtering, it was important to have good and even thermal contact between the insulating sheet and the water-cooled ground plate of the sputtering machine, if hot spots were to be avoided.

The material chosen was polyimide. This material is bio-compatible, comes in liquid form and can be spun on a suitable substrate or carrier such as a silicon wafer to form a uniform film. The thickness of the film can be varied by a combination of changes in the viscosity of the liquid polyimide and the spin speed. /2/ The film is cured partially or fully by heating it to a specified temperature for an appropriate length of time. Details are given later.

The final form of the electrode array has to be sufficiently flexible to negotiate the spiral path of the Scala Tympani, but rigid enough to minimize the possibility of foldback in the canal during the surgical implantation. To help the elctrode array take on the spiral form of the Scala Tympani, tests are being conducted with a shape-memory alloy of nickel and titanium(Nitinol). This material has the property that it can be formed into a desired shape and then annealed at a high temperature. After cooling to room temperature, it can be straightened. Subsequently, when its temperature is brought up to the "transition" temperature, the Nitinol reverts to the shape it had at the time of the high temperature anneal. /3/

The approach is to choose a nitinol wire of the appropriate diameter with a transition temperature just below normal body temperature i.e. 36°C. The wire is annealed after it has been formed into a spiral approximating the shape of the Scala Tympani. The nitinol wire can now be bonded to the electrode array by a suitable adhesive such as silastic. During the implantation process, as the electrode array comes up to 36°C, the nitinol wire starts to force the array into the shape of the Scala Tympani thus making it easy to insert it into the canal. Investigation of this process is continuing.

3. Fabrication

In order to reduce repetition, the following process steps are defined:

i) Small temperature increment (STI) cure

50°C for 1 hour, 100°C for 1 hour, 120°C for 1 hour; elevate temperature 20°C for 20 minutes up to 300°C

ii) Sputter etch to clean surfaces

3 minute sputter etch with Argon at 8×10^{-3} Torr, 100 W rf power

iii) Platinum deposition

Sputter with platinum target; 100 W rf power and 8×10^{-3} Torr Argon pressure.

iv) Positive photoresist process

Follow manufacturers recommendations to obtain at least 2 μm layer of positive photoresist. Followed by pre-bake, exposure, post-bake, development and stripping.

v) Sputter etch to remove platinum

100 W rf power at 8×10^{-3} Torr with Argon for period necessary to etch through platinum layer.

Detail steps in construction of 16 electrode array

1. Silicon wafer cleanup.
2. Spin on 50 μm of polyimide on wafer following manufacturers' recommendations.
3. STI cure to 300°C.
4. Sputter etch to clean surface.
5. Deposit 5000Å of platinum.
6. Spin on 2 μm of positive photoresist and process to expose unwanted platinum.
7. Sputter etch platinum to define bottom layer array.
8. Strip photoresist.
9. Spin on 10 μm of polyimide and partially cure to 250°C
10. Spin on 2 μm of positive photoresist and process to expose electrode terminals and bonding pads.
11. Sputter etch to remove polyimide over electrode terminals.
12. Strip photoresist.
13. STI cure to 300°C.
14. Repeat steps 4, through 9 to produce top layer array.
15. Spin on 2 μm of positive photoresist and process to expose electrode terminals and bonding pads for both bottom and top layer arrays.
16. Sputter etch to remove polyimide over terminals and pads.
17. Strip photoresist.
18. STI cure to 300°C.
19. Remove silicon wafer carrier.
20. Trim electrode to shape.

RESULTS

Fig.1 shows a cross-section of the electrode array.
Fig.2 shows the electrode array after the platinum has been sputter etched.
Fig.3 shows the bonding pads and feedlines of the bottom layer of the array after the pads have been exposed.
Fig.4 shows the bonding pads and feedlines of the top and bottom layers of the array after the pads have been exposed.

Electrical tests were conducted on intermediate and completed samples. Feedline trace resistance was typically less than 250Ω, and interelectrode isolation between coplanar electrode pairs and interlayer pairs was always greater than 100 MΩ. The highest interelectrode capacitance was found to exist between overlapping upper and lower array feedlines, with typical values of 80 pF at 1 kHz.

Impedance characteristics of the individual electrodes in physiological saline were measured by standard procedures, and found to be proportional of $f^{-.915}$. The complex nature of the saline-electrode interface is well known, and can account for this variation from the perfect capacitance relation /4/, over the range 100 Hz - 10 kHz.

Following the determination of the real stimulation site areas according to the procedure outlined by Brummer and Turner /5/, arrays were put on test in physiological saline under lagging biphasic pulse conditions. The injected charge density was calculated to be 300 μCoulombs per real cm^2 per pulse to approach the theoretical nongassing limit of platinum /6/, and the test electrodes were subjected to thirty-five thousand pulse pairs, after which no delamination of the platinum stimulation site from the underlying polyimide was observed.

Flexure cycling was then carried out to assess the durability of the arrays. After fifty cycles of 360° curling, no array trace in any of the samples was found to be open-circuited. Neither liftoff of platinum nor delamination of polyimide was observed. The three dimensional nature of the upper platinum traces as they course over the partially levelled intermediate polyimide layer apparently causes no problems.

At this time, work on the combination of the electrode array and the nitinol memory shape wire is proceeding. Preliminary results are encouraging.

DISCUSSION

As part of the development of the cochlear prosthesis, the concept of a single planar multielectrode array has been extended to a double layer array giving twice the electrode density while maintaining wide feedlines to each contact.

Evaluation of the electrode indicated that interlayer isolation is not a problem. The upper layer electrode array did not appear to have discontinuities due to the uneven surface on which it was formed; and this unevenness having been caused by the feedlines of the lower electrode array.

Preliminary tests have indicated that the addition of a shape memory alloy to aid the surgical implantation of the electrode in the cochlear is very promising.

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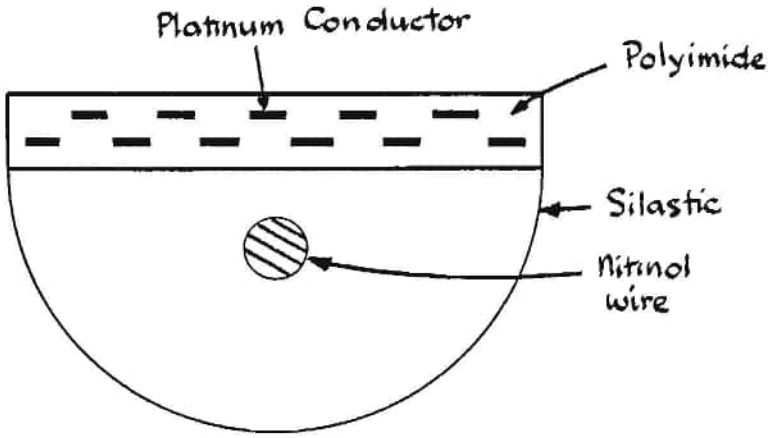


Fig. 1.

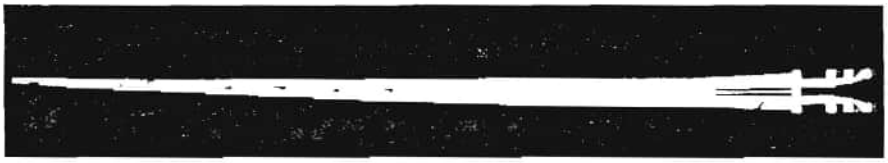


Fig. 2.

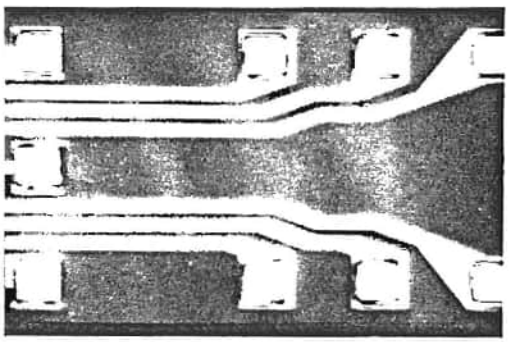


Fig. 3.

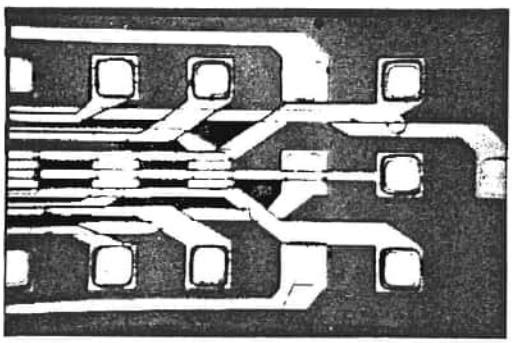


Fig. 4.

INITIAL RESULTS WITH SINGLE-CHANNEL AND MULTI-CHANNEL COCHLEAR IMPLANTS

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SUMMARY

A uniform comprehensive clinical evaluation of different cochlear implant prostheses is ongoing at the University of Iowa. Preliminary results from nine patients with three different intracochlear implants (Los Angeles - single-channel, Vienna - single-channel, and Melbourne - multi-channel) are presented. Early results indicate only minor differences in patient performance among implants and suggests audiologic performance depends upon a high-level cognitive skill related to lip reading ability.

INTRODUCTION

Cochlear implants have become a realistic alternative for the management of profoundly deaf patients. A variety of implants, each with differing electrode designs and unique speech coding strategies, have been developed. With so many design variables and the successes reported by each center, comparative measurements of the present generation of cochlear implants is vital to the development of future prostheses. Comparable data is difficult to obtain since uniform measures of performance have not evolved as rapidly as implant technology. Our research efforts have been directed toward establishing an independent center where uniform comprehensive unbiased investigation of different cochlear implants can be performed. This report provides preliminary audiologic results on nine patients with three different cochlear implants.

METHODS

Nine post-lingually deafened adults with three or more months experience with their device are included in the study. Relevant biographical data on the nine patients is found in Table I. Four patients are using the Los Angeles (LA)/1/ implant, three patients wear the Vienna (V)/2/ single-channel intracochlear device, and two patients are implanted with the Melbourne (M)/3/.

Table I. Biographical data on patient

Patient	Age (yrs)	Etiology of Deafness	Duration of Hearing Loss (yrs)	Duration of Profound Hearing Loss (yrs)	Time Since Implantation (months)
LA1	62	otosclerosis	57	10	21
LA2	64	otosclerosis	22.5	3	7
LA3	53	skull fracture	8	8	29
LA4	66	otoxicity	4	4	60
V1	53	congenital syphilis	45	9	7
V2	23	skull fracture	2.5	2.5	7
V3	56	otosclerosis	45	9	7
M1	39	sudden deafness	30	0.5	4
M2	37	Cogans syndrome	10	8	4

All patients except LA2 had profound bilateral hearing loss and appropriate hearing aids were not useful. LA2 had some residual hearing in his non-implanted ear, routinely wore a hearing aid, but was not able to repeat any W-22 words at any presentation. Tests were performed without his hearing aid.

The audiologic battery is a combination of selected tests from the Minimal Auditory Capabilities (MAC) battery /4/ and 12 additional tests called the Iowa Cochlear Implant Tests /5/. The tests are organized into five categories - everyday sounds, prosody tests, closed-set and speech related tests, open-set speech, and audiovisual tests.

Three randomizations of each of the Iowa tests were produced and three randomizations were re-recorded from the MAC tests. The order of presentation of the tests were randomized within and across subjects. In the audiovisual tests, the sound only version was presented before either the vision or sound-plus-vision tests. All three modality versions of the audiovisual tests were separated by at least three hours of testing with the other tests.

All tests were presented at about 70 dB SPL, and subjects were allowed to adjust their implant to a comfortable setting. The audiovisual tests were presented in a sound field in a large quiet room (background level 43 dBA). All other tests were recorded on Maxell UDBXL-II cassette tapes, played back on a Nakamichi LX-5 tape recorder (with Dolby on) and presented in a single-walled sound treatment room.

RESULTS

A. Everyday sounds All patients except LA4 were able to discriminate some everyday sounds, performance on the identification task was poorer. V3 and M1 were able to identify 50% of the sounds while LA2 could not identify any.

B. Prosody tests Only four patients were able to significantly distinguish whether a sentence was a question or a statement. However, eight patients scored above chance on the accent test (fig 1), and all but one patient scored above chance on the number of syllables test (fig 2). There was a slight tendency to do better with plosive or fricative boundaries than with glide/nasal boundaries on the syllables test.

Fig 1

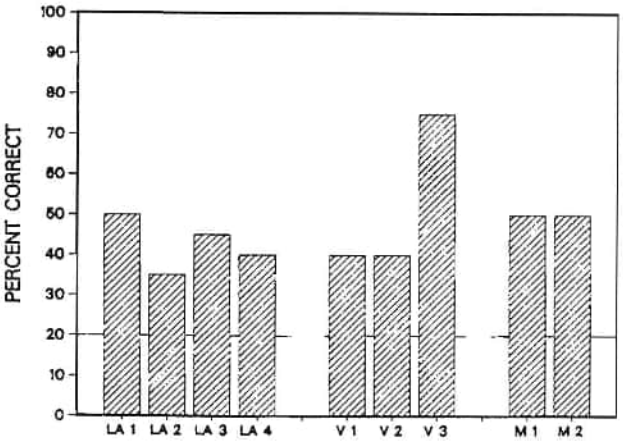
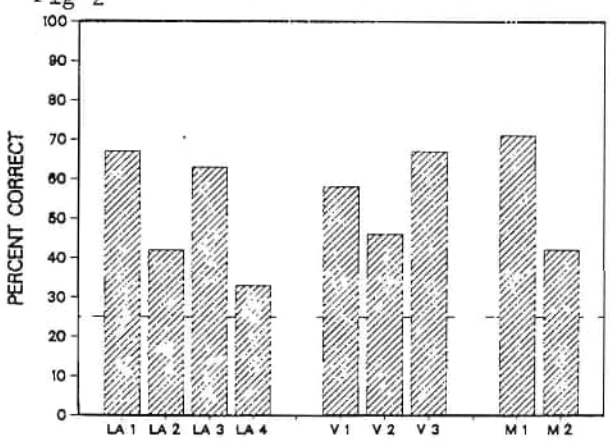


Fig 2



C. Closed-set speech tests and speech related The four-choice spondee and four-choice spondee in noise tests are closed-set. Seven of the patients scored above chance on the four-choice spondee test (fig 3). The dramatic effect of adding noise (at a signal-to-noise ratio of 10 dB) is demonstrated by the observation that only one patient scored above chance on the four-choice in noise test (fig 4).

Most of the patients do very well in the speech related tests. Seven patients performed above chance on the noise/voice test (fig 5) and the female/male test (fig 6). No one, however, could distinguish different speakers if they spoke different sentences.

D. Open-set speech understanding The sound only conditions of the audiovisual tests provide material for open-set speech understanding. When no contest or picture was available (fig 7), only M2 was able to identify some words. But when a picture

Fig 3

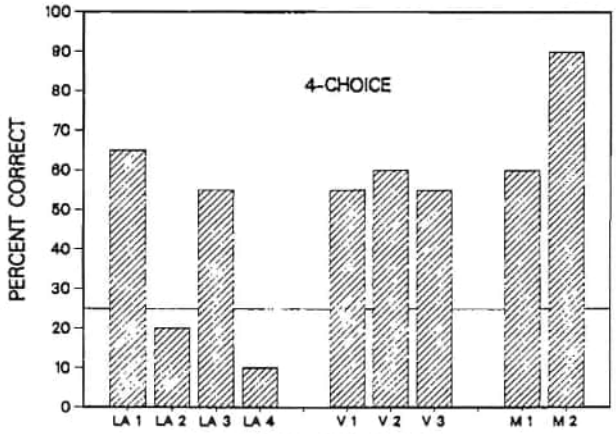


Fig 4

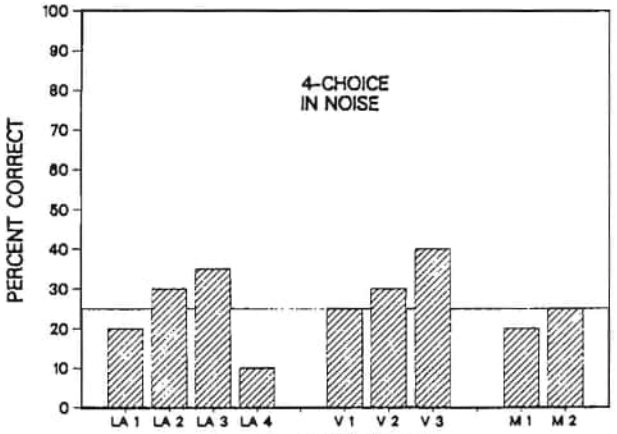


Fig 5

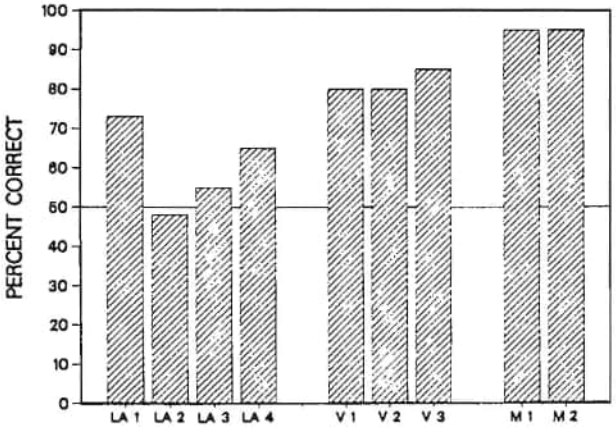
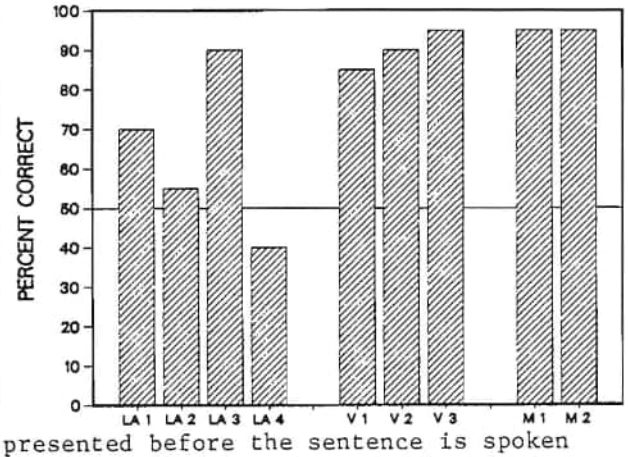


Fig 6



illustrating one word in the sentence was presented before the sentence is spoken (fig 8), seven of the patients repeated some of the words correctly. In addition, LA3, V1 and M2 got some sentences correct when presented live voice by a companion.

Fig 7

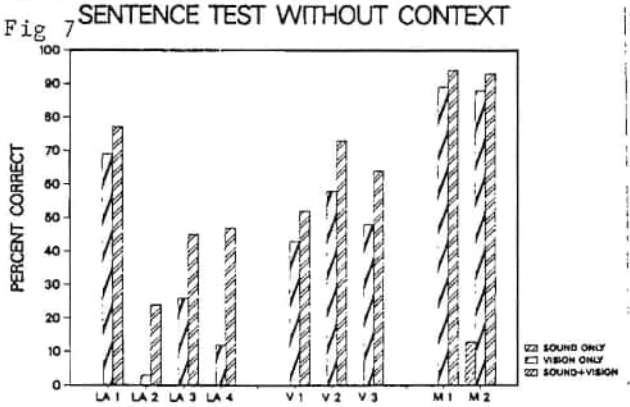
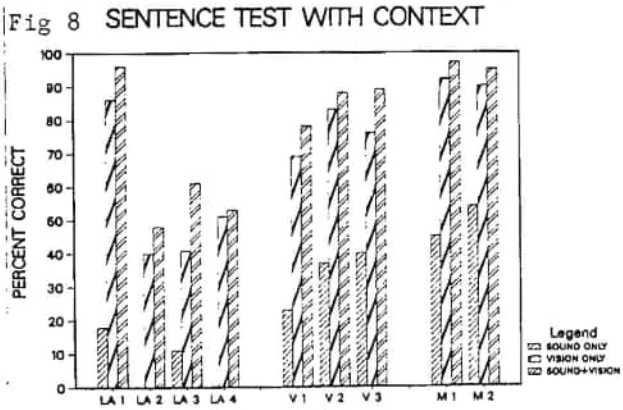


Fig 8



E. Audiovisual tests Binomial confidence intervals applied to the different scores /6/ were used to determine if the implant provided any additional benefit to speech reading (i.e. vision-plus-sound compared to vision only).

On the sentence test without context (fig 6) LA2, LA3, LA4, and V3 showed a significant improvement with the device. In the sentence test with context (fig 7) LA1, LA3, V3, M1 and M2 scored significantly better with the implant.

DISCUSSION

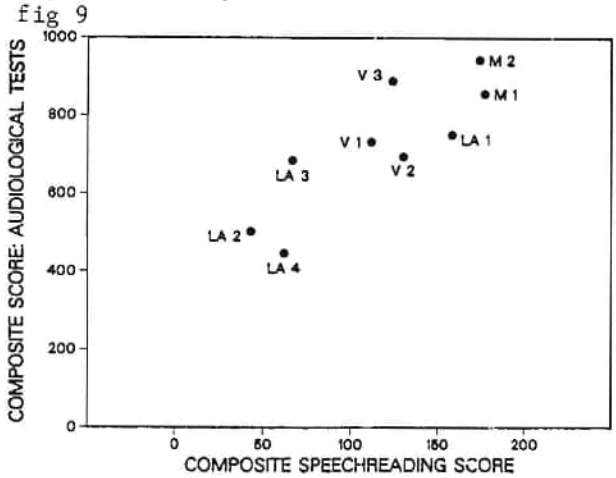
The cochlear implants evaluated in this study provide all patients sufficient information to improve their ability to communicate. They also supply information regarding environmental sounds and warning signals and in some instances it is sufficient for identification of the sound.

Even though most patients performed better than chance on the prosody tasks (question/statement, accent and number of syllables test), it is surprising that their level of performance was not better. All of the implants evaluated in this study should be able to process the voicing frequency (Fo). Even patients with the Melbourne implant which specifically codes Fo as pulse rate, show limited performance on the prosody tests. Some voicing frequency information is being conveyed by all devices as evidenced by the results on the female/male voice test but the processing is not sufficient to discriminate between different speakers of the same gender. Another problem with the present generation of implants is their universal poor performance in noise. Only patient M2 has been able to identify words in open-set presentation of sentences. If, however, contextual information is provided a dramatic improvement was noted. Up to 55% of the words were identified by patient M2. Limited open-set word discrimination was also noted with all three implants in a live-voice test with a familiar speaker such as a spouse. This emphasizes the importance of experience and familiarity with the speaker.

It is obvious from the results that there are large differences among patients. There is also some variability in the rank-ordering among the patients on different tests. Because of these differences, and the fact that the number of patients with each device is small, it is inappropriate to make definitive statements concerning the comparative performance of the three implants at this time.

It is interesting to note that lipreading ability (vision only) correlates ($r = 0.84$; $p<.01$) with audiologic performance (total scores on all tests)(fig 9) irrespective of implant design. One must be careful in emphasizing this point in light of the small number of patients, but lipreading ability may reflect a general high-level cognitive skill necessary to synthesize the limited information provided by the implants. Individual patient differences, i.e. cognitive skills and neuron survival, may effect patient performance more than implant design at this early stage of implant development.

fig 9



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ASPECTS OF SOUND SIGNAL PROCESSING USING THE VIENNA INTRA- AND EXTRACOCHLEAR IMPLANTS[x]

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SUMMARY

The Vienna intracochlear implant consists of a four-channel bipolar molded scala-tympani electrode connected to a four-channel receiver/ stimulator circuit. The Vienna extracochlear implant consists of a single-channel receiver/stimulator driving an extracochlear pair of electrodes. Both of these implants are complemented by the same type of sound processor, which implements a single-channel full bandwidth analog sound signal processing scheme. In the case of the intracochlear implant the external portable sound processor is fitted to the one of the four channels best suited for speech understanding by using a set of selection criteria.

THE DEVICES

An auditory prosthesis consists of two subsystems : an implant comprising the stimulating electrode and an electronic receiver/stimulator circuit, and an external part containing the microphone, the sound signal processing circuitry, the transmitter for the transcutaneous transmission and the battery.

Our development goal was not only an aid for lipreading, but a device which should enable the majority of postlingually deafened patients to understand speech to some degree.

Two different types of implants are presently used, a four-channel intracochlear implant and a single channel extracochlear implant. A detailed description of these implants can be found in /1/ and /2/.

The four-channel intracochlear implant consists of a four-channel molded scala-tympani electrode connected to a four-channel implantable receiver stimulator circuit. Using a set of selection criteria the external portable sound-processor is fitted to the most useful of the four channels. Work is in progress investigating different multichannel coding strategies.

The extracochlear device contains a single-channel implant driving a pair of electrodes mounted externally to the cochlear. The main rationale for the development of this system was to avoid damage to the inner ear. So far it has been mainly used for patients with some residual hearing left that was to be preserved. The external portable sound processor is the same as that used with the intracochlear device.

So far 18 and 13 patients have received the intra- and extracochlear device, respectively, in Vienna.

[x]Supported by the Austrian Science Research Fund.

CODING STRATEGY

Both of the systems use analog stimulation signals. In principle one could also use pulses with these devices, but since they have the capability to use signals covering a frequency range from 30 Hz to more than 10 kHz, it is, of course, quite obvious to make use of the additional dimension afforded by the ability to elicit different percepts by stimulating with different waveshapes.

The use of analog stimulation signals comprising a frequency range from 150 Hz through about 4 kHz makes proper dynamic range compression and proper frequency equalization a necessity. Fig. 1 shows thresholds and uncomfortable listening levels, obtained using a bursted sine wave, together with the properly equalized soundprocessor output adjusted such that conversational speech is heard at most comfortable loundness. The adjustment procedure itself employs a variable frequency sine wave. It is implemented using a microprocessor controlled system.

It is, however, by no means evident, that the frequency equalization procedure involving a variable frequency sine wave gives an adjustment of the processor's frequency response which is optimally suited for the perception of complex speech sounds involving a number of simultaneously present components. Fig. 2 is an example that shows that this is indeed the case. It compares 8-vowel identification results from patient F.W. for the setting of the equalization network as resulting from the adjustment procedure (curve 2), and for one steeper (curve 1) and one less steep (curve 3) setting of the frequency response, both of which give inferior identification results as compared to the original setting.

RESULTS

The effects of inaccurate frequency equalization are similar to effects caused by limiting the bandwidth of the stimulating signal. In order to investigate how important the higher frequency components of speech are, the understanding of one-syllable words and sentences and the ability to identify consonants and vowels have been tested using the full bandwidth frequency equalized signal and using a lowpass filter with a cut-off frequency of 300 Hz. (For the consonant- and vowel-identification an additional configuration using a lowpass filter with a cut off frequency of 900 Hz was also used). The results (Fig. 3) revealed that the addition of the lowpass filtered stimulation signal gave an improvement over unaided lipreading, but that this improvement was much smaller than the improvement observed when the full bandwidth signal was used.

Furthermore, it was found that in the modality "stimulation only",while the patient got 28 % correct for the one-syllable nouns and 55 % correct for the sentences, there was absolutely no understanding of either one-syllable nouns or sentences for the lowpass filtered speech signal. (This is what certainly happens with analog single-channel prostheses without any frequency compensation since in this case low frequencies dominate the percept due to their low thresholds). Consonant identification in the modality "stimulation only" revealed a decrease in correct responses from 81 % to 59 % for the 900 Hz and to 32 % for the 300 Hz cut off frequency. The corresponding values for the identification of the eight German long vowels were : 78 % to 58 % for the 900 Hz and 41 % for the 300 Hz cut off frequency. For a different patient, S.S., the reduction from the full bandwidth signal to the 900 Hz lowpass filtered signal was 56 % to 33 % for the consonant identification in the modality "stimulation only".

It is, thus, apparent that high frequency components of speech even in a range where differences in frequency cannot be discriminated, do contribute to speech understanding, and should not be omitted in an analog stimulation signal. Special attention has to be paid to the frequency equalization.

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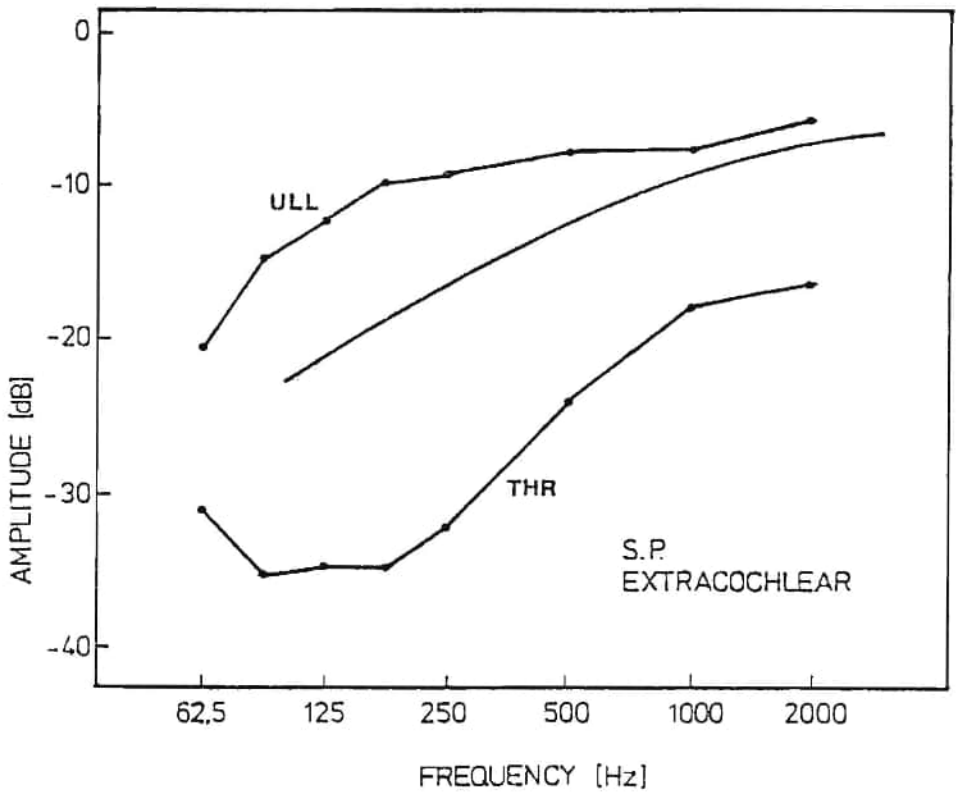


Fig.1: Swept frequency sound processor output compared to threshold (THR) and uncomfortable listening level (ULL). The ordinate is the amplitude at the modulation input of the external transmitter used for the transcutaneous transmission. This voltage is referenced to 1.1 Volt peak.

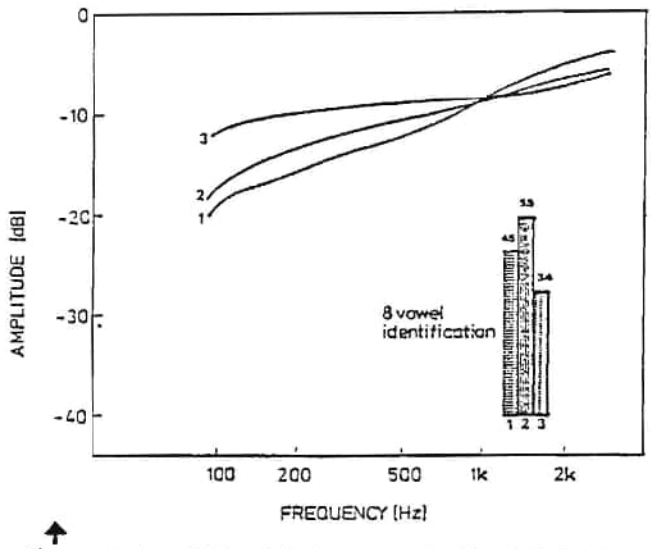
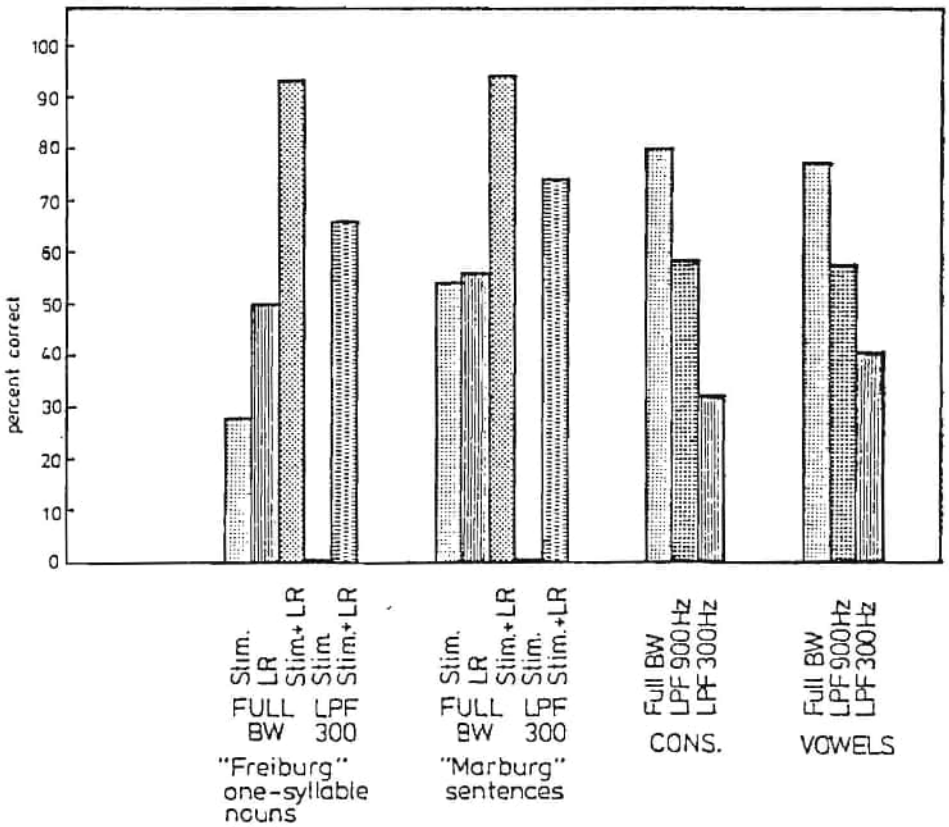


Fig.2: Results of identification tests for the eight German long vowels for correct frequency equalization of the sound processor (curve 2) and two deviating settings: patient F.W., stimulation only. The vowels were presented from tape in the form /hVh/ at most comfortable loudness by a female speaker. There were 160 presentations per test. The numbers give the percentage of correct vowel identification.

Fig.3: Results of speech tests with the full-bandwidth frequency equalized signal and with low pass filters with cut off frequencies of 300 Hz and 900 Hz respectively. 100 of the one-syllable nouns contained in the "Freiburger Test" were used in 5 groups of 60 words each for the 5 test conditions. 20 different "Marburg sentences" were used per test condition. One-syllable nouns and sentences were presented by a female speaker in live voice with no repetitions allowed. The patient was allowed one hour of free conversation with the low pass filtered signal.
For "stimulation only" in the 300 Hz low pass filter condition no items were understood.
The 16 consonants /l/, /r/, /m/, /n/, /ŋ/, /v/, /b/, /d/, /g/, /p/, /t/, /k/, /h/, /ʃ/, /s/ and /f/ were presented in a vowel-consonant-vowel environment using the vowel /a/ in live voice with feedback given after each item. There were 6 presentations per consonant.
The 8 German long vowels /a:/, /ɛ:/, /o:/, /ø:/, /e:/, /u:/, /y:/ and /i:/ were presented from a tape in a consonant-vowel-consonant environment with the consonant /b/. There were 10 presentations per vowel for each condition. The low pass filter had a Butterworth response characteristic and a slope of 48 dB/octave. The filter was inserted between the patient's sound processor and the transmitter. By means of a graphic equalizer care was taken that there was good frequency equalization for equal loudness within the filter pass band.



CLINICAL EXPERIENCES WITH ELECTRIC STIMULATION OF THE ACOUSTIC NERVE x)

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SUMMARY

The limits of indication for the two Viennese Cochlear Implants, namely a four-channel-endocochlear device and a unichannel extracochlear device, are described. Various selection criteria, especially the preoperative electrostimulation test, are discussed. The results of 24 patients, who are included in a clinical study are presented. These results show, that in almost half of the patients a comprehension for open speech could be achieved. Most of the patients who could not reach an open speech understanding improved at least when they combinedlipreading + electrostimulation.

MATERIAL AND METHODS

The Vienna group uses two types of cochlear prostheses, namely a unichannel extracochlear device and a four-channel endocochlear device with unichannel stimulation only. Concerning the multichannel device, each channel differs in dynamic range, pitch discrimination, gap-detection and temporal difference limen, thus suitability for speech perception also differs. The channel best suited to speech transmission is selected through various psychophysical tests. I should like to point out that despite the fact that a four-channel device is inserted into the cochlea only a unichannel stimulation is applied, because the final results could not be improved when all four channels were stimulated. If a multichannel coding strategy is developed in the future that functions significantly better than our present single strategy, then the implanted patients will only require a different speech processor. The previous implant can remain in place. (1,2,3).

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The endocochlear four-channel prosthesis is limited to patients with bilateral deafness, with puretone thresholds above 95 dB, with or without hearing of words, no discrimination of environmental sounds and no visual unaided word- and sentence comprehension, even when hearing aids are used. The extracochlear unichannel prosthesis is limited to patients, who have puretone thresholds of 80 dB and above, hearing of words but no visual unaided word- and sentence comprehension, even with the use of hearing aids. The main difference here is that the patients of this group are able to understand some numbers and to discriminate environmental sounds. This very important function must be preserved. This is only possible with an extracochlear device. Among various selection criteria, like age, general condition, motivation, etc., the most important one is the preoperative electrostimulation test. In these tests the cochlea is stimulated by electric pulses, via a transtympanic electrode which is inserted into the mucous membrane of the middle ear. In this test 30 electric pulses of 3 different frequencies (50, 100, 250 Hz) are randomizly presented and the number of correctly detected frequencies is determined. Detection of more than 2/3 of the stimuli is a useful result for implantation and it seems that there is a good correlation between the result of this test and the final clinical results.

The receiver coils and the electrode are implanted via a retrotympanal approach through the middle ear. From the mastoid cavity the facial recess is opened and the round window explored. After enlarging of the niche to the round window the membrane of the window is removed and the four-channel electrode inserted. In most of our patients the electrode is inserted to a length of 12 - 14 mm from the round window. Further insertion may bear the risk of cochlea damage. The active electrode of the unichannel device is located into the niche of the round window but the round window itself is not opened. The receiver coils of the devices are embeded into circular bone grooves superiorly and posteriorly the mastoid cavity.

RESULTS

The auditory results with electrostimulation only are demonstrated in Tab. 1 - 3. Four patients have "very good" results (Tab. 1). They can understand between 70 - 89% of unknown sentences. In the phoneme recognition test they reach a mean between 77% - 88% correct answers. Also the psychophysical tasks, as gap-detection for low and high frequencies and temporal DL for low and high frequencies correlate significantly with a very good score of sentence-understanding. Presently we experience that the following values of these psychophysical tests are limits beyond those word and sentence understanding cannot be achieved:

Low frequence gap-detection: 55 ms
high frequence gap-detection: 40 ms
low frequence temporal DL: 130 ms
high frequence temporal DL: 80 ms

7 patients have "good results" (Tab. 2). They understand between 13 - 45% of unknown sentences. In the phoneme recognition test they reach a mean between 71 - 83% correct answers, what is only little below the score of the "very good" group. In three patients psychophysical tasks could be performed. They show similar to the previous

group a good correlation to the sentence understanding. In the preoperative pitch test all patients have discriminated more than 2/3 of the stimuli. Five patients have extracochlear and two have endocochlear electrodes. It is obvious from this group that also prelingual deaf can achieve an open speech understanding with the extracochlear device.

13 patients have "moderate results" (Tab. 3). They have no open speech understanding and most of them have no significant values in the phoneme recognition test. The values of the psychophysical tasks in 3 patients are beyond the critical limits and presume that open speech understanding will not be achieved in the future. The mean values of the pitch test are also below those of the previous group (0,77/0,86).

If lipreading is compared with electrostimulation the following results could be achieved:
In the group with "very good" results perception between 97 and 100% of unknown sentences is possible (Tab. 4). In the group with "good results" from 6 patients (Ch.K. can not be classified), 5 improve their lipreading ability when combined with electrostimulation. Only one patient (S.P.) has better results with lipreading alone than with lipreading plus electrostimulation. In everyday life she uses most of the time only her hearing aid; Because of familial problems she refuses to wear the speech processor.

In the group with "moderate results" 10 patients improve lipreading when combined with electrostimulation. 3 patients have better results when they use only lipreading. One of them (A.Z.) has bad results in the psychoacoustic tests. She can not detect the length of the stimulus, shows threshold decrease, unability to discriminate between white noise and sinustones, pitch inversion a.s.o.The 2 other patients are prelingual deaf. One of them (H.H.) did not have enough time to habituate to the use of acoustic information.

DISCUSSION

The risk of a cochlear damage can certainly not be excluded when an electrode is inserted into the scala tympany. An extracochlear device has therefore been developed to avoid the risk of an endocochlear damage. Presently this device is indicated for patients who have a small residual hearing. Our results demonstrate clearly that even with an extracochlear stimulation a comprehension of open speech can be achieved, but only in a smaller number of patients and to a less extend than in patients with endocochlear stimulation. It seems, that with an extracochlear device only a score of open speech understanding up to 50% is possible, whereas with endocochlear stimulation results of up to 90% can be achieved. Nevertheless we must be aware that all conclusions are necessarily obscured because of our poor knowledge of the conditions of the nerve fibres. It will be an important target for the future to find more reliable test methods for a more precise judgement of the quantity of surviving nerve fibres.

Endocochlear stimulation shows better results but as already mentioned the risk of cochlear damage can not be excluded. The stability of the results and some observations we made, when in three patients the device and the electrode had to be replaced by a new one support the opinion that either the risk of damage is small or the consequences of a damage concerning the clinical results are not important.

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PHYSIOLOGICAL PROPERTIES OF THE ELECTRICALLY EXCITED AUDITORY NERVE

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Compound action potential recordings from electically stimulated auditory nerve suggest that temporal response properties depend on the site of spike initiation on the afferent neuron. That dependence may be useful diagnostically in assessing the extent of dendrite degeneration in cochlear implant candidates ou users.
Single fiber recordings have been undertaken to investigate excitation and conduction in teh auditory nerve axon and dendrite. When compared with axonal excitation, dendritic excitation exhibits longer latency, greater latency variability, and longer chronaxie.

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CHOUARD C.H., FUGAIN C. & MEYER B. (Paris) - DESCRIPTION OF THE FRENCH 12 CHANNELS COCHLEAR IMPLANT AND CLINICAL RESULTS.

In the CHORIMAC, the French device designed by the BERTIN Society, the whole speech information is sequentially transmitted to 12 electrodes implanted in the cochlea. An electrode bearer introduced through the round window is now commonly used. Frequencies between 100-4000 Hz and intensities between 40-100 db are only transfered in a 3msec time sampling. The output signal is a positive square wave followed by an equal negative wave. Its voltage varies from 2.5 to 6.5 volts. Its duration varies from 0 to 200 microsec. Its frequency is equal or inferior to 300 Hz. The outside emietter weights 600 g.

Clinical assessment and results are described in 65 implanted patients (among them 15 were less than 18 years old). Voice changes may be objectively observed on sonagrams. Phonetic discrimination depends on the electrical and nervous status of the implanted deaf cochlea. Words and sentences discrimination with reference list, but without lips reading, is commonly obtained. Unknown words discrimination is more difficult and varies from one patient to the other. Discrimination with lips reading progresses elicited by the device depend on the pre operative status and the own possibilities of each patient. Psychoaffective improvement is evident in every cases, specially in 3 cases of autistic deaf-mute children.

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REVERSAL OF DETRUSOR INSTABILITY BY ELECTRICAL STIMULATION

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SUMMARY

Small rhytmic bladder contractions have been observed in many studies of bladder function in the experimental animal (1-4). The etiology of these contractions has not been definitely established. It has been suggested that the contractions are myogenic and orginate within the detrusor muscle but other investigators claim that the contractions are elicited by neural reflex mechanisms. The small rhytmic contractions observed in the experimental animal are very similar to the small, premature detrusor contractions characterizing patients with detrusor instability. Therefore the manipulation of this bladder activity in the experimental animal was used as a model to explain certain mechanisms of the clinical condition detrusor instability.

This communication comprises an experimental study on cats and a clinical study on patients with detrusor instability. The experimental study describes a neurophysiological mechanism offering an explanation of the clinical condition detrusor instability. It also deals with the immediate effects on the bladder during pelvic floor stimulation. The clinical study reports the long-term effects on detrusor instability in a material of patients treated by intravaginal electrical stimulation because of urge incontinence due to detrusor instability or mixed stress- and urge incontinence.

MATERIAL AND METHODS

Animal Experiments

The experiments were performed on 22 adult female cats. The animals were anesthetized with Nembutal (Abbott) 30 mg/kg body weight intraperitoneally, with supplementary intravenous doses to maintain an even anesthesia. The nerve activity was recorded by direct registration of the activity in the peripheral nerves to the bladder. Either of the hypogastric nerves was dissected free and transected close to the bladder. The nerve filaments were mounted on a silver electrode and the recorded nervous activity was amplified, rectified and integrated. The pelvic nerve branches to the bladder were exposed and one or two branches on the right side were transected proximally to the vesical parasympathetic ganglia. The bladder volume was continuously monitored by an isobaric volume recording technique (5,6). Electrical stimulation was delivered by two circular stainless steel electrodes attached to a cylindrical plug introduced into the vagina and secured inside by a suture at the introitus. The dissected pudendal and hypogastric nerves were stimulated through a pair of silver electrodes. The electrodes were connected to a specially designed stimulator through which the shape, duration, frequency and voltage of the pulses could be varied.

Clinical Material

The study comprised 20 patients with urge incontinence due to detrusor instability and 10 patients with mixed stress-and urge incontinence. The diagnosis was established by clinical investigations, including urinary culture, cystourethroscopy, urethral pressure profile measurements, cystometry and isotonic bladder volume registration. The degree of functional disturbance was also assessed from the history and micturition charts. Details of the urethral pressure profile measurement technique, the cystometric technique and the method of isotonic volume registration have been given elsewhere (7-9).

The urinary cultures were negative in all patients. Cystourethroscopy revealed no pathologic findings. All patients had signs of detrusor instability: either a micturition contraction occurring

at a bladder volume less than 200 ml or premature detrusor contractions during bladder filling, either provoked by repeated coughing or appearing spontaneously during filling of the bladder. Two patients had stable bladders according to the cystometrograms but exhibited detrusor instability (transient volume diminutions) in the isotonic bladder volume registrations. Patients with mixed stress-and urge incontinence also had objective findings of stress incontinence: leakage (but not micturition) was observed when the patient, standing with her legs apart, coughed or jumped.

Device for Long-Term Treatment

Technical details of the device have been presented elsewhere (10). It consists of an inflatable electrode carrier made of medical grade silicone rubber with 2 rows of stainless steel electrodes. The positioning of the electrodes was adjusted individually according to findings during primary laboratory stimulation (11). The electronic device was individually adjustable with respect to frequency, pulse duration and voltage. A stimulation of 10 Hz was used, in accordance with previous experimental results (6,9). The voltage was adjusted individually by the patient to an intensity at which she began to percieve the stimulation. The patients used this device 8-12 hours per day.

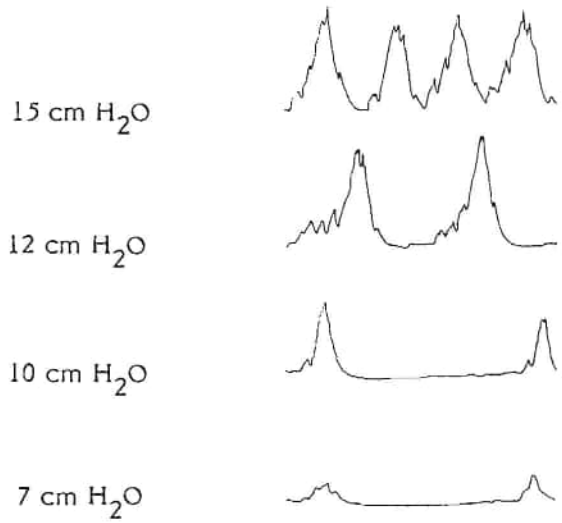
Follow-up of Clinical Material

The patients were asked to record the micturition frequency during 48 hours every month during the treatment period. The consumption of pads was noted. Urodynamic assessments were performed every 12th month.

RESULTS

Animal Experiments

At intravesical pressures below 5-7 cm H_2O there was little or no pelvic nerve activity at higher pressure levels the neurons discharged in 10-15 second long rhytmic bursts separated by silent periods (see Fig). The nervous activity preceeded a small bladder contraction indicating that the bladder response was caused by the efferent discharge. Prolonged continuous efferent activity could occur immediately after pressure changes and at pressures above 20-25 cm H_2O. Rhytmic activity resumed after the tonic discharge. This behaviour indicates that the rhytmicity is primarily determined by a central inhibitory mechanism. Intravaginal electrical stimulation or pudendal nerve stimulation of sufficient intensity caused a complete inhibition of the efference and as a concequence a profound bladder relaxation. The inhibition outlasted the stimulation by several minutes.
Intravaginal stimulation or pudendal nerve stimulation also induced a reflex activation of the hypogastric efference. The latency of the response varied between 35-150 mS. This means that with stimulation of 10 Hz the reflex discharge after one stimulus often encroached upon the early part of the next stimulus cycle. The reflex responses were optimally developed at a stimulation frequency below 5 Hz. Bladder response to direct stimulation of hypogastric nerves revealed that optimal bladder inhibition was also obtained at 5 Hz stimulation. Thus, both the central and peripheral part of the hypogastric reflex pathway seem to be tuned to respond optimally at about 5 Hz (6).



Integrated activity of the pelvic nerves at different intravesical pressures

Clinical Material

Nine women with detrusor instability achieved primary reeducation, i.e. continence and normalisation of frequency and urgency after withdrawal of stimulation for more than 6 months. Recurrences were noted in 3 women: in one of them after less than one year, in another after 2 years and in the third partial recurrence after 3 years. Six patients still remain free from symptoms one to six years affter withdrawal of stimulation. Five patients were free from symptoms during treatment (control of incontinence). Withdrawal of stimulation resulted in recurrence of symptoms. Four patients were substantially improved during treatment but did not achieve perfect continence or normalisation of urinary frequency. Recurrence was noted after interruption of treatment also in these patients. In two patients no effect of treatment was noted. Three women with mixed stress-and urge incontinence presented reeducation but recurrence was noted after 1½ year in two of them. The third one is still free from symptoms 3½ years after withdrawal of stimulation. Control of incontinence was obtained in four women and three patients were improved during stimulation (12).

DISCUSSION

The rhytmic contractions observed in the experimental animals are determined by a central inhibitory mechanism: the bladder is equipped with a self-sustaining positive feedback system, operating so that an intravesical pressure increase may give a reflex contraction of the detrusor through an afferent discharge. This further increases the afference with an enhanced and prolonged contraction. The positive feedback system ensures complete bladder emptying during the micturition contraction. Positive feedback systems are excellent to obtain a sustained and amplified nervous activity but they may at the same time be rather unsafe since they easily become unstable. To prevent this they are usually controlled by inhibitory mechanisms. The central reflex mechanisms involved in this control are essentially unknown and may be quite complex including both a segmental polysynaptic reflex pathway and reflex loops via supraspinal structures (13-16).

Small bladder contractions can also be observed in humans. Such contractions can occur without urge symptoms or incontinence but become clinically significant when beyond proper control (unstable bladder). The overreactivity of the detrusor in patients with unstable bladder may be caused by ineffecitive inhibition of the positive feedback system described in animal studies. This system, however, can be influenced by pelvic floor stimulation.

The long-term effects on detrusor instability observed in our clinical material are more difficult to explain than the immediate effects during an ongoing electrical stimulation. Replacement and modification of synapsis within the central nervous system might be involved in the curative process. It is tempting to propose that disturbances of slow changing systems could be involved in the development of detrusor instability and that electrostimulation normalizes this condition by influence on these systems.

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ELECTROSTIMULATION OF THE CONUS IN A PATIENT WITH PROLONGED BLADDER AREFLEXIA

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SUMMARY

Persistent bladder areflexia is very uncommon following traumatic spinal cord injuries with preservation of the conus area. In such rare cases, the Nashold (1) method of electrical stimulation of the conus is applicable and preferable to indwelling or suprapubic catheter if the patients cannot master self-catheterization.

This communication describes the long-term course in a paraplegic patient who has used conus stimulation to achieve bladder emptying for seven years.

CASE REPORT

A 42 year-old male sustained a complete transverse lesion at the C6 level in July, 1975. His lesion remained complete. Four months after the accident he developed some spasticity in the legs but his urinary bladder was completely flaccid. Ten months after the accident the bladder was still flaccid. Sphincterotomy was performed but still the patient could not empty his bladder. Because of his neurological deficit he could not manage self-catheterization. In this situation conus stimulation, according to Nashold, was considered to be an appropriate procedure.

The device (Avery Laboratories Inc) consists of 2.5 mm insulated platinum electrode pins with 0.5 mm bare tips, mounted 2.5 mm apart on a holder and connected to a radio receiver activated by an external radio frequency transmittor. An alternate pulse signal is delivered to the electrones. The frequency, pulse width and stimulation voltage can be varied.

Before the permanent implantation, test stimulation was performed by means of two electrodes which were inserted percutaneously and placed anteriorly and posteriorly to the conus region (Fig. 1).

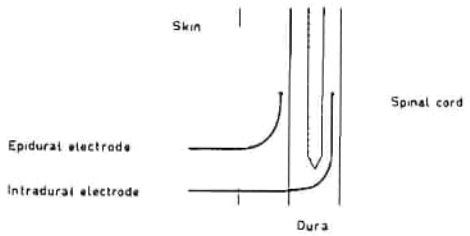


Fig. 1
(For explanation, see text)

Stimulation via these electrodes resulted in a bladder contraction. This was considered to prove that conus stimulation would be successful.

A permanent implantation of the conus stimulator was performed in May, 1976.

Two days postoperatively the bladder was filled with 500 ml Ringer solution. The catheter was withdrawn and at stimulation the patient emptied 250 ml. Urethral pressure profile with and without stimulation showed a small area, giving a marked increase of urethral pressure during stimulation. Another small sphincterotomy was performed at this site. Stimulation now resulted in a better emptying of the bladder with only 50 ml of residual urine. The patient could further reduce his residual urine by repeating the stimulation procedure. In such a way he could empty his bladder almost completely by three sequences of stimulation.

A frequency of 33 Hz was most appropriate. If the stimulation strength was increased slowly it was found that the output voltage required for bladder contraction was generally lower than that producing motor activity in the limbs.

The stimulation equipment has been functioning successfully during seven years since the implant. The patient has had periodic bacterurias but no upper urinary tract complications. He has been followed regularly with cystometries.

In 1982 - seven years after the implant - the situation changed dramatically, and he showed a fully developed micturition reflex on the cystometrogram. This means that he is now able to empty his bladder by external stimulation and his stimulation equipment is no longer necessary for bladder emptying.

DISCUSSION

Extensive sphincterotomy and condom treatment have been advocated in patients with neuropathic bladders but it is doubtful whether this procedure would be adequate in a patient with an acontractile bladder and without any possibility of increasing the intraabdominal pressure by straining. Our patient certainly had to wear a condom since leakage could occasionally be induced by strong movements. This has been a minor problem, however, and he has emptied his bladder at convenient times, which is of importance to him because of his very active life.

Obviously, the long-term stimulation did not damage the conus area, as evidenced by the return of the micturition reflex seven years after implantation. The late return of the micturition reflex is remarkable in itself. It means that synaptic reorganization in the isolated spinal cord segment took place seven years after a transverse lesion. A question which cannot be answered is whether the implanation of the conus stimulator and the stimulation have delayed the return of the micturition reflex or whether the stimulation has possibly created conditions for its return.

In another paraplegic patient we have simplified the technique for conus stimulation. The patient had an areflexic bladder one year after a complete traumatic cervical lesion. We introduced two electrodes in accordance with the test stimulation procedure described above (Fig. 1). The wires from the electrodes were passed through a subcutaneous tunnel to a lateral exit point, 10 cm lateral to the original incision and connected to an external pulse generator. Using this equipment the patient could empty his bladder by intermittent stimulation.The patient developed a reflex bladder after 3 weeks of stimulation, but the detrusor reflex was not sufficient for adequate emptying. During a period, when the stimulation did not function due to technical reasons, the bladder became again areflexic but a reflex bladder was restored when the stimulation had been working again for about one week. Eventually he could manage adequate bladder emptying by suprapubic tapping and the electrodes were withdrawn.

This course supports the hypothesis that electrical stimulation of the conus fascilitates the development of a reflex bladder.

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THREE TYPES OF ELECTRICAL STIMULATORS FOR THE CURE OF URINARY DISORDERS

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SUMMARY

For the cure of urinary disorders, three types of stimulators techniques which uses noninvasive methods find practical applications:

1. The electrical stimulators for cure of urinary stress incontinence with vaginal or anal plug for chronical use
2. The acute maximal functional electrical stimulator for the cure of the urinary urge incontinence for clinical use
3. The electrical stimulator for home treatment of relapse cases of urge incontinence after the clinical treatment by acute maximal electrical stimulation (AMFES).

The three types of electrical stimulation tecniques are clinically proved. The results of treatment showed succesful improvements in the condition of patients in more than 80 % of the cases. More than a thausand patients have been treated in the Ljubljana University clinical centre. The treatment includes the gynaecological and/or urological, neurophysiological, and urodynamic examinations. The treatment by electrical stimulation for the cure of urinary disorders is now an estabilished procedure in our centre. The above mentioned stimulators are commercially available.

METHODS AND TECHNIQUES

Electrical Stimulators with a Vaginal or Anal Plug

Hopkinson and Lightwood first described the possibility of stimulating closing muscles of the urinary tract intra-anally ond intravaginally in 1967. The first vaginal stimulator was developed by De Soldenhoff and McDonnell in 1969 /1/,/2/, and the anal type by Glen in 1969 /3/.

Electrical stimulators for treating urinary incontinence with a vaginal or an anal plug are nonimplantable and consist af an external unit generating the impulses and the electrodes attached to the vaginal or the anal plug.In 1972 vaginal electrical stimulators were available commercially. The success rates in treatment were often quite poor owing to the unsuitable form and frequency of the stimulation impulses.

Subsequently several vaginal or anal stimulators have been developed for clinical use. They were constructed in such a way that the electrical stimulation impulses could be changed. The joint scientific research done by physicians and engineers in the urodynamic laboratory of the Clinical Center in Ljubljana, Yugoslavia, were the tests of the efficiency of stimulation through the vaginal or the anal plug were done, established the fact that the exact duration and form of the electrical current are extremely important

Vagicon and Recticon

Two types of stimulators have been constructed as a result of research- VAGICON and RECTICON.

VAGICON is a nonimplantable electrical stimulator for the treatment of urinary incontinence in female patients. It consists of an external unit containing the electrical circuit, the battery, and the vaginal plug with the electrodes, connected by an electric wire to the external part. The patient can adjust the electric current with the aid of a potentiometer found on the external unit. A button is used to swich the apparatus on and off. The patient herself inserts the vaginal plug.

RECTICON is a electrical stimulator with an external unit identical to that of VAGICON. The plug itself is constructed tor the anal stimulation. Three different sizes of anal plug are obtainable. Recticon is meant for the treatment of urinary incontinence in both male and female patients. Both types of stimulators are to be prescribed by a gynecologist or a urologist following medical examinations. Figure 1 shows an external unit of the aparatus; on the left is the box and on the right the electronic circuit with the supply battery. Both vaginal and anal stimulators have an identical external unit.

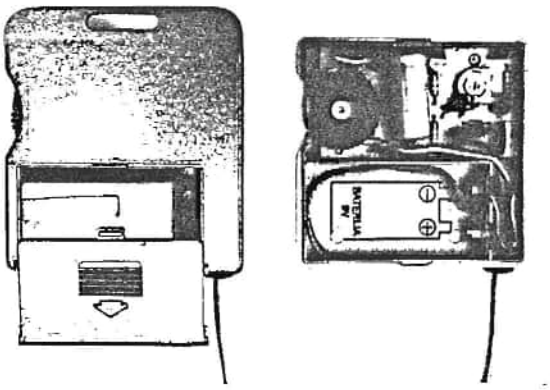


Fig. 1. The external unit

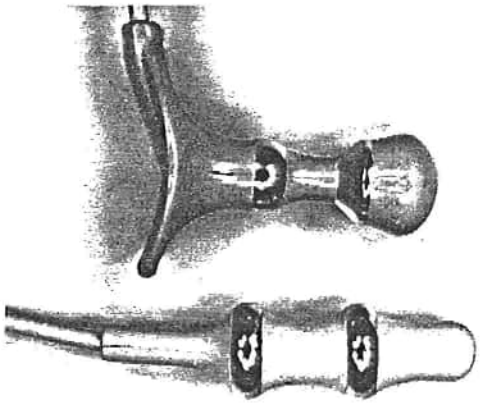


Fig. 2. The plugs

The physiologic needs, and results obtained by stimulation required the development of both a vaginal and anal plug. The plugs are made of silicon rubber and the electrodes of special stainless steel.

New Systems

As already mentioned nonimplantable stimulators are most widely used today for electrical stimulation of the urethral closing muscles; however, recent technical advances have improved the function and reliability of nonimplantable electrical stimulators. In addition to the plug or electrodes, these systems have an external unit containing an electronic circuit and power supply. The external unit is usually a large or small box, which is a drawback in that it detracts from personal appearance, especially of female patients. This disadvantage necessitated the development of electrical stimulator systems without an external unit.

VAGICON-X, an Automatic Vaginal Stimulator

The efforts to eliminate an external unit resulted in the construction of the automatic vaginal electrical stimulator VAGICON-X. The device consists of plastic housing in which the battery supply and the electronic circuit areplaced. The housing has the form of a vaginal plug. The electrodes are placed asymetrically along the plug in such a way that the first electrode lies as near as possible to the exit inits position in the vagina. This position results from the research on the efficiency of the stimulation of the urinary tracts closing muscles. The plug is equipped with a cord at the exit side, by which means the stimulator can beextracted. Physical dimensions of the VAGICON-X are determined by the dimensions of the battery and the electronic circuit. The stainless steel electrodes have a convex shape to provide a better contact with the tissue to be stimulated.

In Figure 3 an automatic vaginal electrical stimulator is shown, with its supply battery.

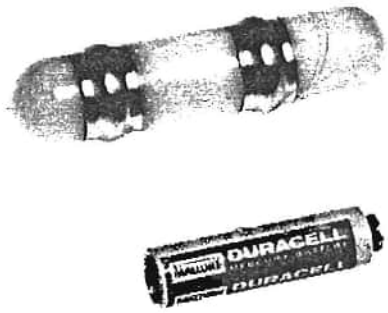


Fig. 3 VAGICON-X



Fig. 4 RECTICON-X

The success of treatment depends on a careful selection of patients suitable for the treatment. Patient history, gynecologic, urologic, urodynamic and neurophysiologic examinations are carried out on all patients in order to make a suitable selection. Provided that patients are suitably selected and that there are no serious contraindications, treatment can be expected to be 80 % successful.

RECTICON-X, Automatic Anal Electrical Stimulator

The device is built into a plastic housing containing a supply battery and electronic circuitry. The housing has the shape of the anal plug shown in Figure 4. The anal mucous tissue in contact with the electrodes represents an electrical load of 100 ohms to several kohms, with parallel capacity up to 20 microF. This load value allows perfect functioning of the stimulator. The electrodes are fixed to the neck of the stimulator, which lies on the anal sphincter. Bouth automatic electrical stimulators VAGICON-X and RECTICON-X have been successfully implemented several thausand times for the cure of urinary incontinence in humans.

ACUTE MAXIMAL FUNCTIONAL ELECTRICAL STIMULATION (AMFES)

For the AMFES a stimulator that generates rectangular impulses is used. The duration of single impulse was 1 msec.; their frequency is 20 Hz. Three different kinds of electrodes are used: anal and vaginal plug electrodes and needle electrodes applied to the pelvic floor muscles. In Table I the range and the mean values of current and voltages applied to 25 patients are shown. The current applied to the patient was increased to the limit at which the pain elicited by the stimulation could still be borne by the patient. The pelvic floor muscles have been stimulated simultaneously with all three pair of electrodes. Some time just one pair of electrodes are used. The AMFES is applied for 15 to 27 min. The pain evoked at the beginning of the stimulation tended to diminish at the end of the session. There is a double influence of FES applied to the pelvic floor muscles: these muscles contract, whereas the activity of the detrusor muscle is inhibited. The bladder capacity increased during and after AMFES had been terminated /4/. This constituted the essential point in treatment of urgency incontinence. The mechanism of urge incontinence improvement after AMFES is not clear. The possible alternatives are the facilitation of the supraspinal neuron or the direct action upon the lower motor neuron. After AMFES voluntary control of the lower motor neuron improves.

Anal plug	6–25 V U = 12.32 V	20–70 mA I = 32.5 mA
Vaginal plug	7–24 V U = 12.86 V	30–70 mA I = 45.7 mA
Needle electrodes	7–30 V U = 14.68 V	6–40 mA I = 15.8 mA

Tab. I Parameters for AMFES

TREATMENT OF INCONTINENCE RELAPSE CASES BY VAGICON-X-AMFES

Urinary urge incontinence is known to be successfully treated by the clinical AMFES therapy In properly selected patients more then 90 % improvements of CMG can be achieved as a consequence of the electrical inhibition of detrusor hyperreflexia and by this detrusor stability and continence /5/. After the clinical treatment, relapse is often observed within one week to six months. Repeated treatment do not require repetition of patient examinations. The patient can continue her treatment at home using the specially made stimulator VAGICON-X-AMFES or VAGICON-AMFES producing the stimuli with parameters necessary for the treatment of motor urge incontinence - peak value up to 100 mAmps.The stimulators VAGICON-X-AMFES and VAGICON-AMFES have been clinically tested in the cases of short term relapse of urge incontinence. After each treatment the bladder capacity increased and detrusor spasms disappeared.

RESULTS

Results of treatment are shown on Table II for a group of stress incontinence patients, and on Table III for a group of patients suffering from urgency incontinence.

Table II. Results of Therapy of Female Patients with Stress Incontinence

Cured	40	59.7%	82.1%
Improved	15	22.4%	
Without effect	12	17.9%	
Total	67	100%	

Table III. Clinical Results of AMFES Treatment in a Group of Female Patients with Urge Incontinence 6 Months After Stimulation

	Number of Patients	*Per Cent*	
Cured	35	62.5	
Improved	16	28.5	91
Unchanged	5	9.0	
Total	56	100	

DISCUSSION

Three types of electrical stimulators techniques described, which use noninvasive methods are clinically proved. The treatment by these methods is now an estabilished procedure in Ljubljana Clinical Centre.

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THE RESULTS OF TREATMENT OF FEMALE URINARY INCONTINENCE BY FUNCTIONAL ELECTRICAL STIMULATION

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SUMMARY

The results of treatment of female urinary incontinence by functional electrical stimulation (FES) are described.

Results of the treatment by FES depend on: indications for treatment, selection of the patients, parameters of stimulation and mode of stimulation. The most frequent indications for treatment by FES are stress urinary incontinence, urge incontinence, mixed (stress and urge) incontinence, recurrent incontinence after operative treatment and some types of urinary incontinence caused by neurogenic bladder.

Especially satisfactory results in treatment by FES occure in urinary frequency (without pathoanatomic substrate - 88%). The results of treatment depend mainly on the appropriate selection of patients. For selection of patients the following procedures are suggested: the patient's history, gynecological examination, urological examination, urodynamic examinations and neurophysiological examinations. Parameters of stimulation which are used: the impulse is rectangular and monophased, the frequency of impulse is 20 Hz, duration is 1 msec, current is 30-120 mA. For treatment of urinary incontinence stimulators of pelvic floor muscles or acute maximal functional electrical stimulation (AMFES) is used. Stress incontinence without anatomical changes and recurrent stress incontinence are treated by FES in a mode of a chronic stimulation whereby stimulators of pelvic floor muscles are applied. A good succes has been achieved in 73% of the patients. 81,9% patients with urge incontinence are cured or improved by treatment with AMFES. In mixed incontinence in 76% of patients succesful results are achieved. However, the results of FES treatment are worse in the cases of neurogenic bladder (only 5o% are cured or improved).

MATERIAL AND METHODS

Functional electrical stimulation (FES) can be used for treating urinary incontinence in two ways: by chronic, i.e. stimulation of longer duration or by acute, i.e. one time stimulation. The type of incontinence determines which of the two methods of stimulation will be used. In the treatment of urgent incontinence good results have been obtained by acute maximal functional electrical stimulation (AMFES); in stress incontinence, however with disfunction of retention mechanism of the bladder, good results have been obtained by chronic stimulation.

In our country the following parameters are used in FES of the pelvic floor muscles: the impulse is rectangular and monophased, the frequency of impulse is 20 Hz, duration is 1 ms, the current used changes according to the type of incontinence.

Female patients may use stimulators temporally or continously. Occasional or constant use of the stimulator depends on the nature of illness, the degree of incontinence, and particularly, on the results of the treatment. The stimulator is applied twice in a day for 1,5 to 2 hours. Longer and more frequent daily applications are not needed. By this method of application (twice a day) the pelvic floor muscles can be sufficiently strengthened and the reflex arch improved. The stimulator has to be used regularly at least three or four months. In some women already after this period, such favour-

able results are obtained that further application is not needed. In recurrence, the patients have to apply the stimulator again. Other patients, however, have to use it constantly.

AMFES is used only in laboratories,clinics and hospitals. It is applied by two electrodes - vaginal and anal.The third,the needle electrode, is no longer in use because higher currents cannot be obtained by it. The current on both the electrodes depends on the peak of sensibility. When the highest point has been reached that the patient still tolerates, i.e. between 80 to 120 mA, the current is no longer increased.

Stimulation lasts 20 minutes. In the first minute it is painful for the patient, later the pain is no longer felt (Kralj 1977 a, Kralj 1979).

In the last time special stimulators for selftreatment at home for AMFES treatment are produced. They are produced with vaginal and rectal plug (vagicon-AMFES, recticon-AMFES) and they are automatic and nonauotmatic. We use them especially for selftreatment of recurrent urge incontinence which occures in 26% of treated patients.

Indications for treatment

1. Stress incontinence:
   a. stress incontinence without a pronounced descensus of the vagina
   b. recurrent stress incontinence following surgery
   c. stress incontinence following radical therapy of gynecological carcinoma
2. Urge incontinence:
   a. motoric urge incontinence
   b. sensoric urge incontinence
3. Frequency
4. Vesico-urethral dissynergy
5. Neurogene bladder (some types of incontinence)

There are no absolute contraindications.

Examinations for selecting patients with urinary incontinence for treatment by FES

1. Patient's history
2. Gynecological examination
3. Urological examination with urethroscopy
4. X-ray examinations
5. Urodynamic examinations
6. Neurophysiological examinations
7. Trial application of functional electrical stimulation

RESULTS

Results of treatment of stress urinary incontinence by FES:

Cured	56 patients or	5o,5%	82 patients or 73,9%
Improved	26 patients or	23,4%	
Unsuccesful	29 aptients or	26,1%	
Total	111 patients	100,0%	

Results of treatment of urge incontinence by AMFES:

Cured	69 patients or	59,5%	95 patients or 81,9%
Improved	26 patients or	22,4%	
Unsuccesful	21 patients or	18,1%	
Total	116 patients	100,0%	

Results of treatment of mixed incontinence (recurrent stress + urge incontinence):

Cured	24 patients or	57,2%	32 patients or 76,2%
Improved	8 patients or	19,0%	
Unsuccesful	10 patients or	23,8%	
Total	42 patients	100,0%	

Results of treatment of frequency ba AMFES:

Cured	11 patients or	68,8%	14 patients or 87,5%
Improved	3 aptients or	18,7%	
Unsuccesful	2 patients or	12,5%	
Total	16 patients	100,0%	

Results of treatment of vesico-urethral dissynergy by AMFES:

Cured	3 patients
Improved	1 patient
Unsuccesful	2 patients
Total	6 patients

Results of treatment of urinary incontinence caused by neurogenic bladder:

Spina bifida 6 patients (3 cured, 1 improved, 2 unsuccesful)
Incontinence connected with paraplegia 5 patients (2 improved)

DISCUSSION

In spite of numerous possibilities of treatment of female urinary incontinence the treatment by functional electrical stimulation (FES) is of an ever increasing value.

Results of the treatment by FES depend on:
1. Indications
2. Selection of the patients
3. Parameters of stimulation
4. Mode of stimulation

Results of the therapy by FES are satisfactory. They are better than those obtained by conservative treatment used to date - by physiotherapy, i.e. Kegl's exercises (Brown 198o). The success of the treatment by FES is quicker than by physiotherapy. In recurrence or deterioration following the treatment by FES the therapy by stimulation is repeated. Results of the treatment by FES are particularly satisfactory in women with stress incontinence without major anatomic changes. In these patients, results obtained by surgery are less satisfactory. The mode of treatment is particularly favourable for recurrence of stress incontinence following surgery and, in stress incontinence following radical gynecologic surgery due to gynecologic carcinoma or following radiation therapy.

Results of the treating urgent incontinence by AMFES are particularly favourable ((82%) and are better than the medicamentous treatment used to date. Success or failure of this mode of therapy can be assessed already during the application of AMFES. In the patients with urgent incontinence, the success of the therapy depends on changes of the cystometric curve, obsérved during the application of AMFES. In the patients where no changes in the cystometric curve are observed during AMFES success of the therapy cannot be expected.

However, the results of FES tretament are worse in the cases of neurogenic bladder (only 5o% are cured or improved). In these cases the recurrences are very common.

In 26% of female patients AMFES was once or several times repeated. AMFES was especially frequently repeated in cases of neurogenic lesions of bladder. In patients with the neurogenic lesions of bladder a recurrence occures very soon that is after one month or even after one week. An improvement in incontinence between the one and the other stimualtion is, however, in such patients to be considered a great success.

The question is raised why in some kinds of incontinence the spinal cord respectively the micturition centre or reflexogenic arch are able to retain an appropriate micturition reflex constantly or for longer period and why on the other hand in some other kinds of incontinence this reflex is retained only for a short period or it is not retained at all. For the time being this question cannot be answered.

A proper selection of the female patients with urinary incontinence is essential for an appropriate choice of the treatment. Urodynamic examinations have a decisive significance. Only on the ground of a proper selection good results can be achieved.

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MAXIMAL ELECTRIC PELVIC FLOOR STIMULATION FOR THE TREATMENT OF URINARY INCONTINENCE

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SUMMARY

Acute short-term maximal electrical self-stimulation (MES) of pelvic floor muscles was clinically tested in 264 patients with different types of urinary incontinence. Good clinical results were obtained in nearly half of the patients. Urodynamic investigations (UPP, CMG) which were done before, during and after MES showed increased values of urethral pressure in patients with stress incontinence who were successfully treated as well as elimination of uninhibited bladder contractions in patients with unstable bladder. Because MES of pelvic floor is a simple, harmless, effective and not expensive it is recomended as a first treatment of various types of incontinence.

MATERIAL AND METHODS

In 264 patients with urinary incontinence of different types (Table I) acute electrical stimulation was applied to the pelvic floor via anal (males) and vaginal (females) plug electrodes. Monophasic square current pulses of 1 ms duration, pulse rate of 20 Hz were used, the current ranging from 15 to 100 mA and the duration of one session was 15 to 20 minutes. The patient was asked to adjust the intensity of stimulation up to level of tolerable discomfort all the time during the stimulation (MES - /1/). Urodynamic measurements (urethral closure pressure profile - UCPP and cystometry - CMG) were performed in supine position before MES, during the first application of MES, and at the end of the observation of the patient. MES was repeated 3 to 4 times in the first month and the effects observed 12 months later.

RESULTS

In the group of patients with stress incontinence in whom MES was not successful the difference in MUCPP before and after stimulation was unsignificant.
The values of CMG (first sensation, maximal cystometric capacity) were increased after the stimulation, but the difference was not statistically significant even in patients with exellent result.
Only in the cases of motor urge incontinence, the elimination of the uninhibited bladder contractions during the first application of MES and after MES was correlated to the success of the treatment with MES.
In four cases the patients noticed better bladder sensation and in three cases suprapubic pain disappeared after the stimulation.

TABLE I: Clinical effects of electrical stimulation in different groups of patients

Type of disorder	Clinical effect				
	Excellent	Gradual improvement	Temporal improvement	Failed	Total number
STRESS INCONTINENCE	15	23	6	36	80
URGE INCONTINENCE	10	20	5	32	67
STRESS AND URGE INCONTINENCE	6	15	3	27	51
REFLEX NEUROGENIC BLADDER	3	10	5	12	35
AUTONOMOUS NEUROGENIC BLADDER - CENTRAL - PERIPHERAL	1 2	1 0	0 0	5 1	7 3
POST-PROSTATECTOMY INCONTINENCE - STABLE - UNSTABLE	2 6	0 1	0 0	8 4	10 11

EXCELLENT — the patient was cured after first or second stimulation

GRADUAL IMPROVEMENT — the patient was cured or significantly improved after the fourth stimulation

TEMPORAL IMPROVEMENT — stimulation produced minimal and short-term improvement

FAILED — stimulation was not successful

TABLE II: The values of maximal urethral closure pressure profile (MUCPP - cm H_2O) in a group of 22 patients with stress incontinence in whom the clinical effect was very good

Age (years)	Before MES	During MES	After MES	Signif.
$\bar{x}$ = 54 s = 11.8 17 - 72	$\bar{x}$ = 49 s = 25.3 20 - 140	$\bar{x}$ = 59.7 s = 32.3 20 - 160	$\bar{x}$ = 84 s = 29.7 30 - 120	$p < 0.05$

DISCUSSION

Using self-stimulation tehnique the patients were able to obtain a rather high intensity of stimulation (up to 100 mA) without significant discomfort. Despite the short-term application of electrical stimulation the effect could be long-term and satisfactory in about half of the patients. MES has the effects on urethral muscles, because MUCPP was significantly increased in patients in whom stimulation was successful and by regulation of some physiological mechanisms /2/ bladder function could be also improved. Bladder sensation could be better and suprapubic pain could be relived after the stimulation. Because MES is harmless, simple, effective and not expensive it should be used as a first method of treatment for various bladder and urethral disorders.

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INTRAVAGINAL ELECTRICAL STIMULATION AND ITS EFFECTS ON URETHRAL CLOSURE AND BLADDER INHIBITION

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SUMMARY

Electrical stimulation has been used as an aid in the control of urinary incontinence. Implanted electrodes or external (anal or vaginal) electrode carrier have been used (1,2,3). Stimulation is intended to activate the closing musculature of the urethra as well as to induce relazation of the urinary bladder sufficiently to prevent leakage of urine (4,5). The method with electrical stimulation has proven to be successful in about 70-80% of the treated patients. Most of the commercially available generators produce continous monophasic or biphasic pulses (6,7). The following study was performed in order to investigate the possibility of reducing the energy consumption, but still achieve sufficient effects on the urinary bladder and the urethra with respect to continence.

MATERIAL AND METHODS

Animals. The experiments were carried out on adult female cats. The animals were anaesthetized intraperitoneally. The arterial blood pressure was continously monitored. During the experiments, the animals were placed in the supine position. The urethra and bladder were exposed extraperitoneally through a low midline incision. A catheter was inserted in a distal direction and connected to a bottle with Ringers´ solution via a photoelectric drop counter, which registered the urethral flow rate. The flow rate was adjusted to give about 100 drops per minute (Fig. 1).

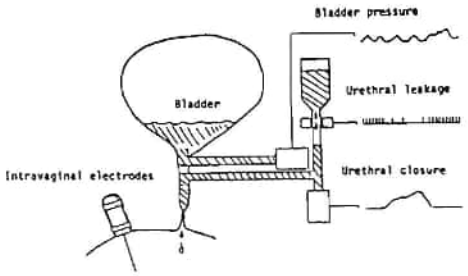


Fig. 1 The experimental arrangement.

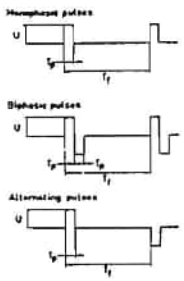


Fig. 2 Generated pulse patterns

Electrical stimulation. The intravaginal electrical stimulation was given from two circular stainless steel electrodes (5 mm apart) attached to a cylindrical plug, which was introduced into the vagina. The electrodes were connected to a stimulator by which the shape, duration, frequency and voltage of the pulses could be varied. The pulse patterns were visualized on an oscilloscope which allowed measurements of voltage and current. The effects of the stimulation i.e. bladder relaxation and/or urethral closure were displayed on an ink recorder. The pulse shapes tested are shown in figure 2.

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The stimulation was given for three minutes with ten minutes interval between consecutive stimulations.
The electrical parameters most appropriate for urethral closure and bladder inhibition were determined from strength duration curves. The measurements were carried out with various frequencies and pulse shapes. After the general pulse shapes were tested, different modulations were applied to the best pulse shape in order to find out if there was any possibility to decrease the power consumption but achieve the same therapeutic effect. The modulated pulse shapes are shown in figure 3.

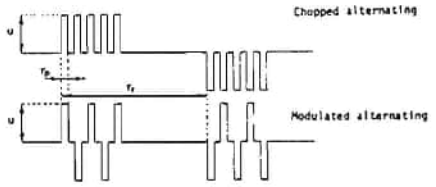


Fig. 3 Different pulse patterns generated in order to minimize the power consumption in comparision to the alternating pulses.

The power dissipated was calculated according to

$$P_m = 1/T_f \int_0^{T_f} u(t) * i(t)\ dt$$

The different patterns were compared concening power dissipation and therapeutic clinical efficacy at the same amplitude in two consecutive stimulations with the different pulse shapes.

RESULTS

This study showed that the alternating pulse pattern was favourable to the monophasic and biphasic pulse patterns, both in respect to urethral closure and bladder inhibition. Experiments with different frequencies showed that the urethral closure was most pronounced at 50 Hz while the bladder relaxation was most pronounced at 10 Hz. The corresponding strength duration curves are shown (Figs 4 and 5). The optimal duration was about 5 ms.

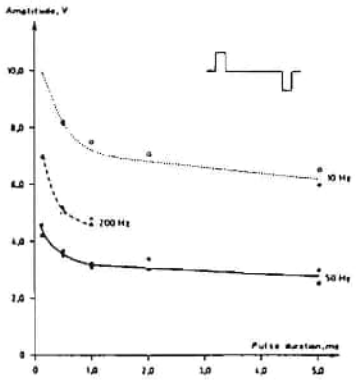


Fig. 4 Strength duration curves for urethral closure, alternating pulses and different frequencies.

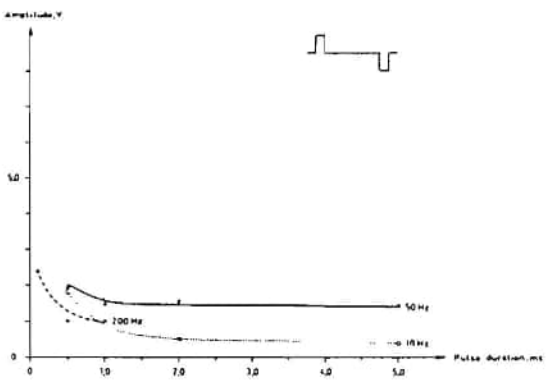


Fig. 5 Strength duration curves for bladder inhibition, alternating pulses and different frequencies.

When comparing the effect of the chopped alternating and the modulated alternating pulses with the alternating pulse shape with respect to urethral closure, the 50 Hz alternating pulse shape was found to be most effective in all cases compared with the modulated alternating pulse

shape and supperior to the chopped alternating pulse shape in 16 of 18 stimulations. The results of the therapeutic effect of the stimulation with the diiferent pulse patterns is shown in figure 6 (urethra).

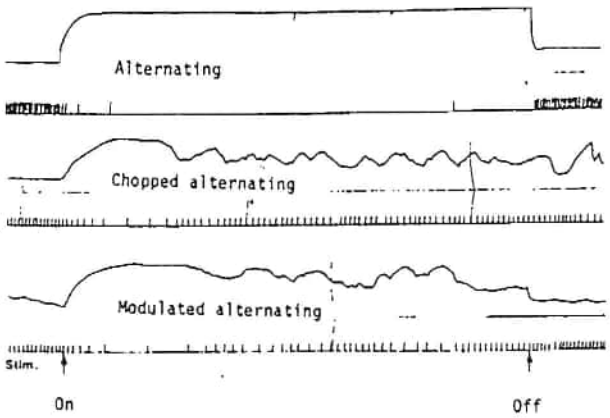


Fig. 6 Urethral closure and urinary leakage during IVS at 50 Hz.

Regarding the effect of the stimulation on the urinary bladder, the three curves indicate inhibition at a fundamental frequency of 10 Hz using the different pulse shapes to be of the same magnitude (Fig. 7).

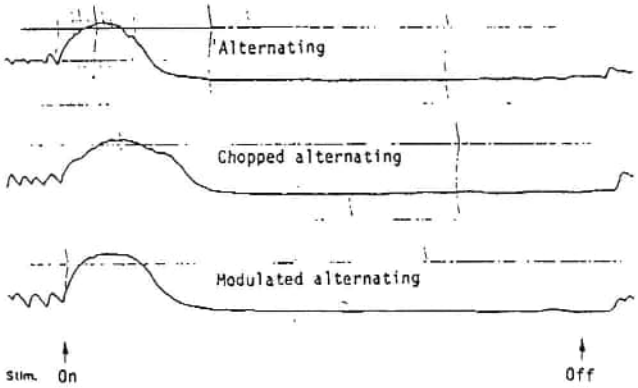


Fig. 7 Bladder relaxation during IVS at 10 Hz.

The power calculations showed that the power could be reduced with 46% and retaining the same therapeutic effect (inhibition) of the uriniary bladder, when using the chopped or modulated alternating pulse shapes. But the therapeutic effect (closure) of the urethra was less pronounced with the chopped or modulated alternating pulse shapes, when the power was 46% of that with the alternating pulse pattern.

DISCUSSION

During the experiments it was shown that the urethral closure was most effective when stimulating with alternating pulses. The therapeutic effectiveness on the urinary bladder was approximately the same for the chopped or the modulated alternating pulses. The power dissipation, however, was reduced considerably with the chopped or the modulated pulses as compared with stimulation with alternating pulses. The reduction could of the dissipated power was 46%. This reduction could be of importance during long-term treatment of patients with inconti--nence:

The energy source in the equipment delivering the pulses should last for a longer period of time; the batteries don´t have to be replaced

or recharged so often.
During long-term treatment it is important criterion that the stimulation do not cause tissue damage. The generation of heat and development of toxic substances through electrochemical reactions are two mechanisms which might cause damage (8). Therefore it must be advantageously to reduce the delivered energy to the tissue.

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EXPERIENCE WITH INTRAVAGINAL ELECTROSTIMULATION IN FEMALE INCONTINENCE

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The therapy of mixed stress-urge-incontinence has been disappointing because operation as well as pharmacotherapy often do not achieve satisfying results.Therefore,32 women suffering from mixed stress--urge-incontinence underwent intravaginal electrostimulation using the Contelle systeme (Gambro),since recently urethral as well as bladder responses have been reported by this technique (1,2).

MATERIAL AND METHODS

The average age of the female patients was 46,6 years (21-75).
8 women had bladder dysfunction presumably related to basic neurogenic diseases: 4 patients had a trauma of the lumbal spine and cauda equina syndrome,4 had a multiple sclerosis.24 patients had no neurological symptoms beside their bladder problems.
Urodynamic explorations were done in all patients before treatment as well as 10 weeks after the beginning.A control examination 1 month after treatment has been stopped is still going on.The urodynamic program included a normal water filling cystometry,incontinence histogram for incontinence staging (3),a micturition study,urethral pressure profile measurements at rest as well as under stress and for classifying the neurological damage we used the Lapides test (4).
Water cystometry was done in supine position with a filling speed of 50ml/min via a 2 channel 12F catheter.Provocation by cough happened every 2 min.Simultaneously intravesical and abdominal pressure,electronically substracted detrusor pressure and EMG of the sphincter ani were recorded.
The incontinence histogram was performed in stting position asking the patient to cough strongly and to perform valsalva maneuvers.The intravesical pressure was recorded by a 5F transurethral catheter. Beside the other parameters flow was registered with a modified DISA flowmeter where the damping was switched off.The flow curve was planimetered after examination.
For the urethral pressure profile we used a 12F 2 channel catheter with one channel open at the top and the other with 2 sideholes 6 cm below the top.The perfusion rate was 2ml/min,the catheter was withdrawn mechanically 1mm/sec.
The intravaginal electrostimulation was done daily for 8 hours during a time of at least 10 weeks.The stimulation was performed in intervals with an active phase of 10 sec. and a rest phase of 25 sec.The stimulation frequency was 20 hertz,the voltage was variable from 2 to 8V in accordance to the pain threshold of the patient.

RESULTS

In general electrostimulation has been tolerated well.1 patient however had strong sexual exitation and treatment was stopped.2 women reported unimportant bleedings from a narrow vagina after colposuspension resp. senile colpitis.Intelligence of the patients was required for cooperation and handling of the quite complex stimulator systeme: 4 patients gave up therapy mostly belonging to the group of less intelligent women because of shame or early disappointment.
Of the cauda equina patients only one showed objective improvement and became temporary continent.
The 4 multiple sclerosis patients achieved normalisation of residual urine and bladder capacity increased significantly.Urgency and frequency improved and the patients felt themselves cured from their bladder symptoms.
The 24 patients without neurological symptoms in general showed significant improvement: The urethral pressure profile increased in maximal closure pressure and planimetered area below the curve.However, in some patients the vaginal applicator seemed to provide a mechanical suspension effect to the bladder neck.Cystometrically bladder capacity and compliance increased and also hyperreflexia decreased.This effect was evident also after the end of treatment.

CONCLUSION

32 women suffering from combined stress-urge-incontinence underwent intravaginal electrostimulation.By this treatment bladder closure mechanism as well as bladder capacity and compliance improved and hyperreflexia decreased.The impact on bladder hyperreflexia seemed to last more constantly after therapy was finished than the effect on the bladder closure mechanisme.

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Stimulation of human median nerve with a random amplitude modulated pulsed signal

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Stimulation of peripheral nerves is usually performed employing a rectangular electrical stimulus of 0.2 msec, stimulating a rather broad spectrum of human afferent fibres. In order to stimulate more selectively, we used an amplitude modulated pulsed signal with a carrier frequency of 20'000 Hz and a pulse envelope of less than 0.5 msec (O.M.Wyss 1963). In 4 healthy subjects in whom the left median nerve at the wrist was stimulated, somatosensory central conduction time (difference in latency between the main negative potential at the neck and the negative response of the contra-lateral scalp) was consistently shorter, compared to stimulation with a rectangular pulse. Moreover, stimulation performed with this amplitude-modulated pulse was reported by all subjects to be more agreeable, suggesting immunity of pain fibres to this stimulus. A selective stimulation of fast conducting afferent fibres is also suggested by the shorter somatosensory central conduction time. Noninvasive selective stimulation of specific peripheral nerves in humans may be possible using similar such pulses.

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The Effect of Electrostimulation of Sciatic Nerve on Upper Airway Dilating Muscles and Diaphragm Activity.

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The effect of electrostimulation of sciatic nerve (ESCN) on the moving average electromyogram activity of upper airway dilating muscles (UADM) — alae nasi (AN), genioglossus (GG) and posterior cricoarytenoid (PCA), and diaphragm (D), was studied in seven anesthetized, tracheotomized dogs during breathing 100% O_2, 3.5% and 7% CO_2 in O_2. At all levels of chemical drive ESCN resulted in an increase of phasic inspiratory activity of three UADM and tonic activity of GG and PCA, with or without change of D activity. Increasing the intensity and duration of electrical stimuli progressively increased the activity of UADM and D, but at any level of stimulation UADM activity increased more than D activity. These findings suggest that reflexes initiated by changing somatosensory activity can result in uneven distribution of respiratory drive and preferential activation of UADM.

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EM-STIMULATION OF NEURAL TISSUES

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SUMMARY

A worldwide controversial discussion has been raised by the question whether nonionizing electromagnetic-radiation below thermal threshold levels can show effects on nervous structures or is able to alter functional pathways of the central-nervous-system. Recent research suggests the possibility of extracorporeal stimulation of nervous structures by EM-radiation, but basic interaction-patterns, that lead to better understanding of effects observed, have yet to be found.

Since several researchers have reported the influence of electromagnetic fields on ion fluxes in neural tissues, an experimental system has been developed at the University of Strathclyde, Bioengineering Unit, allowing initial investigations of ELF-, LF- and LF-modulated RF-fields.

Utilizing clonal cell lines (L 929, PC 12, glia-cells) as an obvious choice for the development of physiological models, a perfusion chamber has been designed and tested that permits, when cascaded, a simplified simulation of regulatory cycles.

Preliminary observations of growth orientation and changes in cellular morphology are described.

METHODOLOGICAL CONSIDERATIONS

The goal of the present investigations is to gain more knowledge and evidence about interactions of non-ionizing EM-radiation with nervous structures, thus finding an explanatory model for observations described and other "unclear and unspecific" symptoms reported.

When detailed data on stress-specific microreactions are lacking, a synthesizing approach for research is almost impossible. Therefore, it is more likely to gain fundamental information on specific stresses by analyzing the changes in functional behaviour of organisms.

It can be taken as a fact that the only realistic way to study EM-interactions with biological matter is by quantitative description of all parameters involved. Carelessness in this direction has led to misunderstanding or misinterpretation of results in the past.

"Without proper instrumentation or a clear understanding of how electromagnetic fields interact with the tissue on a microscopic and macroscopic scale or on the entire body structure, it is difficult indeed to say whether an observable effect may be thermal or non-thermal in origin or is merely an artifact due to the nature of the experimental approach." (Guy, 1972).

For proper correlation of experimental data, this indicates a quantitative description of all technical parameters of the experiments, and a clear pattern for medical evaluation of data.

A possibility of classifying data has to be a facility that tells, whether an effect observed is of thermal or non-thermal nature, followed by a description, whether the observed effect is reversible or irreversible. A further

classification would be whether observed effects are harmless (insignificant), harmful or beneficial.

The final goal of investigations is surely the answer to questions of effects on a human being. Our present investigations suggest experimental studies involving cell and tissue cultures. By this, an understanding of how fields at various frequencies and power levels or their electrical or magnetic parameters interacts with "basic functional biological units", is gained.

The benefit of this approach could be seen in results directly relatable to human physiology. The procedure is justified since cells of higher organized systems are basically pluripotential and, thus by their functional possibilities can partially represent more complex systems. On the other hand, a clearer pattern of effects on different structures will result since interactions of each cell type with radiant energy will likely be different (threshold levels, frequencies).

Systems organized at higher levels and, therefore, consisting of highly specialized and task-dedicated cell types, can be a serious drawback in fundamental analytical experiments because of cellular interactions, including the possibility of masking existing effects.

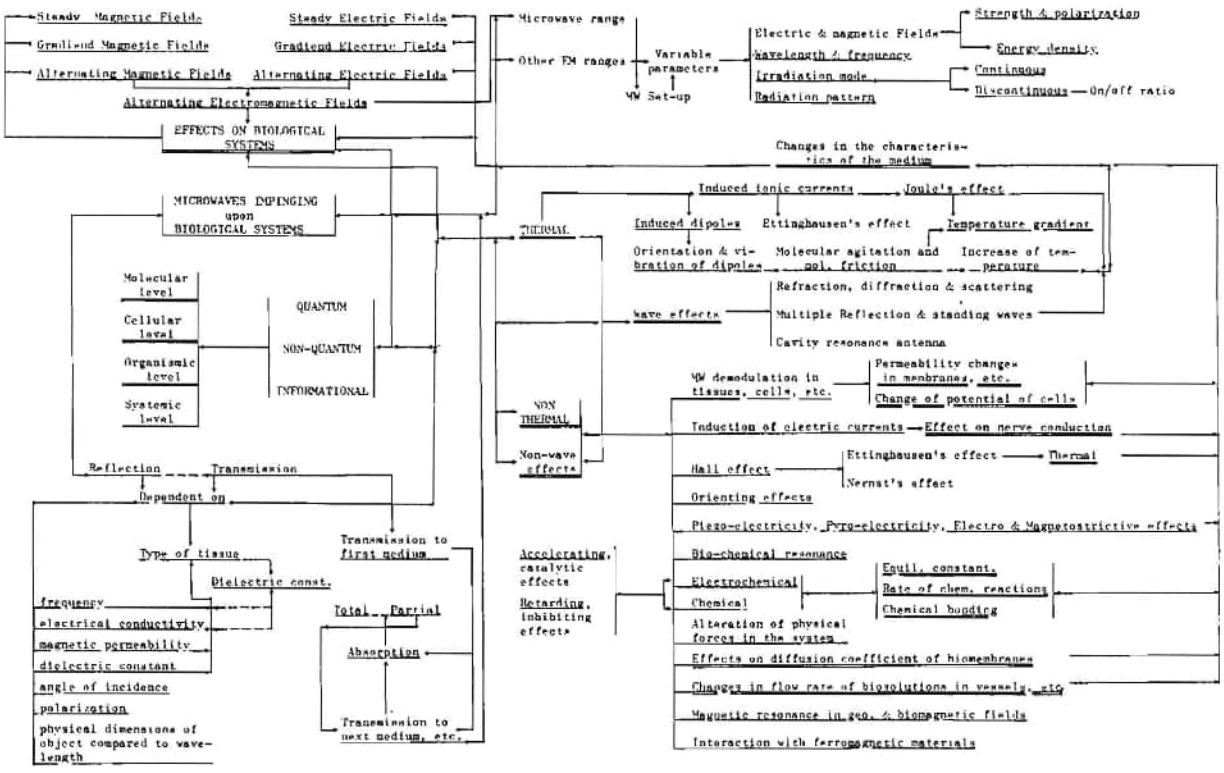


Fig.1 Interaction possibilities of various fields with living matter and experimental considerations to be taken into account.

EXPERIMENTAL METHODS AND INSTRUMENTATION

Successful experimentation can only be performed under completely controlled conditions. Experiments have to be performed in a way that any influencing parameter on the species under observation can be quantified. An effect observed can then be judged whether it is due to the variation of a parameter or an

artifact. This indicates either continuous monitoring of parameters or continuous measurement of all influencing parameters.

L 929 cells were available and used to develop an experimental system for detailed investigations on EM-interactions with neurotransmitter relase in nervous tissues. Although primary cell lines might be useful or required for some investigations, they have to be regarded as "disposable material". Latent infection or limited supply and the resulting necessity of special safety requirements limit the general suitability.

For the present investigation, established cell lines are preferable because then, the properties of the species are known. Furthermore, the choice of a cloned cell line, has the advantage of allowing work with cellular material of similar features. Selecting a suitable cell line with cells adhering to the substrate, monolayers can be grown in petri-dishes, culture flasks, culture tubes or perfusion chambers.

One of the basic parameters in satisfactory cell culture is the growth medium, which depends on the cell line employed. Even when using defined media, most in vitro work requires the addition of serum as a natural component. With L929 cells, Eagles's minimum essential medium (MEM) supplemented with 5% serum was used.

Considerations regarding the optical properties of the medium ought to be made. For optimum result, an optically homogeneous medium should be used. For optimum result, albumen can be added to the medium to equalize differences in the refractive indices, without harming the cells.

With the benefit of reduced danger of contamination, disposables dishes available are perfect for general routine because microscopical examination at low magnification is sufficient, but in the present research morphological examination of living cells is used as a diagnostic parameter, requiring high magnification, the possibilities are limited to special perfusion chambers with an optical performance superior to products industrially available.

The present cell growth system is machined of Perspex (ICI). For future applications Polycarbonate material or PTFE, because of easy sterilization by autoclaving, is suggested. Thermofoil heating elements with integrated temperature sensors (R=20 Ohm/Element)are mounted on top and bottom. When used as microscope stage incubator, the top of the chamber is replaced by a sterile base part of a conventional petri-dish, thus allowing easy access to the specimen. All materials used for the prototype or suggested for future applications have been tested for cytotoxicity.

Because of an optical performance superior to that of synthetic materials, No. 1.1/2 cover-slips are used as optical windows. By designing a chamber with a maximum width of 0.7-1mm, care has been taken so that the design can be used for microscopy with noninverted microscopes and microscopy with inverted microscopes.

Even though no perfusion is necessary in incubator applicatios since sufficient medium is provided to the cells, perfusion is possible and allows complex experiments.

For the present experiments, a simple exposure system for the frequency range of 100kHz-90MHz consisting of an oscillator, a modulator, a driver amplifier, a power amplifier and a resonance circuit has been developed. Power absorption and specific absorption rate (SAR) are determined by the temperature rise in a dummy chamber during a specified period. During an experiment, no heating of the specimen must occur.

OBSERVATIONS ON GROWTH ORIENTATION DURING SYSTEM TEST

During tests performed to check the suitability of the system designed and constructed L929 cells were inoculated in a 60mm diameter petri-dish or in the perfusion chamber in Eagle's MEM without nonessential aminoacids (NEAA). After three days, the cultures were examined by phase-contrast-microscopy and photomicrographs taken for the purpose of documentation.

During these tests changes in cellular orientation were observed. The cells seem to orient in the field they are exposed to loosen partially from the substrate and show the attempt to build formed structures.

DISCUSSION

We are aware that similar results can be obtained by imperfect cell culturing methods but, according to the observations, a relation to exposure seems to exist because cells of the same subculture, grown without exposure, show a perfect monolayer. Furthermore, disaggregating formed structures and culturing the suspended cells without exposure shows a cell growth similar to the growth in unexposed control cultures (random orientation).

More detailed studies would have to reveal if these initial observations of disturbed cell adhesion and cell formation are attributable to field exposure and, if so, in which way they are related to exposure to electromagnetic fields. Moreover, investigations of influences on cell membrane permeability to ions and determination of the rate of DNA-synthesis as indicator of metabolic activity would reveal more informational details about transient changes in cell physiology. Cinematographic time-lapse studies and cell cycle time measurements, together with a determination of changes in the mitotic rate, should give a sufficient base for conclusive data, upon which a more detailed investigation can be based.

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DEVELOPMENT OF A NON TIRING STIMULATION OF THE LATISSIMUS DORSI FLAP AS A MYOCARDIAL SUBSTITUTE

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SUMMARY

In recent years, a considerable amount of interest has been generated by the widespread use of the pedicled Latissimus Dorsi Flap (LDF) for reconstructive surgical problems. The LDF itself presents several advantages as a myocardial substitute: 1) its close proximity to the heart, 2) the large autologous muscular mass it offers, 3) the possibility of inserting it within the thoracic cavity. Previous studies however have shown that fatigue of the muscle and possible tetanisation may occur leading to inefficiency of the transplanted muscle. We have tried to obviate these drawbacks by stimulation preliminary to transplantation so as to prepare the muscle to it's new function.

Five multi-programmable pulse generators (PG) -Medtronic Spectrax- were implanted in the lateral thoracic wall in goats, with modified Spectraflex electrodes in the muscular mass. The PG were programmed in the following manner: rate 30 ppm, progressively increased up to 80 ppm; pulse width 2ms; sensitivity 5 mV; pulse amplitude 5V; mode asynchronous. After 6 months of progressive pacing, electrophysiologic studies were carried out so as to assess the function of the muscle.

MATERIAL AND METHODS

Five goats, race "alpine chamoisée", weighing 28,7 to 45 kg (mean weight 39,3 kg) were operated upon to determine the technical feasibility of this study. Goats were anesthetized with alfaxalone + alfadolone (Alfatesine, o,125 ml/kg/hour intravenously) Ventilation was maintained by a mechanical respirator-Bird Mark 7-.

The goats were placed in the left recumbent position and a cutaneous incision was performed at the level of the right 5th intercostal space. Dissection of the Latissimus Dorsi muscle from all of its superficial surface was carried out.

The muscle was first stimulated with an external variable PG, to determine the threshold level of stimulation. Muscle tension was assessed with a strain gauge (Jauge application - Massy - France), sutured to the muscle. After two hours of a continuous muscular stimulation, with a frequency of 40 ppm, the thresholds were redetermined.

Finally two electrodes (modified Spectraflex) were placed in the middle of the muscular mass (Fig. 1) and a multi-programmable PG (Medtronic Spectrax) was implanted and programmed in the following manner: rate 30 ppm, pulse width 2 ms, sensitivity 5 mV, pulse amplitude 5 V, mode asynchronous.

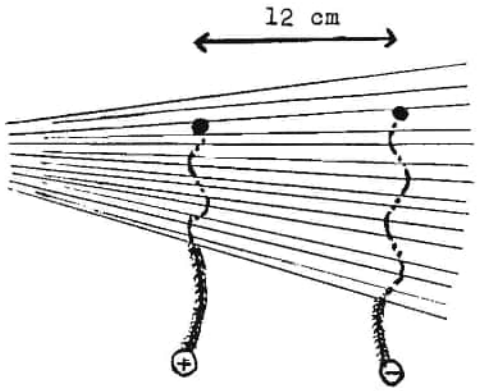
Postoperatively a progressive increase of the frequency of stimulation was performed (10 ppm every two weeks) with a non-invasive programmer (Medtronic Spectrax Model 9701). This experience was based on the principles of the skeletal muscular training.

After 3 months of progressive pacing, the muscle reached a frequency of 80 x minute. This rate was maintained for another 3 months.

RESULTS

No mortality and no morbidity resulted from the implantation of PG in the lateral thoracic wall in goats and its prolonged stimulation over Latissimus Dorsi muscles.

FIG. 1 : 10 cm naked electrodes implanted in the substance of the Latissimus Dorsi.



The excitability of the muscle was studied under general anesthesia in the five goats, and then post-operatively during 6 months in the stimulation programme.

The results of the threshold levels of muscular excitability (Table 1) showed that with this electrophysiological properties, it was possible to pace the Latissimus Dorsi.

Each goat was periodically followed and the external contraction of the Latissimus Dorsi was unchanged.

	INITIAL STIMULATION		AFTER TWO HOURS		AFTER SIX MONTHS	
PULSE WIDTH (mS)	PULSE AMPLITUDE (V)	THRESHOLDS (mA)	PULSE AMPLITUDE (V)	THRESHOLDS (mA)	PULSE AMPLITUDE (V)	THRESHOLDS (mA)
0,2	3,5	1,7	2,5	1,6	1,8	13
0,6	2	1,1	2	1,4	1,5	10
1	1,8	1	1,8	1,2	1,3	8,5
1,4	1,6	0,9	1,5	1	1,2	7,9
1,8	1,5	0,9	1,5	1	1	7,2
2	1,5	0,8	1,3	0,9	1	7
		1,07 ± 0,33		1,18 ± 0,27		8,93 ± 2,27

TABLE 1: Different thresholds of stimulation expressed in milliamperes (mA). Frequency of stimulation: 40 x minute.

DISCUSSION

The usefullness of the use of an autologous muscle in cardioplasty and the numerous problems to be solved in adult and pediatric cardiac pathology, led us to undertake this search on the possibility of left or right ventricular cardioplasty by means of a striated muscular graft (5) (7).

The transposition of a striated muscle to the ventricular myocardium must answer the following three surgical questions:

1) Will a Latissimus Dorsi graft provoke fatal or disabling post-operative thoracic pathology ?
2) What will be the relationship between the muscle and the myocardium ?
3) What is the histological evolution of the muscle ?

As well as two haemodynamic questions:

1) Does the left or right ventricle, on which the Latissimus Dorsi is grafted, have an output equal or better to that before the muscular transposition ?
2) Does the grafted muscle impede the normal heart during the diastolic filling ?

Through our previous research in dogs (4) we have replied to the preceding questions. The intrathoracic transposition of the Latissimus Dorsi has been satisfactory, with a normal post-operative evolution and good lung re-expansion.

The muscle-myocardium relationship and the histological muscular study have shown a good adaptability. The muscle structure was retained and a real anatomical and histological complex muscle/heart was formed.

The haemodynamic and EKG studies have also shown that the Latissimus Dorsi flap on the heart is not be likened to a chronic constrictive pericarditis, as the heart maintains its new output after muscular plasty.

One further question can be formulated: Will the left or right ventricular performance on a healthy and pathological heart be improved by a prestimulation of the grafted Latissimus Dorsi muscle ?.

In fact, the objective of the present study concerns the use of the preserved contractile properties of the muscular graft.

It is possible to stimulate the striated muscle, either directly (2) or by using its nerve (9), to obtain a phasic activity which integrates itself within the left or right ventricular kinetics, and this, in a prolonged fashion (1).

We have taken advantage of the existence, close to the heart, of a large striated muscle having a long vascular-nervous pedicle which facilitates its use in plastic surgery, to achieve a successful cardioplasty. Taking into account that this method of cardioplasty can be conducted without cardiopulmonary bypass, the operative risk is smaller.

The sequel of the Latissimus Dorsi transposition from the thoracic wall to the interior of the thorax is practically nil. The muscle's large width permis to entirely surround both ventricles.

A cardioplasty technique with a Latissimus Dorsi muscular flap can be considered to replace noncontracting myocardium with contractile tissue, having the potential for growth and possible differentiation.

The technical feasibility, histological adaptability and electrophysiological properties of this muscular flap makes its use, in reconstructive cardiac surgery, probably appropriate for dysplasic, ischemic, tumoral and other acquired or congenital anomalies.

The development of this non tiring neuromuscular biocompatible stimulation of the complex heart-Latissimus Dorsi flap with a specially programmed pulse generator is desirable in the treatment of all chronic cardiac insufficiencies without myocardiac reserve.

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METHODS OF INCREASING THE EFFECTIVENESS OF INVASIVE STIMULATION

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SUMMARY

Small effectiveness of contemporary implanted stimulators has induced the author to propose and test new method (in laboratory as well as in vivo). The obtained results show the possibilities of the further improvement of stimulators and methods of stimulation in order to support the activities of human extremities in case of traumas such as damage to a spinal cord.

PROBLEM

Most of the stimulation methods known up to date show very low effectivity [x]. This is a result of small effectiveness of applied stimulators, which in its turn is determined by specific work conditions, namely:

/i/ stimulator is always implanted into a conducting medium and each voltage impuls is accompanied by current leakage into surrounding tissues;

/ii/ an implanted stimulator is the one of not numerous devices which have to work in semilocked circuit;

/iii/ an electric current in the conditions of "conducting biologic background" never flows through a definite pathway, independently on a shape and dimensions of electrodes applied.

An evaluation of effectiveness of different stimulator types is commonly made by their comparison, what can lead to certain optimization of stimulator constructions, but doesn't allow any quantitative estimation. Here, an attempt of quantitative estimation of stimulator effectiveness is made on an example of yougoslovian pipe stimulator for stimulation of peroneal nerve in the control of drop-foot during walking of hemiplegic patients. The stimulator is usually implanted parallel to the nerve trunk. From the comparison of nerve and stimulator diameters it follows that only 9% of stimulator current flows through the nerve [1]. It can be shown, moreover, that only about 1/3 of nerve surroundings is influenced by stimulating current. It follows, therefore, that stimulator effectiveness is near 3% and 97% of stimulation current are dissipated in surrounding tissues.

Therefore, to obtain the required stimulation effect, stimulator developers have to apply comparatively high voltage. The possibility of its increasing is, however, limited from at least two reasons. The first is the effect of pain which can occur during stimulation of too high voltage, and the second is the problem of capacity of feeding batteries, which are implanted together with the stimulators.

The present work is an attempt to decrease electric current losses in the living tissues during stimulation. It seems that such a decrease, due to improving of stimulator effectiveness, can result in lengthening of life-time of implanted stimulators without any change of power sources.

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x) Effectivity of stimulation methods is an intentional functional or terapeutic effect obtained by given energy or power transmitted from stimulating device to the organ stimulated.

xx) Effectiveness of stimulator is a possibility of getting the required level of muscle or nerve response as a result of given voltage or power on stimulator's electrodes.

MATERIALS AND METHODS

Three methods of increasing of FES [x] effectiveness are proposed, namely:
- a method of controlled disturbance of electric field,
- a method of suspension (saturation with metal),
- a method of connection (paving).

The common feature of these methods is maximizing of an amount of electric current directed toward the stimulated organ and minimizing current losses in the surrounding tissues.
Since the stimulation is carried out in the conducting medium, there are only two possibilities of directing the stimulation current toward the chosen point:
- by decreasing of conductivity of the medium surrounding the stimulator, what seems to be impossible;
- by increasing of conductivity of whole stimulated organ (a method of suspension [2]) or of specific pathway between the stimulator and stimulated organ (a method of connection [3]); both method are possible and will be presented below.

I. A method of controlled disturbance of electric field

An essence of this method is an artificial deformation of potential lines of an electric field generated by a stimulator. This deformation is obtained by introducing into required region of organism metallic or insulator elements. An application of certain combination of such elements of appropriate properties and shape can result in specific condensation of stimulating current.

II. A method of suspension

An essence of this method is creating of an artificial motor point in stimulated muscle by injecting metal particles into it. This artificial motor point substitute an axon tree within a muscle which has disappeared as a result of nerve damage. A muscle is stimulated in the region of an artificial motor point and stimuli are transmitted to subsequent muscle fibres by artificially created connections which conductivity is greater than that of surrounding tissue. In such a way an artificial motor point is directly connected with majority of muscle fibres. Therefore the resistance of muscle tissue, which results usually in big voltage decrements for fibres distant from stimulating electrode, is significantly decreased. Due to such muscle treatment, a stimulation current flows not only through the under-electrode muscle part, but through nearly all muscle section.

III. A method of connection

This method utilizes the fact that an electric current flows through a pathway of smallest resistance. Such a pathway could be created, if comparatively big well-conducting elements are placed close one to another between the electrode and stimulated organ. Due to such a procedure in chosen region current density is greater than in another ones.

The ideas presented above has been tested by experiments in vitro and in vivo.
The experiments in vitro, oriented toward testing controlled disturbance of electric field, has been carried out on the two- and three-dimensional models of conducting tissues. The two-dimensional model was the conducting paper, on which conducting or insulating elements were introduced by conducting or insulating paint, respectively. The three-dimensional model was the tank filled with Ringer solution into which a model of stimulator together with different combinations of disturbing elements, was immersed. Three-dimensional distribution of electric field was measured in the one quarter of space around the stimulator.
Two another methods have been tested in vivo. The experiments were carried out on the biceps femoris muscle of the rabbit. During thase experiments a force responce to the stimulation was measured.

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[x] FES = Functional Electrical Stimulation

RESULTS

A series of in vitro experiments has confirmed an effectiveness of controlled disturbance of electric field. The most effective field condensation has been obtained by placing "nerve" and stimulator parallel one to another and introducing an appropriate combination of insulating and conducting elements between them.
The method of connection has been tested by comparison. One pair of stimulating electrodes has been attached directly to one of the muscles under investigation, whereas another pair has been placed on the skin above the same muscle of the another leg. Between the second electrode pair and the muscle metallic particles were injected. Stimulation of both muscles with the same voltage resulted in nearly the same force output in both legs of a rabbit. As follows from these results this method allows to substitute implanted device by external one without any change of stimulation effect.
Another series of experiments was directed toward testing of a method of suspension. Metallic particles were injected directly to the muscle tested. Several parameters responsible for the final effect of stimulation have been optimized experimentally. Those were: a total volume of metal injected; dimension of metallic particles; stimulation rate; duration of one stimulation cycle; stimulation voltage; total number of stimulation cycles. Since none of optimal values of parameters listed above had been known before, the Gauss' method of multiparameter optimization has been applied, i.e. optimal values of two parameters have been established, then the next parameter has been optimized etc.
During these experiments, it has been shown that the voltage required to obtain the same force output (5N) in the injected muscle was 2.4 times lower than in control muscle.

DISCUSSION

It has been shown that during stimulation only few percent of stimulator energy is utilized. Several methods of decreasing energy losses and therefore increasing stimulator effectiveness, have been proposed. Experimental testing of these methods has confirmed their usefulness.

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TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) IN SEVERE ANGINA PECTORIS

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SUMMARY

The short-term effects of transcutaneous electrical nerve stimulation (TENS) were studied in 10 patients with severe angina pectoris. All patients showed an increased working capacity, decreased ST-segment depression and reduced recovery time during TENS. Equally good results of TENS concerning these variables were obtained in a long-term study in 23 patients with severe angina pectoris. It is concluded that TENS may be included in the short and long term treatment of severe angina pectoris.

INTRODUCTION

Patients with severe angina pectoris often are restricted in their daily activities. In spite of advances in pharmacological therapy as well as the introduction of aorto-coronary bypass surgery, many of these patients still have severe symptoms.The purpose of this investigation was to evaluate if transcutaneous electrical nerve stimulation (TENS) on the chest could reduce the chest pain and increase the working capacity in patients with severe angina pectoris.

PATIENTS

Ten male patients between the ages 40 and 65 years were studied. All patients had severe angina pectoris (functional class III or IV, New Your Heart Association).All patients had been considered for bypass surgery: one patient had been previously operated upon, two patients were current candidates for surgery and the remaining seven patients were not considered suitable for surgery. The antianginal pharmacological treatment was to be regarded as optimal and had been carefully titrated as to compounds and doses.

METHODS

The study consisted of three subsequent parts:

1. A run-in period (3-5 days) to familiarise the patients with the test situation, to further confirm that they were suitable candidates and to individually standardize an exercise test for each patient.
2. A treatment period (4 days) when the individually standardized exercise test was performed twice daily with and without TENS treatment according to an alternating schedule.
3. A post-treatment period (2 days) to obtain the post-treatment value of the patient's working capacity.

The following variables were used to assess the effect of TENS.

1. Maximal total work during exercise.
2. Pulse rate, blood pressure and the product of pulse rate and blood pressure before, during and after the exercise tests.
3. Pain and dyspnoea reported by the patient were recorded during and after exercise testing. Chest pain and dyspnoea were graded according to a scale ranging from 0 to 5 where 0 signified no discomfort, and 5 maximal discomfort. All patients

were urged to continue their exercise to levels producing grade 5 in either pain or dyspnoea.
4. The electrocardiographic characteristics of the patients were analyzed by using 12 channel EEG before and after each exercise test. The ST-segment depressions and heart rates were measured.
5. Recovery time after maximal work is defined as the time needed until disappearance of pain or dyspnoea (stage 0).

A commercially available transcutaneous nerve stimulator was used. The stimulator delivers constant current 0.2 ms pulses and a pulse frequency was set to 70 Hz. The intensity of the stimulation was individually adjusted to a level immediately below that producing pain. Silicon rubber electrodes (3 x 12 cm) were used. The electrodes were placed on the patient's chest at the site of the most intense pain.

To evaluate the statistical significance, Wilcoxon's matched pairs signed ranks test was used. All tests were two-sided and statistical significance was defined at $p<0.05$.

RESULTS

All ten patients completed the study. No complications or adverse effects were observed.

When comparing data with and without TENS, the following statistically significant differences were observed. Patients receiving TENS showed an increased working capacity (16-85%), decreased ST-depression and a reduced recovery time. The mean values are given in Table 1. Blood pressure, heart rate and the blood pressure heart rate product were not influenced.

	Run-in period	Treatment period		Post-treatment period
		Without TENS	With TENS	
Mean exercise tolerance (Wmin)	559	549	700	567
S.D.	222	203	233	207
Mean ST-segment depression during exercise (mm)	3.1	3.2	2.1	3.1
S.D.	1.8	1.6	1.3	1.7
Recovery time (min)	4.7	4.3	1.7	4.3
S.D.	2.8	1.4	0.6	1.8

TABLE 1

COMMENTS

The favourable effect of TENS on angina pectoris was confirmed in a later long-term study on 23 patients with severe angina pectoris (1). Following a common run-in period the patients were randomly allocated to TENS treatment and to a control group.

The treatment period lasted 10 weeks and was followed by a post-treatment period that was identical for both groups. The TENS treatment group was instructed to self-stimulate one hour three times daily and in addition to stimulate during anginal attacks. The results were equally good as in the presented study with respect to working capacity, ST-segment depression and recovery time. Moreover, the TENS treatment group showed a significantly decreased frequency of anginal attacks and intake of nitroglycerine.

Considering the analogous results of both studies there is now ample evidence to support the value of TENS in the treatment of severe angina pectoris.

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THE EFFECTS OF POLARIZATION ON HUMAN EPILEPTIC FOCI

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SUMMARY

In three patients suffering from chronic epilepsy with drug-resistant complex-partial seizures the effects of weak direct polarizing currents applied to the primary epileptogenic focus, that had previously been localized by chronic depth-EEG (SEEG) recordings and was proven in all 3 patients to be restricted to unilateral mesiobasal limbic structures (amygdala, hippocampus), were studied before surgical removal of these structures. During polarization scalp- and depth-EEG were simultaneously recorded. We report preliminary results and show that anodal (positive pole) polarization tends to decrease epileptic spike incidence, whereas cathodal (negative pole) polarization tends to have the opposite effect. In one case the latter induced a seizure originating in the polarized structures. Intracerebrally evoked responses recorded within the hippocampal formation were altered in shape by a weak polarizing current across the hippocampus, the phase of the mainly biphasic potential with opposite polarity to the applied field being increased in amplitude and duration. These effects were reproducable and related to current intensity. The effects on background activity were more variable: anodal polarization sometimes reduced it, and both polarities equally activated rhythmic delta waves in the polarized hippocampus in one case. No side effects (except the induction of one seizure) were observed during polarization. The patients were unable to tell whether they were under the influence of dc-currents or not. In one patient, however, a marked behavioral alteration with psychotic features occurred during the night following polarization. During the next two months this pat. remained completely seizure-free.

MATERIALS AND METHODS

Three patients with drug-resistant complex partial seizures, undergoing our evaluation protocol for surgical epilepsy therapy,that includes chronic depth-EEG recording (SEEG) (20), were selected for this study. The following conditions were met: 1.SEEG had shown a strictly unilateral mesiobasal limbic seizure origin, 2. therefore it was planned to perform the so-called "selective amygdalohippocampectomy" (21) within the next weeks, and 3. informed consent was given.

For depth recording and stimulation we used multiple-contact hollow-core electrodes of 1 mm diameter, each consisting of 10 Teflon insulated helically wound stainless steel wires ending in two groups of 5 poles. Each pole is cylindrical with a tissue contact length of 0.8mm and a real surface area of $3.8mm^2$ (7).

At the end of the SEEG-exploration, when the depth electrodes were still in situ, weak dc-currents were applied between the poles situated in the epileptogenic amygdala (E1.1) or hippocampus (E1.2) and a large (5x5 cm) scalp electrode placed over the ipsilateral fronto-temporal region, using a 9 V-battery powered constant-current device with additional continuous monitoring of current flow by an amperemeter in series (Fig.1).

In patient 3 we applied a weak dc-field between the epileptogenic hippocampus and the overlying white matter, using two different poles of the same depth-electrode (Fig.4, E1.2/1-5), and studied the influence of the dc-field on EEG-responses recorded within the hippocampus (Fig.4,E1.2/2-3,b) and evoked by electrical pulse stimulation (1 Hz, 0.7 msec,10 V) of the ipsilateral amygdaloid complex (Fig.4,E1.1/1-2). During each investigation we started with very low initial current flow (1 μA) for short periods (10 sec) and closely observed EEG-activity and behavior. If no significant changes occurred, we stepwise increased duration (up to 2 min) and intensity of the dc-current, (normally up to 60 μA, only once up to 200 μA).

FIG.1
PAT.1
(PAT.2)

LOCATION OF DEPTH-ELECTRODES

Schematic view of two multiple-contact hollow-core electrodes located with their inner contacts in the amygdaloid complex (E11) and medio-posterior hippocampus (E12), and with their outer contacts within the grey matter of the anterior (E11) and medial (E12) 2nd temporal gyrus.
Polarizing current was injected by a constant-current device through the innermost amygdaloid contact in pat.1 (E1/1, fig.1 shows anodal polarization of the right amygdala, EEGs recorded during polarization are shown in fig.2b), or by the innermost hippocampal contact in pat.2 (E2/1, EEGs see fig.3). Current return was provided by a large (25^2cm) ipsilateral fronto-temporal scalp electrode.

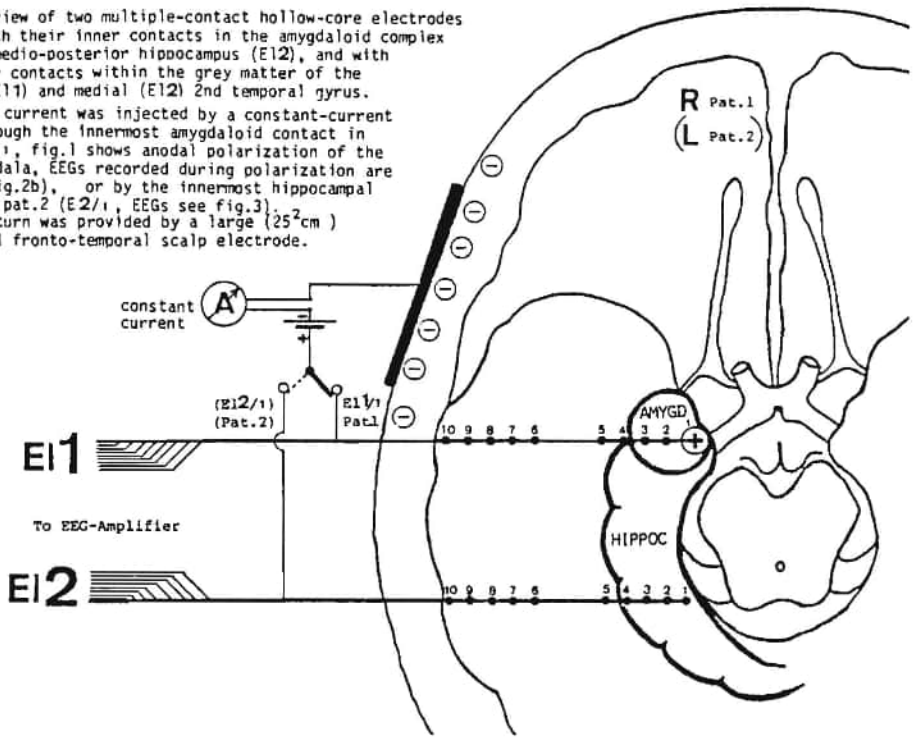


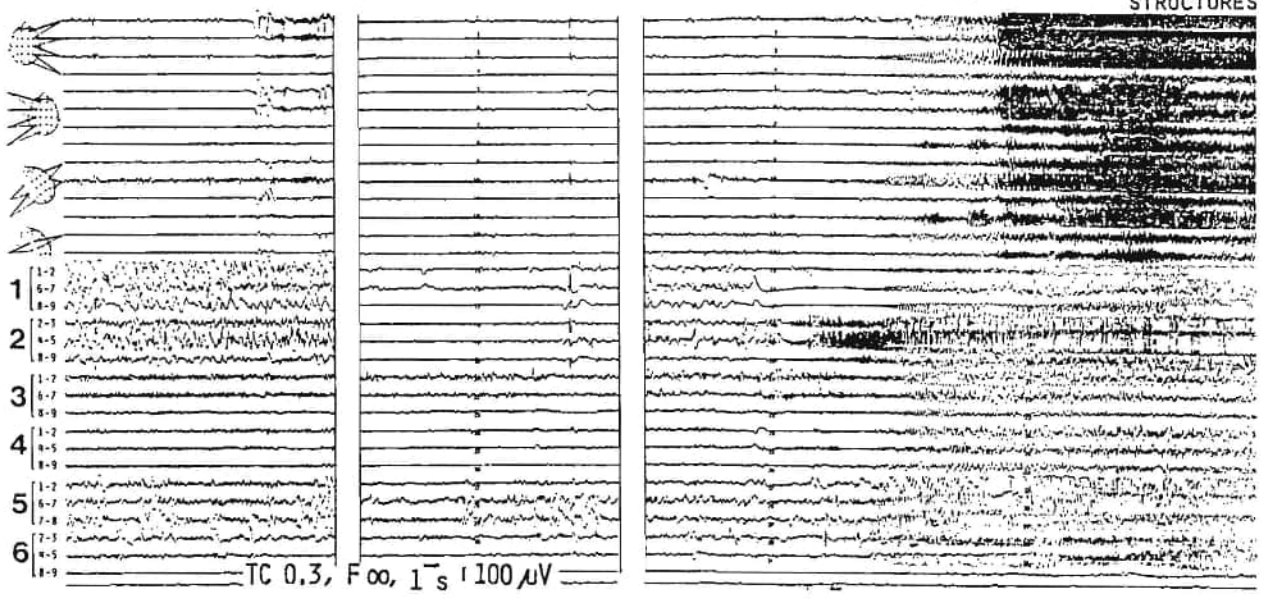
FIG.2
PAT.1

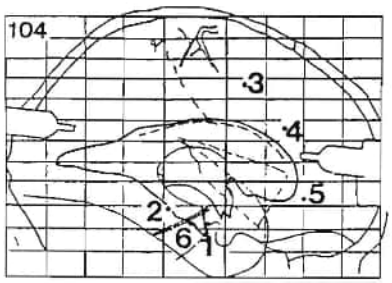
COMBINED SCALP- AND DEPTH-EEG RECORDING PERFORMED DURING POLARIZATION OF RIGHT AMYGDALA

a NO POLARIZATION

b ANODAL POLARIZATION OF RIGHT AMYGDALA

c CATHODAL POLARIZATION OF RIGHT AMYGDALA→SEIZURE ORIGINATING IN THE POLARIZED STRUCTURES





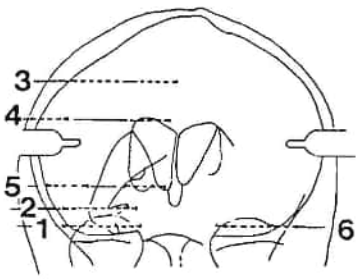
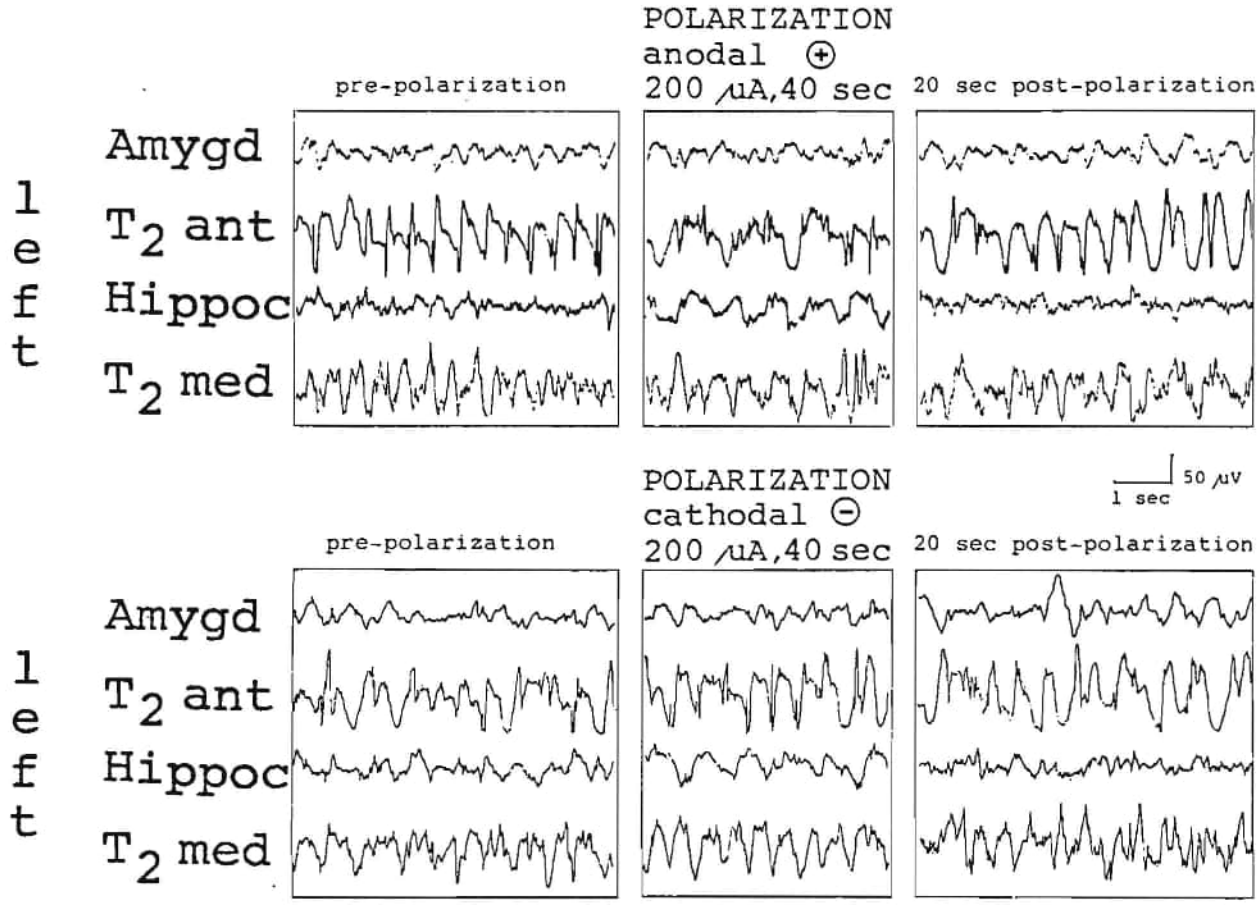


FIG.3
PAT.2 POLARIZATION OF LEFT HIPPOCAMPUS

by innermost contact of electrode no. 2 (surface 4 mm^2)
current return by large left fronto-temporal scalp electrode (25 cm^2) (see Fig.1)

Influence on depth-recorded EEG



After surgery histo-anatomical studies will be performed on the removed tissue to verify the exact electrode location, to assess the extent of possible micro-lesions caused by current flow, and to measure the amount of Fe -ions that have been released by the electrode wire during anodal polarization.

RESULTS

Because of the small number of patients and obvious reasons that did not allow us to use rigid experimental protocols, we can report only preliminary results. Nevertheless, polarization of the amygdalohippocampal complex showed a reproducable and sometimes marked effect on depth- and surface-EEG. In all 3 patients epileptic spike incidence was decreased to a variable extent by anodal polarization, whereas cathodal polarization had an opposite effect and induced one seizure originating in the polarized structure (Fig.2c). In patient 2, although anodal and cathodal polarization had an opposite effect on spike incidence (Fig.3), both facilitated rhythmic 1.5-2/sec activity in the hippocampus. Mainly biphasic intracerebrally evoked potentials were recorded from the hippocampus in patient 3 (Fig.4). The phase having an opposite direction to the applied dc-field was increased in amplitude and duration and vice versa. The patients never reported any sensations or mood change during polarization, they could not even tell, whether the current was switched off or on. In patient 1, following polarization, a transitory psychotic state of 2-3 days duration developed, for the next two month he was completely seizure-free, then seizures gradually recurred.

FIG. 4
PAT. 3

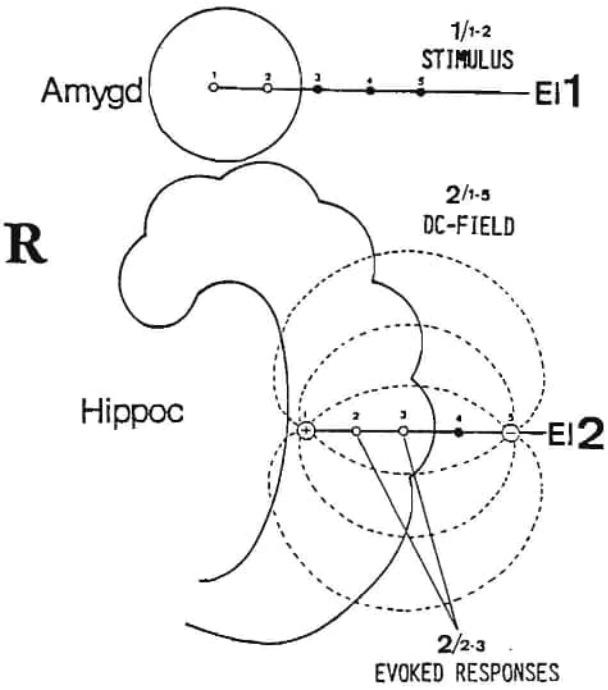
EFFECTS OF POLARIZATION OF R. HIPPOCAMPUS ON RESPONSES EVOKED BY STIMULATION OF R. AMYGDALA

a SCHEMATIC ELECTRODE LOCATION

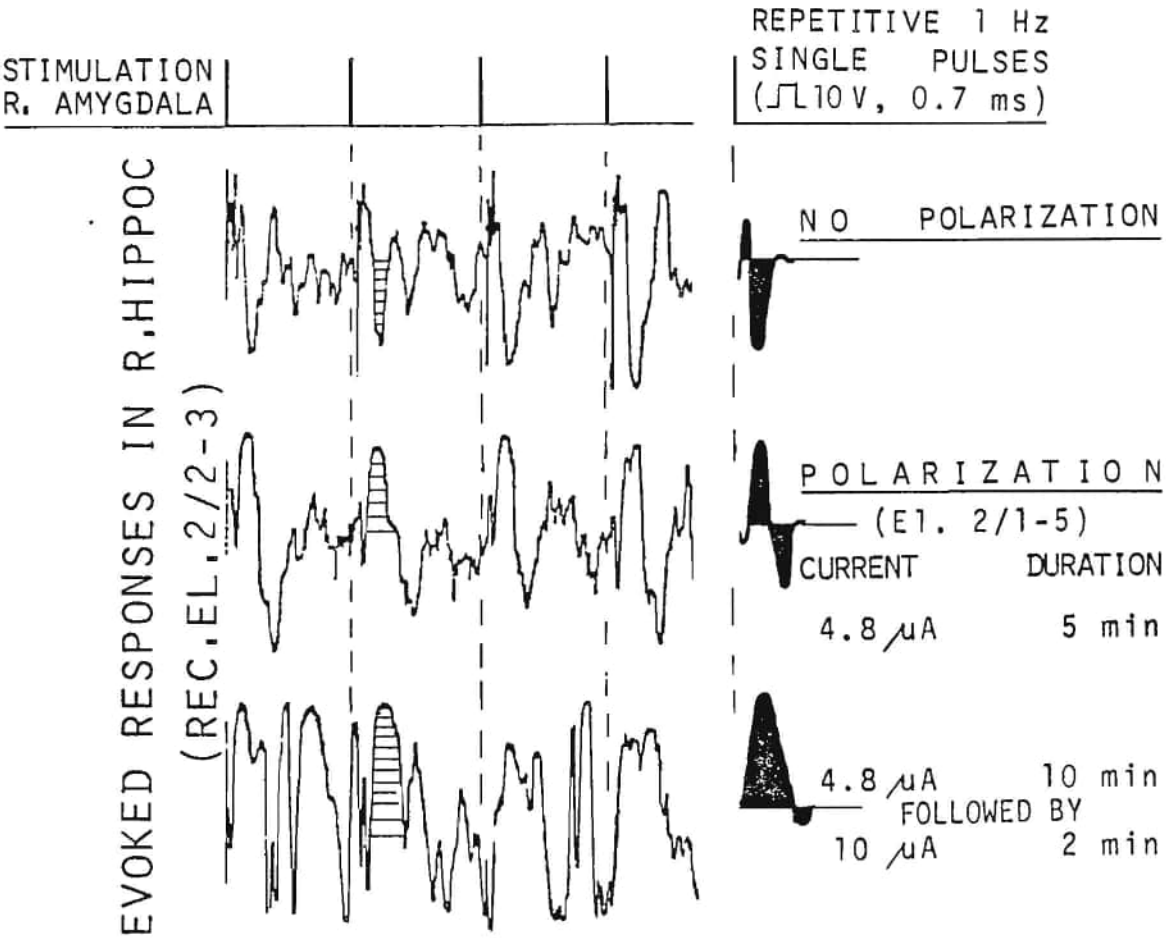
EEG-responses are evoked by electrical pulse stimulation
(1 Hz, 10 V, o.7 msec)
of the right amygdaloid nucl.
(El 1/ 1-2)

DC-current (4,8 and 10 µA) is applied across the right medio-posterior hippocampus
(El 2/ 1-5)

Depth-EEG responses are recorded within the right medio-posterior hippocampus
(El 2/ 2-3)



b EVOKED EEG-RESPONSES



D I S C U S S I O N

Although the natural occurrence and influence of externally applied pulsed currents on neural tissue are quite well understood, comparatively little is known about the effect of weak direct continuous currents and the underlying mechanisms of action. Polarized direct currents can influence tissue-growth and -regeneration, of clinical importance are studies demonstrating activation of osteogenesis by direct cathodal currents (23) and tumor regression by direct anodal currents (14).Extracellular anodal polarization of peripheral axons increases potential-differences across the nerve sheath (i.e.leads to hyperpolarization), raises the treshold, increases the amplitude of response to stimulation, increases the duration of the spike, and decreases the absolute refractory period (4).

In the last century there was a great interest in the effect of electricity on mental function, the application of "galvanic" (direct) current with one electrode placed on the head and the other at some distant part of the body was therapeutically used in diseases as "neuroasthenia" and "melancholia" (16). Different behavioral effects (sedation, stimulation) of different polarities were repeatedely reported. In 1870 Fritsch and Hitzig (13) observed that a surface-positive (anodal) direct current had a stimulatory influence on the cerebral cortex, whereas a negative current inhibited it. Some recent work suggests a beneficial effect in patients with various forms of depression by anodally polarizing the scalp with weak currents (up to 1 mA) over prolonged periods (rev. see 15). Crow (9) reported a transient reduction in fear feelings in psychiatric patients after anodal intracerebral polarization (up to 1 mA, 10-20 sec.) of frontal white matter what he attributed to axonal blockings. Bishop and O'Leary (5) showed that surface positive (anodal) polarization of the cortex modifies evoked potentials, the negative wave being increased and the positive wave being reduced in amplitude and time.Later experiments of various authors confirmed this observation and showed that anodal polarization increases firing rate of single cortical (3,6) and hippocampal (22) neurons in direct relation to current density, whereas cathodal polarization has the opposite effect. If current flow is long enough (several minutes)persistent after-effects in the same direction could be observed for several hours (3).Beginning with the work of Rusinov (17)it was suggested that low dc-fields influence the associative and connective functions of the brain. Anodal polarization of the scalp over the vertex with less than 0.3 mA was reported to shorten reaction time in humans (11).Furthermore,anodal polarization of prefrontal cortex in monkeys facilitated behavioral learning (20).These effects were confirmed with different species and tasks,cathodal polarization having an opposite effect.The optimal current density was found to be in the range of 20-50 uA/mm^2 (1).Naturally occurring weak dc-fields are discussed because of their possible role in learning phenomena (2).In recent years,partly due to improved recording techniques,there was a growing interest in physiologically occurring weak dc-shifts within the brain,especially their correlation with cognitive and activation events (rev.see 18). Furthermore, shifts of the cortical dc-field are observed during and after epileptic seizures. Still very little is known about the mechanisms underlying epileptic behavior in neurons, but changes in the local dc-field seem to modulate the repetitive activity of single neurons and influence generation and spread of epileptic activity.

Therefore it can be expected that polarization of the adequate polarity and strength might exert an inhibiting influence on focal epileptogenic activity and its propagation, especially in topically well organized brain structures.To test this hypothesis we polarized epileptic mesiobasal limbic foci in drug resistant patients before surgical removal of these structures.
Our preliminary results support the hypothesis that weak dc-currents can influence the activity of human epileptogenic neuronal populations.Some of the observed phenomena are clearly polarity-dependant.Direct anodal polarization of the amygdalohippocampal complex seems to inhibit spontaneous epileptic activity in these structures.Further careful studies are necessary to assess the possible clinical value of polarization in epilepsy.

A serious limitation on further clinical research is the fact,that very little is known about the electrochemical mechanisms involved during dc-current injection in brain tissue.There is the possibility of damage by electrolytic lesions.Currents of 3-8 mA applied for 1-3 min daily can produce tissue necrosis (10).Tissue damage might happen when the natural buffering capacity is exhausted and gross pH changes occur with further current injection.The critical current density appears to be in the range of 1mA/mm^2 (8). With a maximal current density of 53 µA/mm^2 we remained well below that level. The surgigically removed amygdala of pat.1 showed some Fe-loaded macrophages in less than 100 µm distance from the electrode, but no signs of tissue damage due to polarization.

Several possible mechanisms for the action of dc-polarization at the neuronal level have been suggested, e.g. changes in membrane properties (of the dendritic tree, of axonal terminals, and of glial cells) and changes in local ion concentrations (e.g. potassium), which both might alter synaptic function.

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ENDOSCOPIC ELECTROMYOGRAPHY OF THE LARYNX

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(Director: Prof. Dr. M.E. Wigand)

SUMMARY

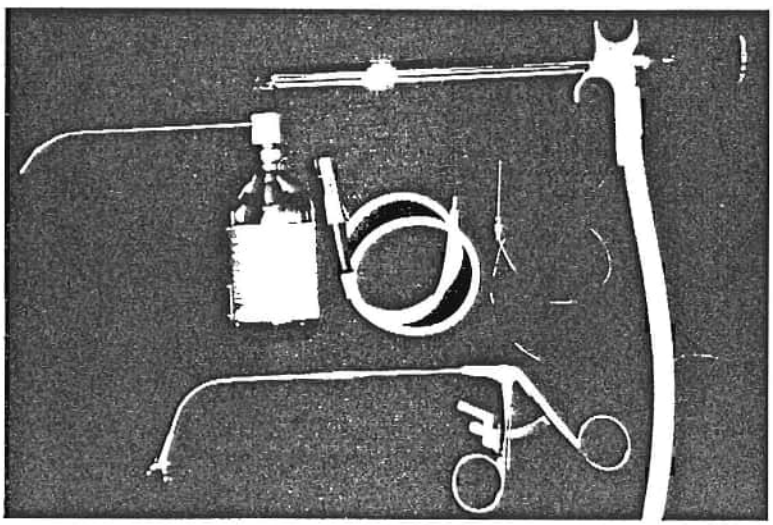
In facial nerve surgery as in functional surgery of the recurrent nerve, electrodiagnosis provides most valuable criteria of indication. A method of direct electromyography of the laryngeal muscles in the awake patient has been established using a zoom endoscope for the placement of needle-electrodes. The formerly used bipolar needle-electrodes are now replaced by hooked-wire-electrodes consisting of 80 µ copper wires. These electrodes are easy to apply transorally with minimal discomfort to the patient. With these electrodes even speaking and singing is possible. Electromyography and in addition neuromyography by electrostimulation of the laryngeal nerves by cutaneous surface electrodes permit a better diagnosis and prognosis of laryngeal nerve lesions. Furthermore, a reflexarc of the upper and lower laryngeal nerves can be tested with electric stimulation and measurement of the response activity similar to the trigemino-facial reflex. With the aid of this recurrent nerve neurography, both evaluation of laryngeal palsies and the prediction of sequelae are considerably enhanced.

MATERIAL AND METHODS

Electromyography of the laryngeal muscles has been up to now of minor importance, because

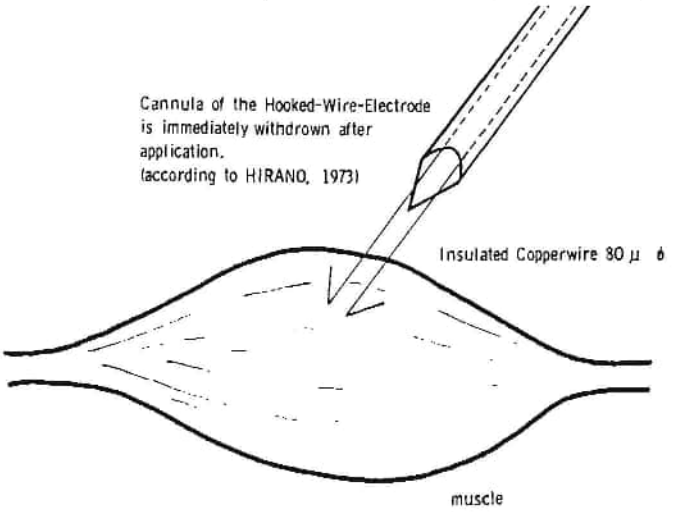
- the transcutaneous, blind insertion of needle-electrodes /2/5/ could not provide selective records of muscle activity
- controlled placement of needle-electrodes needs general anesthesia /1/3/ and
- therefore prevented the recording of voluntary activity.

We have tried a new access to electromyography of the larynx in the awake patient, using 90 endoscope after von STUCKRAD /6/, and a special electrode applicator(fig.1).

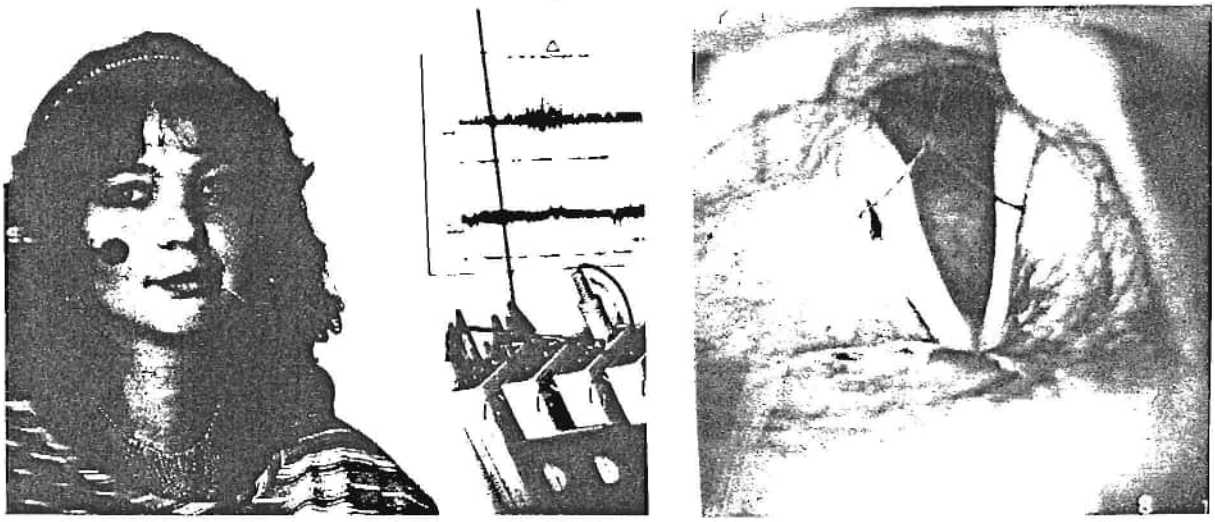


The application of electrodes into any wanted muscle of the larynx is performed with this magnifying endoscope and an optimal supervision after superficial spray anesthesia of the pharynx and larynx without any other medications.

Similar to the technique of taking specimen out of the larynx under local anesthesia, the optimal optic control enables the application of the first used bipolar needle-electrodes into the posterior crico-arytenoid muscle or the vocal muscle, even simultaneously, or the now used 80 μ in diameter copper wire electrodes, which are preferred for voice disturbance investigations. As the foam-rubber model demonstrates clearly, the application needle is withdrawn immediately after inserting the electrode, which stays in place even during speaking and swallowing with help of a little hook at the end, which is not isolated. Since two copper wires are drilled together, this electrode represents an ideal bipolar electrode, that stays exactly in place (fig.2).



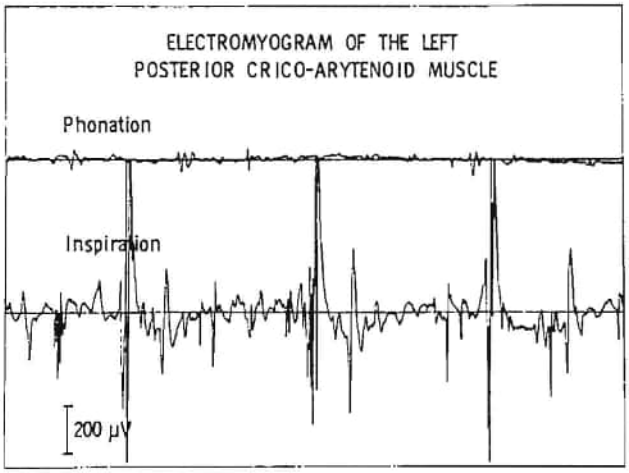
With this procedure the patient is able to inspire, phonate and even to sing with the electrodes inserted and in place with only minimal discomfort (fig.3,4).



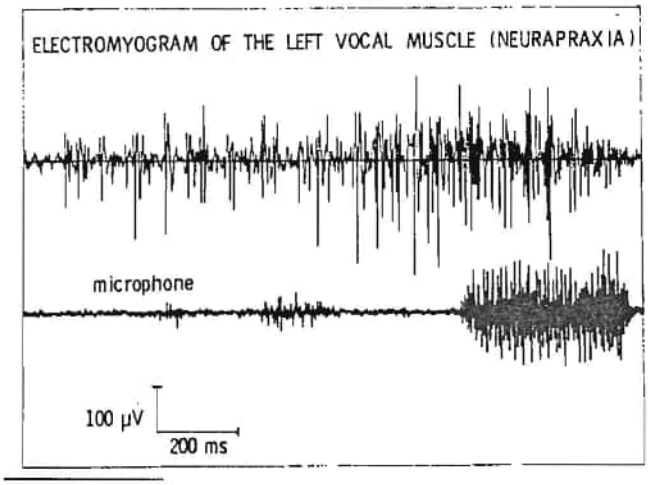
Simultaneous recording of the patients voice with the microphone allows correlations of special muscle activities to inspiration or phonation.

RESULTS

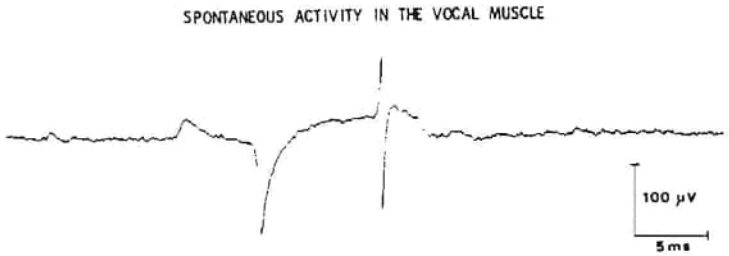
The intact laryngeal muscles have typical pattern of voluntary activity in the electromyogram: the posterior crico-arytenoid shows only some basic activity during phonation, but an increase of both, frequency and amplitude during inspiration (fig.5).



A reverse activity is recorded from the vocal muscle, where voluntary activity starts about 350 ms before the onset of voice, if it is unimpaired (fig.6).



In cases of degeneration of the laryngeal nerves the occurrence of pathological spontaneous activity, for instance positive sharp waves or fibrillationpotentials may be observed (fig.7).



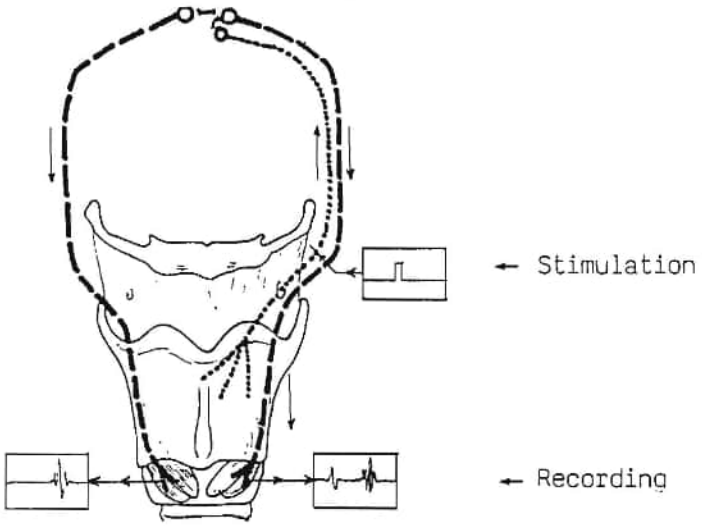
Thus an early diagnosis of the initial signs of beginning denervation of the larynx is possible for the indication of immediate surgical interventions.

Since 1976 we have examined more than 1500 laryngeal palsies by electromyography of the larynx. In one group of patients the prediction of vocal cord recovery was controlled one year after electromyography and an adequate prognosis was found in 138 of 184 patients (=75%), recovery better than predicted was seen in 28 patients and recovery worse than predicted in 18.

Apparently electromyographical examination of the paralysed larynx did not answer all the questions neccesary for an exact diagnosis. Similar to investigation of facial nerve palsies we therefore established a neuromyography and reflexmyography of the laryngeal nerves in the awake patient.

MATERIAL AND METHODS

By simulation of the upper laryngeal nerve in the region of its penetration through the hyothyroid membrane with surface electrodes a first potential can be induced in the cricothyroid muscle after 4-6 ms as a stimulated electromyogram similar to electroneurography. In addition, the same stimulus of the superior laryngeal nerve provokes a second answer after going up and down the afferent and efferent laryngeal innervation along the vagus nerve system (fig.8).



This second or reflectory potential is seen 18-20 ms after onset of stimualtion by 0.5 ms impulses. This second potential can be measured although in the laryngeal muscles innervated by the recurrent laryngeal nerve. Using the endoscopic electromyography of the larynx for inserting the electrodes into these muscles answer potentials can be recorded with typical latencies, if there is only a partial or no degenerative paresis. Otherwise there is no stimulus reaction with a worse prognosis of the palsy.

RESULTS

More than 300 patients with vocal cord paralysis could be examined with this method. The most impressive results are given immediatly after neck surgery if there is a loss of vocal cord function. In a group of 90 patients the findings were controlled one year after onset of the paralysis. An adequate prognosis was given in 83% concordant and additional 8% discordant to the electromyography. This means a correct prediction of the outcome of the palsy in more than 90%.

DISCUSSION

The combination of the electrodiagnostic methods given with the technique of endolaryngeal electromyography, neuromyography and stimulation of laryngeal reflexes along the vagus nerve system enables a precise diagnosis and prognosis of laryngeal nerve lesions within two or three weeks /7/8/. According to the time table for electrodiagnosis of the larynx a degenerative palsy can be excluded with EMG, NMG and RMG immediately after onset of paresis and at least two weeks afterwards. The differantiation of axono- and neurotmesis is more difficult, but seems to be possible in cases after surgical intervention, when there is no electric activity and no electric response in the laryngeal muscles. These diagnostic tools give better chances for functional nerve repair /4/9/10/, than the traditional attitude of expecting control, which up to now has been the consequence of the laryngologist's lack of appropriate test procedures.

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DIRECT ELECTRICAL STIMULATION OF THE POSTERIOR CRICOARYTENOID MUSCLE

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SUMMARY

To provide for an adequate air passage in patients with bilateral recurrent nerve palsy the glottis-opening muscles were subjected to respiratory-rate controlled stimulation.
Clinical aspects of bilateral recurrent nerve paralysis and currently available therapeutic approaches are reviewed.
The design of our experimental study including the surgical technique, the configuration of the electrodes,the parameters of stimulation and the histochemical findings in the posterior cricoarytenoid muscle are discussed.

MATERIAL AND METHODS

Bilateral recurrent nerve lesions acutely threaten the patient's life and require emergency tracheotomy or endolaryngeal surgery for glottic expansion.The loss of one vocal cord associated with this mutilating operation prompted us to employ direct electrical stimulation of the glottis-opening muscles to provide for an adequate passage of air.

The following problems were investigated:
(1) Is direct electrical stimulation of the posticus muscle possible?
(2) If so,is the abduction obtainable sufficient for normal breathing?
(3) What is the optimum timing after recurrent nerve lesions for stimulation to be effective?
(4) Can the residual muscle fibers be kept functional by electrical stimulation?
(5) What electrodes are most suitable?
(6) What are the most useful stimulation parameters?
(7) What is the best surgical access and what is the optimal electrode localization on the muscle?
(8) What is the normal histology of the posticus muscle?
(9) What are the histological changes produced by recurrent nerve lesions as a function of time?

To find answers to these questions animal experiments were carried out in sheep.Recurrent nerve lesions were produced on one side and monopolar electrodes were implanted with the tip on the ipsilateral posterior cricothyroid muscle and its subcutaneous lead ending at the skin surface.
The electrode we used was a 35 cm coiled steel wire(Ethicon® steel wire polyfil 4-0).Except for its ring-shaped tip it was insulated with silicon and carried a plug at one end for connecting it with the external stimulater unit.

To implant the electrode a skin incision was made along the anterior border of the sternocleidomastoid muscle at the level of the cricoid cartilage.The superficial cervical fascia was dissected for exposure of the cricopharyngeal portion of the pharynx,which was equally dissected so that the posticus muscle came into view. With 5-0 silk sutures the electrode tip was attached to the muscle belly and its silicon sheet spaced 3 cm from the tip with 3-0 silk sutures to the thyroid cartilage.This ensured adequate stability of the paralaryngeal electrode and prevent slipping of the electrode tip.The long end of the electrode was led subcutaneously to the posterior part of the neck and emerged at the skin surface. Stimulation was done at weekly intervals.Abduction of the vocal cord was monitored by direct laryngoscopy with jet respiration at a normal respiratory rate.
Histochemical examinations of the sheep posticus muscle were performed prior to and 3 weeks after producing the recurrent nerve lesion.

RESULTS

As our research project is still in its early stages,we are currently unable to provide answers to all of the above questions. However,there is evidence to show that direct electrical stimulation of the normal sheep posticus muscle is possible and that it produces sufficient abduction for adequate air passage.
For stimulation a square wave current of 1 to 5 mA,a pulse frequency of 30 to 50 Hz and a pulse duration of 1 to 15 msec.was used.

We also examined denervated muscles with implanted electrodes and found direct stimulation to be possible within a 3-week period after denervation.However,the response in terms of the abduction obtainable was inadequate.This may be attributable to the use of monopolar electrodes which generate an excessively large field so that the adjacent muscles of the neck are equally activated. Placing the skin electrodes as close as possible to the posticus muscle appeared to solve this problem,because it prevents contraction of the other cervical muscles and enhaces the abduction of the vocal cord.
A square wave current of 5 to 10 mA with the muscle electrode serving as cathode,a pulse frequency of 30 Hz and a pulse duration of 10 msec. appeared to optimally suited for stimulation.
The extend of abduction obtained within the first 3 weeks was the same without any substantial losses.

Histochemically (ATPase,mitochondrial stain,NADH-diaphorase) the normal muscle showed a type I (slow) to type II (fast) fiber ratio of 36 : 64%.
Three weeks after severing the nerve supply increased connective tissue and fatty infiltration were found to be present,but there was still an adequate amount of intact muscle fibres.The ratio of muscle fiber types was not significantly changed.

DISCUSSION

The preliminary results obtained with direct electrical stimulation of the glottis-opening muscles were encouraging and prompted us to continue our experiments and extend them to include long-term studies.In fact,it would be of interest to establish whether or not

chronic respiratory-rate controlled stimulation of the denervated posticus muscle is capable of preserving the muscle substance or ensuring adequate function.There is evidence to suggest that bipolar electrodes substantially augment the abduction obtainable by stimulation.Further experiments will show whether these can sufficiently expand the glottis to allow for an adequate air space.

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SPINAL CORD STIMULATION IN PERIPHERAL VASCULAR DISEASE

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SUMMARY

The results of twelve patients with severe, intractable symptoms of arterial disease receiving spinal cord stimulation are reported. Seven of twelve patients showed clinical improvement. Five of seven patients with severe or moderate rest pain obtained complete or very marked relief. The mean claudication distance in ten patients increased from 65 to 212 metres during epidural stimulation of the spinal cord. Exercise tolerance as measured on a bicycle ergometer increased by 61%. These changes were associated with small increases in cutaneous and muscle blood flow. In those patients who responded clinically, the improvements seen were maintained as long as spinal cord stimulation was continued. There was no clinical response to transcutaneous (placebo) stimulation and five patients did not respond in any way to spinal cord stimulation.

INTRODUCTION

During the use of spinal cord stimulation for chronic neurological disease we observed that blood flow in the lower limbs of patients improved over a period of days (1). Nine patients with vascular disease had spinal cord stimulation and showed a favourable clinical response (2). We were impressed by one of our patients with multiple sclerosis and co-existing arterial disease causing intermittent claudication; spinal cord stimulation improved the claudication distance. A trial of spinal cord stimulation in peripheral vascular disease was therefore begun and results have been reported (3).

MATERIAL AND METHODS

Patients

Twelve patients were studied and all had severe and disabling arteriographically proven peripheral vascular disease which had not responded to conventional therapies such as by-pass grafts and lumbar sympathectomy. They were accepted for a trial of spinal cord stimulation after full explanation of the procedure. Four had given up smoking at the start of their illness, the others agreed to limit their smoking to a mutually agreed level. The protocol had the approval of the hospital ethical committee. Electrodes were implanted percutaneously and permanent implants made in those giving a favourable response (4). Objective assessment of their circulatory status was made as follows:-

a) Claudication Distance:- This was measured several times prior to and during stimulation at fixed times of the day and over the same course at the same speed. In two cases a treadmill at speed 2 Km/hr. was used.

b) Exercise Tolerance:- Patients were required to maintain an output of 100 watts on a bicycle ergometer for as long as possible and the time measured. The mean time of 3 determinations prior to and during stimulation was taken.

c) Cutaneous Blood Flow:- Measured by a Xenon 133 clearance technique (5) in both legs just below the head of the fibula and the dorsum of the feet.

d) Muscle Blood Flow:- Was measured in the calf muscles by Xenon clearance at rest and during exercise on a bicycle ergometer.

Stimulation was of the cord dorsum and produced a pleasant bilateral tingling sensation in the legs. Pulses at 33 Hz and 0.2 msec duration and of approximately 8mA were used (6). Avery stimulators were used and were kept on for most of the day

x) Supported by The Medical Research Council (U.K.).

and night. The changes described took place over several days.
e) Placebo Stimulation:- Seven patients received transcutaneous stimulation in the lumbar paravertebral region before spinal cord stimulation. This lasted for 2 weeks and gave a similar sensation.

RESULTS

Seven patients responded favourably such that stimulation significantly altered their life style, the other five did not respond. Two case histories are given.
Case 1 L.M. This 67 year old male insulin dependent diabetic developed intermittent claudication in both legs in 1977. A translumbar aortogram showed widespread disease unsuitable for surgical reconstruction. In July 1978 he developed cellulitis and gangrene of the right second toe. This lesion healed as a response to lumbar sympathectomy but in December 1978 continuous rest pain developed and an indolent ulcer on the right fourth and fifth toes. At the time of stimulation (May 1979) he had severe claudication at 55 metres. Within a fortnight of stimulation the rest pain was relieved, claudication distance had increased to 400 metres and the ulcer had become dry and almost healed. Stimulation was therefore continued through permanently implanted electrodes and at present, 48 months after the start of stimulation, claudication is no longer a problem, mobility being limited by mild arthritis. The ulcer has remained healed and there is no rest pain.
Case 2 H.M. This 34 year old woman had a ten year history of severe Buerger's disease affecting both legs and arms. In the past she had had bilateral lumbar sympathectomies, a right Gritti-Stokes amputation and a right cervical sympathectomy. At the time of stimulation she had left calf claudication at 100 metres, severe rest pain at night in the left leg, pain in the right stump and pain in the right hand. All of these symptoms had been stable for approximately nine months. Despite repeate warnings and psychiatric help, including ECT, she had been unable to give up smoking. Her level of smoking, however, had been stable for some time before the period of stimulation. In response to stimulation there was a marked increase in her claudication distance, a reduction in rest pain in her stump and left leg and some reduction in the pain in her right arm. She was therefore offered permanent stimulation, became free from leg rest pain and was able to walk approximately 1 Km without pain.

This improvement has been maintained but she began developing symptoms due to digital ischaemia in her left hand. These progressed rapidly until there was gangrene of the left thumb and index finger. An angiogram showed that the distal part of the limb was being perfused almost entirely by the interosseous artery. Additional electrodes were placed in the lower cervical spine at a level intended to produce a stimulator sensation in the hand but did not halt the progression of gangrene or in any way relieve the pain associated with it. Her hands improved after cervical sympathectomy. She remains improved and is working on her feet for 16 hours a day 30 months after the implant.

In two of the five failed patients no dorsal column stimulator sensation was achieved, for the other 3 no reason for failure of the technique was found. Two patients have subsequently died, one of ruptured aortic aneurysm and one of myocardial infarction 1 week and 2 years 8 months after stimulation was commenced.

Clinical Changes.

Seven patients had severe rest pain night and day and five obtained complete or marked relief. In case 2 above rest pain persisted in the arms but disappeared from the legs. Three patients had indolent ulcers; in one this healed within 2 weeks, in one other there was no change and the third died of ruptured aortic aneurysm after only one week of stimulation. Claudication distance was measured carefully in 10 patients, 6 of whom gave a good clinical response. Prestimulation claudication distance was 65 ± 45 metres and after 2 weeks of stimulation this rose to 212 ± 147 metres, a statistically significant increase. This change made a great contribution to the patients life enabling some to go shopping for the first time in years.

Objective Tests.

The full range of tests was not completed in all patients. Seven patients in whom exercise tolerance was measured increased their output from 3929 ± 1961 joules to 6328 ± 3421 joules (61%) but this did not reach statistical significance at the 5% level. An increase in both skin and muscle blood flow was observed in four patients who responded well to stimulation but skin blood flow did not change in the non responders. Results are given in table 1. None of the seven patients having transcutaneous stimulation showed any change in claudication distance or exercise tolerance.

Follow Up.

Six of the seven patients giving a good clinical response had permanent implants and have been followed up to 4 years. All have maintained the improved claudication distance. Those with pain relief have remained pain free. Four patients have now been followed for longer than 2 years, one for one year and one for 4 months. Two patients had equipment failures and their condition regressed but improved again after repair.

Discussion.

Objectively measured changes with spinal cord stimulation and the absence of change with transcutaneous stimulation effectively rule out the placebo response as the reason for favourable results. The time course of changes and the stage of the disease in which they were observed were most unlike the natural history of the disease (7,8).

We do not know how spinal cord stimulation works but there seem to be four possible mechanisms:-
A. Pain Relief: Pain relief by spinal cord stimulation is well known and it may release some vasoconstriction which accompanies pain.
B. Sympathetic Nervous System: Stimulation may be able to excite the sympathetic cholinergic vasodilator fibres and inhibit the alpha adrenergic vasoconstrictors.
C. Prostoglandius and Prostocyclius: Antidromic stimulation of nerve roots produces vasodilation in animals which can be blocked by proctoglandin inhibitors (9).
D. Local Vascular Control: In the presence of obliterative disease of large vessels the local circulation may not make appropriate adaptation perhaps because of hypoxia. Increases in blood flow can be produced pharmacologically indicating some circulatory reserve (10, 11).

The follow-up for these few patients is encouraging and appears better than that for those receiving spinal cord stimulation for multiple sclerosis (12).

TABLE

Effect of Spinal Cord Stimulation (SCS) on blood flow in peripheral vascular disease. Mean and standard deviation given in ml/min/100G. P calculated by paired t test.

	Patients Responding				Patients not responding		
Site	n	Before SCS	During SCS	P	n	Beford SCS	During SCS	P
Skin L.Foot	4	5.45±1.13	6.90±1.64	0.02	4	2.40±3.50	1.68±1.71	NS
L.Leg	4	3.33±1.86	3.32±0.70	NS	4	1.33±0.04	1.38±1.31	NS
Muscle Rest	4	1.10±0.68	2.20±1.13	0.05	1	1.2	1.2	NS
Exercise	4	3.68±1.45	5.244±2.93	NS	Not done			

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NEUROPHYSIOLOGICAL ASSESSMENT IN EPIDURAL SPINAL ELECTRICAL STIMULATION (ESES)

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SUMMARY

Functional changes due to epidural spinal electrical stimulation (ESES) can be assessed not only by clinical observation, but also by neurophysiological methods. In spastic movement disorders Silent Period (SP) recordings and in bladder dysfunctions urodynamic investigations have shown an improvement due to ESES. Registration of spinal evoced scalp potentials (SESP's) offers a further method of assessment in longterm treatment with ESES.

METHOD

ESES is applied for treatment of various chronic pain conditions as well as to improve central motor disorders and bladder dysfunctions, mostly in patients suffering from demyelinating diseases and post-traumatic or postinflammatory spinal cord lesion(s). For routine application of ESES usually clinical assessment and the patient's experience is sufficient for decision, whether further stimulation should be performed or not. The primarily benefit of neurophysiological assessment is to get objective data concerning changes due to ESES.

Recording of Silent Period (SP)

In order to prove the effect of ESES on spasticity, in twenty patients the SP was measured before and during the period (up to six weeks) of ESES treatment. Under isometric conditions (one half to threefourth of maximum achievable force, measured in kp) an electromyographic (EMG) recording (M. biceps brachii, M. abduct. poll. brev., M. abduct. dig.V, M. rectus fem., M. tib. ant., M. soleus) was carried out with application of various supramaximal stimuli to the respective innervating nerve (N. musculocut., N. medianus, N. ulnaris, N. femoralis, N. peroneus, N. tibialis).

Urodynamic Investigation

In nine patients with bladder dysfunctions an urodynamic investigation (pelvic floor EMG registration simultaneously with vesical and rectal pressure recording) before and under ESES treatment was performed, as well as recordings of miction frequency, urge and urge incontinence and determination of the residual urine. Urodynamic criteria of assessment were: bladder volume at the first onset of detrusor contractions, pressure trace shapes of detrusor contractions before and during voluntary or unvoluntary voiding, EMG pattern at the time of voiding, effective bladder capacity (maximum bladder capacity minus residual urine).

Spinal Evoced Scalp Potentials (SESP's)

During the clinical test stimulation period as well as after implantation of the Radiofrequeny Receiver, SESP's were recorded using the method already described (3). The applied stimulus strength was at the level of tolerable intensity and below the threshold for producing

motor action (due to spinal root stimulation).

RESULTS

Silent Period (SP)

Nine out of the total of twenty patients with spasticity showed a priori and later on normal SP values. Out of eleven patients with shortened PS's three patients showed an increase and six patients a normalisation of the SP in the investigated muscles within six weeks of treatment (6).

Urodynamic Investigation

In seven patients out of nine there could be observed an increase of the effective bladder capacity and later onset of first autonomic detrusor contractions during ESES therapy. The shape of the pressure trace during the detrusor contractions usually was smoother during and after stimulation. In two of these seven cases the urodynamic recordings showed a decrease, in one case an increase of detrusor-sphincter dyssynergia. Only five of these seven (nine) cases experienced a remarkable benefit.

Spinal Evoced Scalp Potentials (SESP's)

Two patients with Multiple Sclerosis, who were treated by ESES, showed a further increase of N1 and P1 latencies and a decrease of amplitudes. These patient did not report deterioration of their status but a change of stimulus sensation.

DISCUSSION

The effect of ESES on spasticity has been proofed by H-reflex depression (9) and change of tonic stretch reflex toward normalisation (2), also by the increase up to normalisation of the SP, as we could observe this in nine out of eleven patients with shortened SP (6). These neurophysiological results prove the effect of ESES more as such, but they are less appropriate for determining the extent of clinically relevant improvement (5). The positive influence of ESES on bladder dysfunction could be verified (1,7,10) as well and the shown results are similar to our observations. Urodynamic investigations seem to be a valuable criteria for the decision of definitive use of ESES in patients with bladder dysfunctions followed by upper motor neuron lesion(s).
In long term care of ESES patients you will see various dysfunctions of the stimulation system. Frequently patients report modified or absent sensations. By the methods described sofar (8), however, sometimes no satisfactory clarification can be obtained. An additional differentiation between technical defects, neuronal tissue and environmental changes promises (4) the described (3) technique of SESP's recordings in patients with implanted receiver systems.

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LONG TERM FOLLOW UP OF SPINAL CORD STIMULATION PATIENTS WITH MULTIPLE SCLEROSIS

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SUMMARY

In the Wessex Neurological Centre 50 patients have had spinal cord stimulation (SCS) carried out since 1976. Of these, 27 patients had multiple sclerosis (MS) and 41 studies of SCS were performed (i.e. many patients had repeated studies in order to investigate consistency of response). Of the 27 patients with MS, six had unsatisfactory stimulation by our criteria (defined below) and none of these had any clinical response. Of the 21 patients with good stimulator sensation, 19 showed a clinical response (90%). However, in terms of improved function sufficient to alter their lifestyle, the numbers were smaller (about 65%) and almost entirely confined to improvement in bladder dysfunction.

Follow-up of patients indicated that improvement was maintained for four months to three years four months, with a mean of one year three months.

MATERIAL AND METHODS

Since 1976 SCS has been carried out at the Wessex Neurological Centre on patients with MS, pain and peripheral vascular disease. This communication concerns only the MS patients.

The original patients form part of a Medical Research Council (of G.B.) funded trial and initial temporary SCS was repeated three to six months later in order to examine consistency of response. In all, 27 patients with MS (fulfilling Schumacher's[1] criteria) had 41 studies of SCS.

SCS was carried out as described previously.[2,3] The epidural electrode was manipulated with symmetrical stimulation sensation into the legs and feet but this optimum stimulation was not always achieved. In some patients only unilateral or, more usually, root stimulation was achieved.

Patients were assessed clinically, physiologically, and urodynamically.[3,4] With two exceptions, patients were followed up indefinitely.

RESULTS

Type of Stimulation: In five patients mock stimulation was carried out (either cutaneous electrodes or epidural electrodes with no batteries) and there was no change in these patients. Nine patients had incorrect (i.e. unilateral or root stimulation) and there was no response in these patients. Symmetrical stimulation was subsequently introduced by manipulation of electrodes.

In six patients it was impossible to achieve satisfactory stimulation by our criteria. None of these six showed any clinical or measurable change. Twenty-one patients had good symmetrical stimulation sensation and 19 showed clinical and measurable response. All patients with pain (a not unusual manifestation of MS)

responded. Patients with motor symptoms occasionally showed improvement in flexor spasms and spasticity. There was increase in walking speed (30%) in five out of nine patients but this did not reach statistical significance. Fatigue and endurance were often improved but we have not been able to quantify this. Cerebellar and sensory symptoms showed either no response or an insignificant change.

The major change was in bladder function. Overall, 65% of patients with severe bladder disturbance showed improvement. Improvement in bladder symptoms were as follows:

Incontinence	58%
Urgency	63%
Hesitancy	71%
Frequency	63%
Stream	71%

Objective changes were seen in terms of improvement in detrusor instability (54%) bladder capacity (46%) and residual volume (50%).

It was not possible to predict from a detailed knowledge of pre-stimulation symptoms and urodynamic findings which patients would achieve a favourable response to SCS.

Complications: There have been no significant complications of SCS in the Southampton series. Minor skin infection occasionally occurred during the trial period of stimulation. Occasionally the electrode lead would erode through the skin, after implantation, and would need replacing. The major problems are due to electrode slippage and breakage of the electrode lead. A method for locating leads damaged in implanted systems has been described[5]

Long Term Benefit: The long-term effect of SCS is still uncertain because of poor follow-up information. All the patients in the Southampton series with the exception of two who were lost to follow-up, have been kept under regular supervision. Of the first 12 patients who were followed for over a year, six cases developed technical problems due to displacement or broken electrodes. One patient found the apparatus unacceptable. In only one case was the failure at one year due to failure of clinical response. However, although all six technical failures were re-stimulated through new electrodes, only one responded clinically to this second period of stimulation. The range of time for improvement following SCS was from four months to three years four months with a mean of one year three months. About three-quarters of the patients in the Southampton series, undergoing long term stimulation, lost the beneficial effect of stimulation at about one year.

The loss of response is not equal in all aspects of the neurological state. That is there is not a steady decline of all neurological manifestations. Mobility is lost first and any improvement seen in mobility following SCS is usually reduced to 50% or lost within the first 6-12 months. Bladder function is usually maintained much longer.

The reason for loss of response of bladder function in the Southampton series usually coincided with technical failure. Despite this, restimulation did not usually produce a consistent response and this is in contrast to the original period of 10 days of initial stimulation followed three to six months later by a second period of stimulation and permanent implant.

DISCUSSION

In a recent paper[6] reviewing the UK experience of SCS in MS in 90 patients there was a considerable degree of improvement in both the symptomatic and the objective

measurable changes produced. The number of patients receiving SCS at a single European centre (Zurich - Prof. Jean Siegfried, Personal Communication) exceeds the total of the number of patients treated in the UK. It was interesting therefore to compare results. In summary, the indications for SCS were similar and the long-term success was about the same. It is not known why the beneficial effects of SCS last only for about one year but presumably the natural course of the disease is responsible. Nevertheless, the alleviation of bladder symptoms, even for one year, represents a significant contribution to management. If one compares this kind of response with the response to therapy in other progressive neurological conditions, then it becomes less disappointing. For example, a recent review of Parkinson's disease[7] indicates that 62 of 178 patients had stopped Levodopa treatment within two years because of side-effects and inadequate response. No neurologist would regard this poor response as an indication for not treating patients with Levodopa.

There is a widespread misunderstanding about the nature of SCS. It is not, and never has been, advocated as a treatment for multiple sclerosis but is a treatment or technique for treating the neurological deficit caused by multiple sclerosis. The technique of SCS should always be looked at in this light.

CONCLUSIONS

SCS has an objective and beneficial effect on bladder dysfunction of MS in about two thirds of patients. This improvement is seen in patients who had previously been treated by standard techniques with poor or no response. Other manifestations of MS are unlikely to respond to SCS, with the exception of pain, and in some cases, spasticity and spasms.

Published accounts of the long-term benefit are incomplete and the outcome remains uncertain because of poor follow-up information and further detailed studies of the effects of SCS are necessary not only to determine the long-term benefit but also in order to arrive at a clearer understanding of the mechanism of action, so that this form of treatment can be exploited more effectively.

There is room for technical improvement since the need for accurate placement and the tendency for later slippage of electrodes make SCS a time-consuming procedure. Most centres where SCS is carried out would agree that the procedure should only be performed where adequate facilities are available for X-ray screening with image intensification, urodynamic assessment and the measurement of neurological disability.

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SPINAL CORD STIMULATION IN PERIPHERAL VASCULAR DISORDERS

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SUMMARY

Twentysix patients with advanced peripheral vascular insufficiency in the extremities were treated with electrical spinal cord stimulation. Healing of ulcers and/or prevention of amputation occurred in 16 patients and 19 patients reported significant pain reduction. Measurements of skin temperature and arterial toe pressure confirmed an increased peripheral blood flow by stimulation.

INTRODUCTION

In 1976 Cook et al. (1) reported that spinal cord stimulation (SCS) could improve patients with circulatory disturbances in the lower extremities. In the present study SCS has been used on patients with severe vascular insufficiency in the extremities. The effect of stimulation was evaluated by clinical observations, measurement of skin temperature and arterial toe pressure.

PATIENTS AND METHODS

Twentysix patients (8 women and 18 men; age ranging from 21 to 79 years with an average age of 66 years) were studied. All patients had severe signs and symptoms of peripheral vascular insufficiency in the extremities but not suitable for reconstructive vascular surgery. Eighteen patients had arteriosclerosis, five Raynauld's disease, one diabetes mellitus and two patients had posttraumatic vascular insufficiency.

SCS was performed by means of percutaneously inserted epidural electrodes. In most cases only one epidural electrode was used. When the lower extremities were affected, the epidural space was punctured in the upper lumbar area and the tip of the electrode placed at about T 10 in order to get adequate paresthesias at stimulation in the affected feet and toes. When the arms were affected, the upper thoracic area was punctured and the tip of the electrode placed at about C 5 to get adequate paresthesias in the hands and fingers.

The following electrical parameters were used: 100 Hz, 0.2 msec pulse width and an appropriate amplitude for comfortable paresthesias. The patients were asked to self-stimulate for at least 1 hour every third hour during day-time. However, most patients stimulated themselves more because of the beneficial effect on the ischemic pain condition.

The clinical effect of stimulation included observations concerning the healing of the ulcers and the patients' verbal report of their pain.

The peripheral arterial toe pressure measured by means of a strain gauge method. An increase of 20 mm Hg was considered significant.

The skin temperature was registered by a transducer technique and by thermocamera. An increase of 1° C was considered significant.

For various reasons only 15 patients were measured upon with the objective physiological methods mentioned above.

RESULTS

With respect to wound healing and/or prevention of amputation, success was obtained in 16 of the 26 patients. This refers to 11 of 18 patients with arteriosclerosis and 5 of 5 patients with Raynauld's disease. Significant pain relief was obtained in 21 of the 26 patients.

The skin temperature was significantly increased at stimulation in 11 patients of 15 investigated.

The arterial toe pressure was significantly increased in 10 patients of 15 investigated. There was no significant increase in the systemic arterial pressure in response to stimulation that could explain the pressure at the toe level.

DISCUSSION

The results are good in patients with arteriosclerosis and Raynauld's disease. It seems to us that SCS must be considered as the method of choice in patients with arteriosclerosis when reconstructive vascular surgery is not possible and in patients with Raynauld's disease as an alternative to sympatectomy.

The operating mechanisms of the stimulation are unclear. Three possible mechanisms may be considered: Firstly, it has been shown in animal experiments that an antidromic activation of C-fibers in the posterior roots increases the local skin blood flow. Such a mechanism seems not probable because the patients did not use a stimulation strength high enough to activate afferent C-fibers.

Secondly, the stimulation might activate ascending pathways to supraspinal autonomic centers responsible for a more general vasomotor fiber adjustment. If this had been the case, one would have expected a general vasomotor response and not only the local changes.

Thirdly, the stimulation may have activated segmental spinal mechanisms inhibiting sympathetic fiber discharge, primarily to the vessels in the extremities. This explanation seems to be the most plausible one.

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ANTERIOR SPINAL CORD STIMULATION IN THE TRANSTHORACIC APPROACH TO THE SPINAL CORD

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SUMMARY

49 patients suffering from trauma of the vertebral column and consequent affection of the spinal cord with transverse lesion were operated on by means of the transthoracic and thoracoabdominal approach. Out of these 49 patients 18 patients underwent intra- and postoperative spinal anterior and posterior epidural stimulation and examination of the stimulation effect by means of cortically evoked potentials. The prognosis according to the tendency of recovery of the spinal cord function was good in patients showing "neuronal continuity". Until now it is impossible to get any exact prognosis about the extent of the recovery to be expected. Apart from the diagnostic possibilities of evoked potentials, little therapeutic effects of stimulation of the spinal cord could be observed consisting in the fact that the rehabilitation time was shorter and spasticity was lessened.

PATIENTS, MATERIAL, AND METHODS

49 patients suffering from a traumatic spinal cord injury were operated on by transthoracic and thoracoabdominal surgery (1, 2). Out of these 49 patients 18 patients underwent an intra- and postoperative spinal cord stimulation. These patients were examined.

Surgical and stimulating procedure:

After transthoracic decompression (1, 2) of the spinal cord, a bipolar electrode was placed at least two vertebral segments ventrolaterally epidurally above the lesion. After this procedure cortically evoked potentials were recorded and motor effects on muscles below the lesion were observed and these special muscle groups were listed. Next, an electrode was placed at least two segments below the lesion and the same procedure was repeated. Before closing the thorax, two electrodes were placed above one ventrally and one dorsally, and two electrodes below the lesion, one ventrally and one dorsally. The position of the electrodes was checked by X-rays, and afterwards the wires of the electrodes were led out of the wound.

From the first postoperative day on,

a) stimulation was made and evoked potentials were recorded,
b) the effect of stimulation was checked (muscle movements) and the patient was asked about his sensations,
c) then we made a "therapeutic stimulation" (this was done in 8 patients only). After stimulations, lasting half an hour, an interruption of two hours was necessary.

The intensity of stimulation was chosen in such a way, that motor effects could just be noticed and/or that the patient felt little sensation in the lower extremities.

The stimulation and record of evoked potentials were effected by a DISA 1500 EMG apparatus. Stimulation parameters: Frequency 5 Hz, intensity: 2-4 V with constant currency, amplifier sensitivity, 5 uV/dIV, the band-pass amplifier ranged from 5 Hz and 5 kHz. The record was carried out with scalp needle electrodes from the sensory hand area of the best approachable side ($\bar{C}3/\bar{C}4$) with reference to the vertex (Fz). At least 256 average passages were necessary. The latency and amplitude of the primary cortical cpmplex (N20/p28) were examined. Intra- and postoperatively evoked potentials were elicited above and below the lesion and were compared with one another.

RESULTS

Figure 1

Example for dorsal column-stimulation above and below the lesion: traumatical transverse lesion in D6. Cortical evoked potentials recorded from $\bar{C}3$-Fz eliated from dorsal column stimulation in C6, D4, D6, D8. Normal in C6, D4, pathological changed in D6, abolished in D8.

Table 1

Number of patients with intra- and postoperative stimulation N = 18 patients
Patients with temporary implanted electrodes for therapeutic stimulation (up to 4 weeks) N = 8 patients

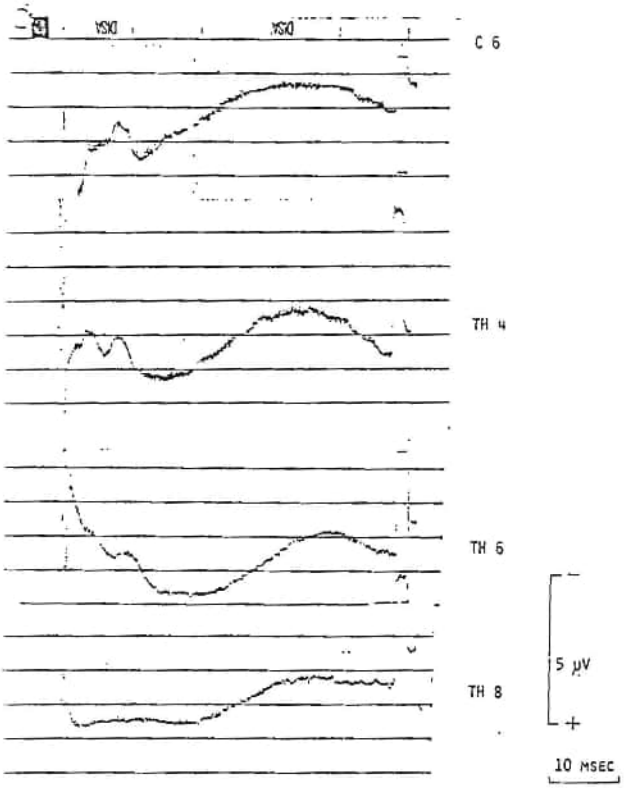


Figure 1

Table 2

Correlation: intraoperatively evoked potentials - postoperative ability to walk N = 18 patients

Intraoperatively evoked potentials elicited below the lesion

	positive	negative	no assessment possible
ability to walk	9	0	3
no change	0	4	0
"useless motor activity"	0	0	2

In all patients, who were able to walk after operation, the cortical primary response (N20/p28) could be recorded, although there was a more or less delay of latency of the potentials elicited below the lesion in comparison with potentials elicited above. In four cases with no infralesionally evokable potentials without artefacts, post-operative ability to walk never appeared.

DISCUSSION

Anatomical lesions of the vertebral column with consequent injury of the spinal cord can to be shown in an excellent way with CT and computertomographic myelography. But, in contrast to this, until now there is no satisfactory way of examination dealing with the recovery of functional activities of the spinal cord after an injury. The aim of our investigation was the attempt to make a statement of an eventual recovery of the spinal cord function by means of epidurally elicited intra- and postoperatively evoked potentials as well as epidural stimulation of the spinal cord. The questions, which arose, are listed as follows:

1. Is there any possibility to make a prognosis about recovery of the spinal cord by means of evoked potentials ?
2. Could any lesion of the spinal cord appear through the surgical procedures ?
3. Is there any possibility to examine the spinal cord function in the postoperative phase by means of the evoked potentials ?
4. Could apart from this diagnostic procedures, any "therapeutic" effect be reached through stimulation of the spinal cord ?

As we have touched a new field of neurophysiology, no definite, but only a preliminary answer to the questions listed above was possible and further investigations will be necessary. Experimental studies have shown that the prognosis is the better the sooner evoked potentials returned after an injury (3, 4). According to our findings the point of time of the operation is important as well. The prognosis

is the better the less the difference between the potentials above and below the lesion is. In the postoperative phase it was possible to stimulate not only the dorsal columns, but also the ventrally passing motor tracts, each of them separated from the other. In two cases there was no response after stimulation of the ventral tracts. In spite of this fact a considerably latency-delayed potential could be reached by stimulating the dorsal columns. But it was not reproducible and so we classified this finding as "no response". Clinically, no improvements of motor deficits could be observed in this patients. Nevertheless, there are more and more experimental signs that the pyramidal tract and the dorsal column work independently of each other (5).

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ATTEMPTS TO UTILIZE THE STIMULATION OF THE SPINAL CORD IN THE TREATMENT OF TRAUMATIC INJURIES OF CERVICAL SPINE.

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Since the publication of the report by Cook /1/ stimulation has been used in treatment of spinal cord diseases. At the same time at the Rehabilitation Clinic in Konstancin first attempts were made to apply stimulation directly to the spinal cord within the first hours or days after injury to the spinal cord /4/. The present report aims at presenting the effects of direct stimulation of the spinal cord after injury in terms of achieved neurological improvement and quickened formation of bladder automatism.

MATERIAL AND METHODS

60 patients with spinal cord injury in the cervical /36 cases/ and thoracic segments have had electrodes implanted surgically hitherto. We shall confine our considerations only to the effects of treatment of the cervical spinal cord injuries, since it is the cervical spinal cord segment that we have stimulated most frequently so far, and were able to select representative groups of patients with equal degree of spinal cord damage.

Electrodes were implanted during decompression of the spinal cord from anterior approach, usually with partial or complete resection of the vertebral body. After removing fragments of the vertebral body compressing the cord and after forming the bed in the adjacent bodies, the electrodes were inserted under the bone graft or under the vertebral bodies adjacent to the damaged one. Then a canal was made in the subcutaneous tissue of the neck or in the subclavicular region where the receiver of the stimulator was placed. The implanted stimulators were designed in our Clinic and had been used for stimulation of peripheral nerves. The stimulator was supplied externally by means of imparting energy in electric coupled circuits. The stimulator emitts rectangular impulses, duration of which can be regulated exact to 0.2 - 1.2 msec, frequency range being 30 - 80 Hz and amplitude 0 - 20V. The following parameters are usually used: impulse duration 0.7 msec, frequency 45 Hz, amplitude of tension up to several volts, individually regulated. The stimulation was performed with the use of a specially designed programming device. Series of impulses of 5sec each with intervals of 30sec were

applied for 5min. Then 30 min. break followed and the 5 minut stimulation was repeated. The daily training lasted 3-4 hours and was carried on within 3-4 weeks after surgery.

COMPARATIVE CLINICAL EVALUATION OF ELECTROSTIMULATION OF THE SPINAL CORD.

Clinical evaluation of the effects of stimulation in spinal injured patients can only be made in comparison to a group of patients with similar degree of spinal cord injury who underwent surgical decompression by the same method. Otherwise it is imposible to assess the degree of neurologic improvement or automatism formation due to surgical decompression of the cord or due to stimulation. The compared groups comprised patients of corresponding age, who had same kind of decompression and surgical stabilization at the same period time, but in one group only the stimulation of the spinal cord was applied. Each group was divided into subgroups according to the symptoms of complete or incomplete injury to the spinal cord. Thous groups, as mentioned before, were compared with respect to obtained neurologic improvement and time elapsed from injury to the formation of bladder automatism. Neurologic improvement was evaluating by comparing groups of 15 patients with the same degree of spinal cord injury assessed on admission and then recording the change of neurologic condition after treatment. In case of complete injuries there was loss of active movements and of all kinds of sensation from the level of spinal cord injury downwards.
Incomplete injuries are traditionally divided into 3 groups:

1. Loss of voluntary movements with traceable deep sensation in feet,
2. Extensive paresis with active movements of no functional use /muscle strength below 3^{o} acc. to Lovetts scale/,
3. Paresis of slighter degrees rendering the basic life functions possible.

Table I presents the comparison of neurologic improvement obtained in the group of complete and incomplete injuries of the cervical spinal cord.:

neurologic state before - after treatment	anterior decompression	decompression + stimulation
C - 3	-	1
C - 2	2	4
C - 1	3	2
1 - 3	4	8
1 - 2	6	2
C - C	10	8
1 - 1	5	5

Table II presents comparison of bladder automatism formation in the stimulated and unstimulated groups:

automatism formation /in weeks/	spinal cord injury			
	complete		partial	
	decompr.	decompr. +stimulation	decompr.	decompr. +stimulation
3 - 5	-	4	2	6
6 - 8	3	6	5	7
9 - 12	3	3	6	2
13 - 16	6	2	2	-
17 - 20	2	-	-	-
over 20	1	-	-	-
average	13.2weeks	7.7weeks	8.9weeks	6.2weeks

DISCUSSION

It seems that - although the clinical material is not vast yet - the the presented data are convincing and clearly show beneficial effects of stimulation on injured spinal cord. The obvious necessary condition of neurologic improvement in the complete spinal cord injury group is the decompression and implantation of stimulators at the earliest possible time after injury, within a few or several hour preferably. The patients with symptoms of complete injury presented in the Table were operated on within 24 hours after injury.
Table I shows that stimulation influences not the incidence of neurologic improvement so much, as it leads to better quality of the improvement. Significant neurologic improvement, i.e. by two degrees of our scale, at least, was obtained in 43% of stimulated patients, whereas only in 20% of the unstimulated group.
The effect of spinal cord stimulation on the control of the functions of neurogenic bladder had been reported earlier /2,3,5/. This effect is also clearly seen in our comparison.

It follows from the presented data that stimulation of the spinal cord makes it possible to improve effects of treatment of spinal injured patients and it seems to be worth while continuing research in this field.

CONCLUSIONS

1. The application of stimulation of injured spinal cord yields good results in patients in the early post-trauma period.
2. The analysis of the data confirms the favourable effect of spinal cord stimulation on the formation of bladder automatism.
3. The results we have obtained hitherto allow the conclusion that the stimulation of spinal cord exerts beneficial influence on better results of treatment of the discussed group of patients and continuation of investigations into this field is by all means purposeful.

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THE ROLE OF BIOMATERIALS RESEARCH FOR ELECTRICAL STIMULATION

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SUMMARY

Materials problems are especially critical, when implants are used for the functional stimulation of living tissues. However, the roles of materials, surface conditions, and designs for the electrode-tissue interactions are not yet fully understood, the ideal materials or material combinations for the insulation of leads, for the encapsulation of devices or for transcutaneous implants have still to be found, and there are many open questions as to the effects of long-term stimulation on tissues, materials, and devices.

In this review, the state of the art in biomaterials research will be discussed in respect to the specific problems associated with electrical stimulation.

ELECTRODE MATERIALS

The materials used as electrodes in stimulating as well as in recording systems must first of all exhibit electrical and mechanical stability in the corrosive physiological environment. For the performance of an implanted electrode, however, not only the material composition, but also so different factors as surface roughness, design, type of surrounding tissue, local electrolyte concentration and pH, interfacial proteins and other macromolecules, kind and density of the stimulating current, duration of stimulation, etc. are important.

Of all the metals in use for electrodes,platinum and platinum alloys exhibited the most acceptable behaviour in vitro and in vivo for current densities below 0.02 A/cm^2. Since the threshold current densities for the stimulation of most tissues are in the range of 0.1 to 1.0 A per cm^2, not only the more corrosion-susceptible alloys of ignoble metals, but even the noble metals platinum, iridium or gold will show increasing surface degradation (= corrosion) due to electrochemical reactions which cause damage to the electrode and to the surrounding tissue (1). This corrosion damage can be prevented in capacitative electrodes, where a thin, dielectric oxide film"insulates"the electrode surface. This could be the advantage of using the refractory metals tantalum or titanium, and anodized tantalum was regarded as the safest electrode material for chronic high-current density stimulation (2), although with some charge-storage limitations. It was also observed that the protein film which is deposited on an electrode surface, can act in the same way as the oxide film thus making the electrode capacitative (1).

On the other hand, the effect of the electrode material itself on the surrounding tissue can also show that noble metals, despite their chemical inertness, may not be as biocompatible as for example the refractory metals tantalum and titanium. This could be demonstrated in own experiments (3), where gold exhibited an inhibitory effect on in vitro cell growth and in vivo bone formation, while tantalum and titanium were well tolerated.This interdigitation of electrical and mater-

ials influences on the tissue response was well demonstrated in a recent study on electrical stimulation of bone formation (4), where direct current stimulation was performed at current densities of only 0.02 and 0.2 $\mu A/mm^2$, and the effect of electrodes manufactured from 6 different metals and alloys was compared. It was shown 1) that the osteogenic effect decreased considerably with the noble metals platinum and gold at the higher current level, while the ignoble stainless steel performed better, and 2) that around unstimulated gold and silver electrodes the reparative bone formation seemed to be more impaired than around platinum and the ignoble alloys. It is astonishing, but typical for the state of the art, to note that such comparative studies are only scarcely found in the literature. More basic knowledge in this respect would be desirablesince it is necessary to distinguish between the tissue reaction due to the presence of an implanted electrode itself and the effect of short and-even more important- chronic stimulation on the target cells and the surrounding tissues, as for example in endocochlear auditory prostheses (5).

As mentioned before, also the type of tissue into which the electrode is implanted, can be important. For example in neural tissue, silver is toxic even as a passive implant, and the same deleterious effect was found for carbon (1) which is regarded as one of the most inert materials in other tissues.

SURFACE CONDITIONS AND DESIGN OF ELECTRODES

An important factor for the tissue response to an implant is it's surface condition. While the role of surface charge, interfacial forces, hydrophilicity, and thrombogenicity is quite well studied for blood contacting materials, these aspects just begin to attract more attention in other implant situations such as in soft or hard tissue. Also here the nature of the proteins primarily adsorbed to the implant surface is determining for the cellular reaction and for the future fate of the implant.

There are, however, more obvious surface properties like roughness (microstructures) or porosity (micro- to macrostructures, depending on pore size)which must be considered. It has been repeatedly demonstrated that a roughened surface makes a given material more irritating and creates a so-called foreign body reaction, which is not observed around the smooth form of the material (1,6). On the other hand,cells and tissues will adhere on rough surfaces which can prevent the also deleterious effect of motion for the interface reaction. Therefore, smooth electrodes will be selected for neural tissues where only minimal irritation is desired and only minimal implant motion is to be expected, while for muscular electrodes and especially for cardiac pacemaker electrodes a rough surface and -even better- a porosity for tissue ingrowth can be successfully used for better implant fixation (7). One has to keep in mind, however, that the increased surface area of such implants puts higher demands on the corrosion resistance of the electrode material, and that fibrous tissue ingrowth and eventually enhanced encapsulation with scar tissue will interfere with keeping the impedance as low as possible.

This latter consideration relates also to the design of the electrode tip which should be implantable without greater traumatization and should not cause biomechanical trauma during function. This could be shown, for example, in own experiments with "non-traumatic" and "traumatic" pacemaker electrode tips (8). Traumatic, screw shaped tips were found penetrating the endocardium even when they were only laid onto endothelial surface, because of the implant movements during cardiac motion. The resulting fibrous tissue reaction, however, was greatly enhanced if the electrode was in fact inserted into the myocardium. The elevation of the threshold for stimulation is the price for a more

accurate and durable electrode fixation.

MATERIALS FOR INSULATION AND ENCAPSULATION

The materials which can be used to insulate electrodes or leads from the target cells and the surrounding tissue, or which can encapsulate and tightly seal an electronic device from the body fluid and moisture, are mainly plastics (silicone rubber, epoxy resin, TEFLON^{R}) or inert carbon materials, ceramics or glasses. Another way of solving the water-permeability problem is the welding of metallic cans of either stainless steel or titanium. Besides corrosion the leaking of the welds required again additional plastic encapsulation. All the encapsulants and insulations must be sterilizable, cause minimal tissue irritation, and in general be biocompatible.

Another aspect is the constant motion of these soft tissue implants which requires a mechanical suitability not only capable to protect the lead or device from breakage, but also to withstand the mechanical stresses while undergoing the degradative attack of the physiological environment which is a major problem in most of the plastics in medical use. Evidence for this "biodegradation" could be presented and related to the morphological appearence and histochemistry of the interfacial tissue and cells (9). The more "degradable" a material, the more intense and long lasting is the cellular reaction characterized by macrophages and multinucleated giant cells. The presence of such a foreign-body-reaction, however, which is opposed to acute or chronic inflammatory reactions by some authors, can no longer be regarded as indicative for bioincompatibility. Improvements in the histological techniques made it possible to detect foreign-body-cells also around implant materials which were up to now classified as biocompatible because they seemed to be encapsulated solely by a fibrous connective tissue. Such differences in histological findings could be demonstrated, for example, in a recent study on MACOR^{R}-glass ceramic (10), a material which is also in use for pacemaker encapsulation.

Finally, in this section one of the most difficult problems with biomaterials applications should be discussed: the transcutaneous implants. Leads of stimulating or recording systems which pass through the skin or, for example, from the middle ear cavity into the endolymphatic space of the cochlea, require a tight seal which resists mechanical motion and occludes the drainage of exudate or infection, the latter of which is considered the main cause for failure (11). This goal could only partially be reached by coating the transcutaneous (transmucosal) portion of the device with velours or felts from plastics or even with processed biological materials like collagen sponge which allow for connective tissue ingrowth thus preventing the deleterious downgrowth of the respective epithelium. Because of the not yet adequate chemical and mechanical compatibility of the available materials the ideal system has still to be found. This example can teach us, however, that we still have to be modest when we look to the success which we reached in solving even simply looking problems with biomaterials applications.

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PACKAGING TECHNIQUES FOR IMPLANTABLE ELECTRONIC DEVICES AND SENSORS

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SUMMARY

With advances in microelectronics and integrated circuits designed to perform complex functions, the primary controlling factor in determining the lifetime of any implantable electronic devices today is the reliability of its package. The most sophisticated biotelemetric device will perform only as well as the materials used to protect its circuitry against an agressive environment such as that found in the bodies of both humans and animals alike. It is difficult to categorize the best packaging materials currently available. The optimal biomaterial for all occasions has not yet been developed. Many packaging materials may serve to fulfill special requirements, but no one material is superior for all applications. One class of materials may outrank another in terms of performance based upon a specific quality or a particular function. It remains essential, however, that the packaging engineer not only base the selection on the inherent properties of the material, but also carefully consider all possible consequences when the material is interfaced with another material exhibiting dissimilar characteristics. This article reviews the literature with emphasis on techniques acquired from research on implantable instruments at the Electronics Design Center at Case Western Reserve University, in the areas of hard shell encapsulation package and implantable sensors.

MATERIALS AND METHODS

All packaging materials should fulfill two major functions : 1) Protection of electronic and mechanical components of the instrumentation systems from hazardous body environments. 2) Compatibility with the body of the subject whether the material is totally implanted, percutaneously connected, or attached to the surface. Many materials are presently known to be acceptable. /1-4/

The major considerations in selecting a packaging material & technique are :

I. Protection of components from moisture penetration and mechanical stress

(1). Moister Permeability :

Polymeric material has various moisture permeability. It's ability to keep moisture out of package depends on the material and the thickness of the package as shown in Figure 1.

The permeability is also very sensitive to the material preparation, and the packaging procedure and environment. They are not generally suited for long term implant applications. Common polymers used for biomedical device package and their typical moisture transmission coefficient are given in Table 1.

(2). Adhesion :

The adhesion of the polymer to the underlying surface modifies the effect of moisture permeability. If the package has voids the water vapor will condense and weaken the bonding surrounding the void causes breakdown of total package. Therefore it is quite frequently one would select a good adhesion polymere with suitable moisture permeability over others with lower permeability but poor adhesion for packaging.

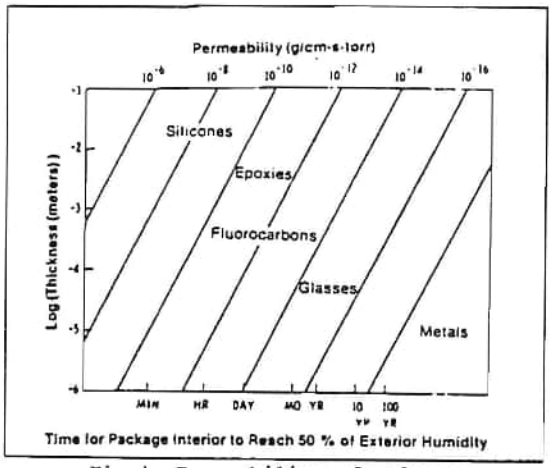


Fig.1. Permeability of polymers.

Polymer (2-mil films)	Moisture Vapor Transmission (Measured at 86° F and 90%-98% R.H.) g/mil/100 in² · 24 hr
Polymonochlorotrifluoroethylene:	
Aclar 33-C	0.015
Kel-F	0.02
Trithene	0.02
Ethylene/vinyl acetate copolymer (Elvax 260), 1-mil film	0.20
Polyvinylidene chloride (Saran)	1
Parylene C	1
Polytetrafluoroethylene (Teflon)	3
Polyethylene	21
Polyethylene terephthalate (Mylar)	48
Polystyrene	120
Silicone rubber, 1-mil film	170

Table 1 : Common packaging polymers and their moisture transmission coefficient.

(3). Hermeticity : (nearly zero permeability)

Glass, ceramic and metal enclosure, when properly sealed, can provide a hermetic environment for the electronic devices. In this case the package can be considered not permeable to moisture in the expected life time of the device. Techniques of sealing of this groups of material will be discussed later.

(4). Mechanical Rigidity :

To protect the components from external stress and to maintain their integrity.

(5). Long term stability :

Under thermal cycling, mechanical vibration and various electrical operating conditions the package should remain stable in its life time.

II. Biocompatibility :

(6). Metallic conosion and polymeric degradation. The possibility and the effect of the product of these chemical reactions need to be considered.

(7).Thomboresistance and other Toxi effect of the material in contact with tissues.

(8). Sterilization :

Varies sterilization methods including steam, dry heat, cold gas, radiation and sporicide solutions need to be considered in term of the properties of packaging material and electronic components.

III. Implant operation considerations

(9). size at weight
(10). shape and surface condition
(11). methods of fixation of implant in the body
(12). cost, repair or replacement

For medium and long term implant, 3 kinds of materials have been sucessfully tried

1. Glass : the high dielectric strength, high volume and surface resistivity, low dielectric loss, low thermal conductivity, good biocompatibility, and the ability to be made of various shapes make glasses attractive packaging materials, especially for small packages. Pyrex glass with metal feed through or metal-glass joints had been sealed with laser or small localized heat source. These devices had been implanted in animals and lasted several years without package failure.
   However the glass has poor tensible strength its brittleness limit the use of glass for large packages.
2. Ceramic
   Ceramic is chemically stable, mechanically strong and is a good insulator /5/. However like glass the tenside strengten is poor and is brittle. A type of machinable ceramic MACOR (from Corning) was used sucessfully to house telemetry and stimulation electronics implanted in the body for over 2 years and is still functioning. The main body of the package is machined from a block of MACOR. A close tolerance cover is sealed to the main body box with thin layer of epoxy.
   MACOR offers : Proven biocompatibility, good machinability, high fracture energy, high thermal shock resistance and minimal outgassing /6/.
   Current effort in using CO_2 laser to seal macor is been pursued. If sucessful, it will be an important packaging material for long term implants.
3. Metal
   Metal can be made to various forms and sealed by soldering, brassing, as well as resisitive, laser, and electron beam welding to fabricate hermetic packages. However most metals corrodes. For example, KOVAR is a iron-Nickel-cobolt alloy, it is used extensively in electronic industry, but even with conventional gold plating. KOVAR packages corrodes in VIVO and produces toxic products.
   The titanium is generally accepted as the choise for its excellent corrosion resistance, light specific gravity, and good mechanical strength.
   Tantalum is similar to titanium, can also be used for implant package.
   Hermetic seal of titanium can be made with laser or electron beam welding, glass-metal feed-throughs with Pt and Ti wires can be made.
   These hermetically sealed titanium package is expected to have life time of exceeding 10 years. For applications where metal package can be used, it is clearly the choice of the present time.

In micro-sensor package, no satisfactory material or technique has been found for long term implant package. Sensors has the unique requirement that the sensitive area has to be in communication with the tissue or body fluid in order to sense the parameters. The size requirement of the micro sensor package made the problem very difficult. At the present, there is no material that can protect the micro-sensor leads and electronic components and yet to allow bio-signals to communicate with sensors without produce interferences over long period.
Currently polymeric materials were used or special techniques developed for a special sensors. Additorial research is needed in this area.

RESULTS

Small size pyrex glass package for telemetry units has been sealed by laser and micro-torch to indicate a life time in VIVO better than 2 years, expected lifetime is much larger than this.

MACOR ceramic was used for medium term implants that require insulator as the packaging material such as in all RF powered implants. In this case the Macor is machined

to form a box and a cover with close fit (tolerance on the order of 10-20 u). After the electronics is prepacked and coated with polymers and assembled in the box, cover is sealed with thin layer of spoxy. The leakage path of the moisture has very small cross-section thus may extend the life time. Telemetry devices using Macor has been implanted in animals with life time over 2 years and is still functioning.
Titanium flat pack with wire feed-throughs and sealed with laser beam is currently used for implantable intracranial pressure monitoring system as shown in Fig. 2. Animal evoluation has passed 4 months test, no failure due to packages were observed.

DISCUSS

For package of implant electronics there are several choices, but for sensors, better technique is to be developed. New materials and new approaches and techniques are needed.

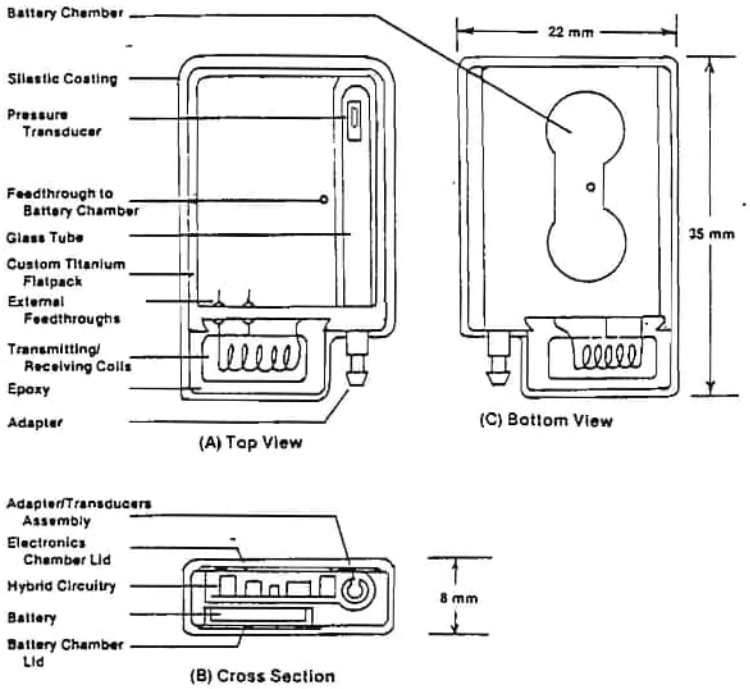


Fig. 2. Intracranial pressure
Monitor transmitter package

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ASPECTS OF CORROSION PERTINENT TO NEUROLOGICAL PROSTHESIS

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SUMMARY

Weight loss and electrochemical techniques have been applied to carry out preliminary studies on the corrosion of Kovar and a solder. These metals were assessed either as single items, or when coupled to gold or to a platinum alloy respectively. The variables used were the electrolytes, created by various proportions of CO_2 and O_2 in deionized water, and temperature which was set at values of 303 K, 318 K, and 330 K. In sealed systems, i.e. temperature the only variable, after 750 hours exposure corrosion losses of Kovar were increased by factors of 1.38 (SD = 0.13) and 1.95 (SD = 0.28) at temperatures of 318 K and 330 K respectively, compared with losses at 303 K. In contrast to the Kovar overall losses, which were within the range of 9.8 to 27.5 mg cm^{-2}, the solder losses ranged from 1.2 to 3.1 mg cm^{-2}. The electrochemical techniques proved useful in showing that the corrosion limiting step was a diffusional process, and in yielding information about the nature of the corrosion films formed and the type of corrosion occurring. Of the electrochemical methods used, the AC Impedance technique was found the more generally useful in that in addition to electrochemical data, information of a surface physico-chemical nature was also obtained.

MATERIALS AND METHODS

Introduction.

Two of the ways in which a neurological prosthesis may fail are (a) adhesion loss of its encapsulant and (b) corrosion of its metallic components. With this problem in mind, the following is an account of some preliminary work involving the effect of variation in environmental temperature and composition, on the corrosion of certain metal alloys.

The simple model envisaged consists of two metal couples encapsulated in a (silicone) rubber (1,2). The couples consist of solder (62/36/2, Sn/Pb/Ag) with a thick film metal conductor (Pt/Au), and Kovar (54/29/17, Fe/Ni/Co) with gold (3). It is proposed that the encapsulant is permeable to water vapour, oxygen and carbon dioxide, i.e. this basic model excludes considerations involving any through diffusion of ions such as chlorides etc. It is suggested that, in the course of time, the encapsulant may lose adhesion and become detached from the underlying microcircuit, creating voids into which water vapour can condense and into which oxygen and carbon dioxide can then dissolve (4,5). Thus an electrolyte containing protons, bicarbonate ions and dissolved oxygen can contact single metals and bridge metal couples.

Environments.

Tests were carried out at three temperatures, using four gas compositions passed into de-ionized water. The temperatures were 303 K, 318 K and 333 K, whilst the gas mixtures (volume %) of carbon dioxide and oxygen used were 13/87, 50/50, 87/13 and 100/0 respectively.

Test Types.

Two series of tests were carried out, involving (a) simple weight loss determinations, and (b) electrochemical techniques. An essential difference in electrolyte composition between these tests was that the weight loss determinations were carried out within sealed systems, whilst the electrochemical techniques were open to the atmosphere.

Weight Loss Determination.

Samples of Kovar and solder were prepared, size 10 mm x 10 mm x 1 mm, washed, rinsed and dried using pure acetone, de-ionized water and filtered warm air. A sample of each was weighed and then placed in separate 500 ml screw capped bottles. Four stock electrolyte solutions were prepared at 303 K, using one of each of the various gas compositions, and the pH and conductivity of each solution measured. Then 450 mls of each was added to the bottles such that samples of the metals could be tested in each of the four electrolytes at each of the three temperatures. The bottles were then firmly screwed closed and sealed, and placed in water baths set at 303 K, 318 K, 330 K. The bottles were agitated four times daily for 30 days. Then the seals were broken, the specimens removed, dried, examined, corrosion products removed and finally reweighed. The pH and conductivity of the solution in each bottle was again measured.

Electrochemical Methods.

Four electrochemical techniques were used. These are outlined below, and an indication is given of the nature of the results which may be produced. The techniques are Potential Monitoring, DC Polarization, Zero Resistance Ammetry and AC Impedance.

Potential measurements require a reference electrode (e.g. SCE) and a high impedance millivoltmeter. In oxygen containing solutions a more positive potential usually indicates film formation or passivation, whilst a more negative potential suggests a low oxygen content and hence a low corrosion rate. Importantly, the presence of crevice or pitting corrosion displays characteristic 'spikes' or 'saw-tooth' changes in the potential response. In the DC Polarization technique, a potentiostat is used to sweep the potential of a specimen from (typically) 500mV ± the rest potential whilst recording the current flowing (6,7). The slopes of the potential vs. log (current) plot yield Tafel constants which are characteristic of the anodic and cathodic processes (8). The polarization resistance (Rp) is estimated from $\Delta E/\Delta i$ at the rest potential, and the corrosion current is calculated using Rp and the Tafel constants. Zero Resistance Ammetry (ZRA) can be used when the anodic and cathodic areas are well separated. Thus the corrosion processes in galvanic couples may be studied. The two specimens, (one anodic and one cathodic), are connected to an amplifier so that a current is supplied which constrains the specimens to the same potential. This current is then the corrosion current flowing when the two specimens are connected together, and depends upon the presented areas of the two specimens. The AC Impedance technique is a sophisticated method of studying corrosion processes, and requires a Frequency Response Analyser (FRA) and a computer to present the data (9). A small sine-wave (of selected frequency) voltage is applied, and is correlated with the resulting current (at that frequency). Pairs of voltage and current are obtained over several decades of frequencies. The data is modelled by a computer in terms of probable physico-chemical processes occurring in the corrosion system. This technique can yield an overall view of reacting surface properties and processes at the same time. Thus, relationships between voltage and current in the 10^4, 10^3 and 10^0 hertz order, are largely determined by solution resistance, surface films and species diffusion effects respectively.

The above techniques were used on Kovar and solder specimens suspended in test cells open to the atmosphere, at the given three temperatures, whilst the given various

gas compositions were continually passed into de-ionized water in the cells. In addition, currents flowing between Kovar and gold (18 carat), and between solder and a platinum/gold alloy, were measured using Zero Resistance Ammetry.

RESULTS AND DISCUSSION

Conductivity and pH.

The initial conductivities ranged from 23±1 x $10^{-6}\Omega^{-1}$ for 13% CO_2 87% O_2, to 55±5 x $10^{-6}\Omega^{-1}$ for 100% CO_2 electrolytes, whilst the corresponding pH values ranged from 4.45 ± 0.05 to 4.1 ± ·2. After 30 days of the weight loss work, the final values of conductivity ranged from 110 x $10^{-6}\Omega^{-1}$ to 160 x $10^{-6}\Omega^{-1}$ for the Kovar specimens, and from 22 x $10^{-6}\Omega^{-1}$ to 56 x $10^{-6}\Omega^{-1}$ for the solder specimens. The corresonding pH values ranged from 4.9 to 5.5 Kovar, and from 4.5 to 5.3 solder.

Weight Losses.

The Table displays the weight losses incurred by Kovar with variation in temperature and electrolyte composition. It is seen that the 50% CO_2 50% O_2 produced electrolyte causes the greatest losses, and that the losses increased as the temperature increased. The averaged corrosion loss increase factors, due to temperature rise from 303 K to 318 K, and from 303 K to 333 K, are 1.37 and 1.94 respectively.

TABLE

WEIGHT LOSS (mg cm^{-2}) OF KOVAR (54,29,17,Fe,Ni,Co) AFTER 750 hrs. EXPOSURE TO AQUEOUS SOLUTIONS WITH VARIATION IN GAS COMPOSITION AND TEMPERATURE (SEALED SYSTEM)

GAS COMPOSITION VOL.%		TEMPERATURE (K)		
CO_2	O_2	303	318	333
13	87	12.4	18.0	25.1
50	50	15.1	18.4	27.5
87	13	10.1	16.8	23.7
100	0	9.8	11.8	15.6

In contrast to the Kovar weight losses, those incurred by solder ranged from 1.2 mg cm^{-2} to 3.1 mg cm^{-2}, with the electrolyte produced by the 87% CO_2 13% O_2 gas mixture causing most corrosion.

Electrochemical Studies.

At all three temperatures, the potential of Kovar decreased by at least a factor of x 2 as the oxygen content of the gas mixture was decreased. This, combined with the actual potentials found, indicated that the oxides and/or hydroxides formed on the metal surface were only partially protective. In contrast, the solder potential only fell by some 15% as the oxygen content decreased. This suggested that whilst a film did form on solder, the overall reaction with oxygen was slower than with Kovar. The DC Polarization results, i.e. the Tafel constants values, from the 'potential-log (current)' plots, showed that the limiting processes for the corrosion

of both Kovar and solder were diffusion controlled, at all oxygen flow rates. At 303 K the slope $\Delta E/\Delta i$ at the rest potential - the polarization resistance (Rp) - fell by 33% for the solder and 50% for Kovar as the oxygen flow changed from high to low rate; and an increase in temperature to 318 K also caused a fall (slight) in Rp for both metals. These results suggested that decreasing the oxygen concentration (within limits) and increasing the temperature increases the corrosion rate, bearing in mind a reasonably constant relationship between the anodic and cathodic Tafel slopes, and further suggested that the oxide and/or hydroxide corrosion product formed became less protective as temperature was increased. It was noted that Kovar showed passivating tendencies when its potential was raised well beyond the rest potential. The Zero Resistance Ammetry work displayed quite different behaviour between the Kovar/gold couple, and the solder/platinum alloy couple. The Kovar couple, especially at the lower temperature and higher oxygen content, showed persistent periodic current fluctuations. This suggested that the coupling to gold raised the Kovar potential to produce(only) partial passivation, which effectively created a large cathodic area which promoted development of localized small areas of high anodic (corrosion) current density, i.e. corrosion pitting. The fluctuating current, yielding the characteristic 'saw-tooth' pattern, suggested a dynamic situation of pit repair and breakdown. At the lower temperatures, the current response of the solder couple also fluctuated. Over a period of several hours the amplitude of these fluctuations decreased giving, finally, a smooth response. However, this smoothing did not occur at 333 K. The current flow in general was proporitional to the oxygen flow rate, i.e. a change in flowing gas composition from 50% to 13% oxygen caused a 30% decrease in the current flowing. An increase in temperature from 318 K to 333 K caused an increase in current flow for both couples. However, at 318 K after some hours a sharp current decrease was observed; no such decrease was noted at 333 K. These observations suggested that, whilst increased temperature and oxygen flow rate induce a higher rate of corrosion film formation, the higher temperature promotes the formation of a less protective film. The difference in corrosion response indicated that Kovar suffers localized attack whilst solder does not. The AC Impedance technique was used to study the corrosion of solder. The plots showed two arcs for all oxygen and temperature values. The main arcs had maxima in the frequency range 55 ± 15 Hz which did not change in diameter with applied potential. This response could be modelled with a 0.25 ± 0.15 μF capacitor in parallel with a resistor; further, the modelled value of this resistor increased with increased oxygen flow, and decreased (slightly) with increased temperature. These effects indicated the presence of a porous surface film, some 20 nm thick, with the variable degrees of corrosion product pore blocking being functions of oxygen flow rate. Additionally, the response suggested that the protection afforded by the film decreased slightly as the temperature was increased to 333 K. Finally, the maximum of the low frequency arc, (less than 1 Hz), its modification to a straight line when anodically polarized at lower temperatures and lower oxygen flow rates, its diameter reduction when cathodic polarization was impressed or a higher temperature used, suggested that the corrosion process is increased with temperature and oxygen diffusion controlled.

COMMENT AND CONCLUSION

Neurological prostheses, in which the implanted micro-electronic part comprises a thick-film circuit encapsulated in an adherent rubber or resin, appear to offer a service life approximately 5 years, (10). Since it is, in general, not practicable to test in a simulated in-vivo environment over such time scales, modern technological progress in creating new designs of prosthesis also creates a demand for in-vitro testing and assessment. Thus, some form of valid accelerated test is necessary. Clearly, the dominant degradation mechanisms occurring in an in-vitro test must correspond and relate to those pertinent to the in-vivo situation, in addition to proceeding at higher rates.

The failure of an encapsulated prosthesis, in this context, can be conceived as including two general effects, i.e. adhesion loss of encapsulant and corrosion of enclosed metal components. Studies upon adhesion involving accelerated testing has

concerned the action of water at temperatures up to 340 K, and the influence of design and stress, (11,12). Amongst much more information, such works included lap-shear joints involving Kovar specimens and an alcohol evolving R.T.V. single-pack silicone adhesive, immersed in de-ionized water at temperatures between 310 K and 373 K. The adhesive failure time decreased with increasing temperature, with the time/temperature relationship expressable in terms of an overall activation energy of 0.48 eV (4.63×10^4 J mol^{-1}). Bearing in mind the limitations involved in comparing 'activation energies', it is still interesting to note that the presently reported work on corrosion for Kovar demonstrated a corrosion loss/temperature average activation energy relationship of 0.19 eV (1.82×10^4 J mol^{-1}), over the range 303 K to 333 K. The tentative indication is that adhesion is rather more sensitive to temperature change than corrosion.

As a final comment, this preliminary study suggests that the use of both AC Impedance and DC Polarization methods, carried out on sealed electrolyte systems, would constitute a very useful basis for an accelerated in-vitro corrosion test procedure. This is considered so because, in addition to yielding information upon corrosion rates with temperature, the dominant processes occurring could be constantly monitored and thus any deviation from in-vivo processes would be immediately recognized.

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SOLID STATE SENSORS IN CLOSED LOOP CONTROL OF PROTHESES x)

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SUMMARY

As the physiological understanding and electronic technology advances, closed loop control of protheses, such as cardiac and respiratory pacing, artificial organs, neuromuscular control and automatic drug delivery systems, become within the reach of medical research and health care communities. The key hardware element to be developed is the proper sensors used to access the state of controlled parameters in order to close the control loop. Many solid state sensors have been developed recently. A brief review of the sensors that may be applicable to the control of protheses is made. Two examples on pressure and ionic concentration sensors are used to illustrate the promise of electronic technology in developing biomedical microsensors, eliminate the problem of shielding connecting wires from the sensor to the following processing circuits. Other functions such as temperature compensation, off-set voltage adjustment, digital coding, alarm, etc. can be incorporated to make it a real intelligent sensor.

A partial list of the physical and chemical parameters that can be sensed by solid state sensors is given in Table 1. More detailed information can be found in the literature and the references [1-6].

Two examples, one in pressure sensors and another in pH sensors are given to illustrate the progress and the problems in the development of solid state biomedical sensors,

Table 1. Potential solid state sensors for biomedical measurement

Quantity measured	Principles or devices used
Electrical potential	Active and passive electrodes
Electrical impedance	Electrodes (driven)
Temperature	Thermisters, diodes, infrared sensors
Sound	Microphone
	Capacitive and Piezoelectric
Ultrasound	Piezoelectric
Light	LED and detection, transmission, reflection
Magnetic	Hall devices, flux sensitive transistor
Pressure and time	Piezoresistance, capacitive sensors
Flow	Differential pressure sensor, thermal gradient, ultrasonic and optical doppler
Displacement, Velocity, Acceleration	Accelerometer
	Magnetic and optical
	Position sensor, Doppler sensor
Imaging	X-ray, ultrasound, optical sensors
Time	Delay and elapsed time counter

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Humidity	Resistance and capacitance changes, Dew points
Gas concentration	Solid state gas sensors
Ion concentration	Ion selection electrodes, Ion sensitive FET
Biomolecules	Enzyme electrodes

As well as the problems in adopting these sensor technology for medical applications.

SOLID STATE MICROSENSORS

With the advanced solid state technology that makes the large scale integrated circuit popular at low cost and high reliability, the sensors for biomedical systems can be designed with many advantages such as : (1) Microsize and weight. (2) Consume small power. (3) High performance and uniform characteristics between devices. (4) High reliability once it is fabricated properly. (5) Mass producable, potentially can be made at low unit cost. (6) May be integrated with preprocessing circuit on the sensor chip to raise the system performance and offer ease of interfacing with other circuits.

The possibility of integrating signal processing circuits with sensors, can be very valuable in upgrading the signal performance and simplifying the system design. For example the sensor with high output impedance can be fabricated with an amplifying circuit that provides high input impedance to interface with the sensor at the same time to have low output impedance to reduce the external interference and power line pick up. This can increase the signal to noise ratio.

PRESSURE SENSORS

Pressure (P) is a common biomedical parameter that is important to cardiovascular, respiratory and locomotive systems. The same sensor with small modification can be used to measure Force (PxA), stress, strain, displacement, acceleration ($= \frac{F}{M}$), flow (ΔP), etc. However long term implantable pressure sensor with time stability of 1 % per year and the size and weight for small animals are still to be developed. In the past decade significant progress has been made to characterize the device to understand the stability problem and to develop design techniques. As a result of these progress, many industrial pressure transducers are now available with high performance and low cost. The biomedical implantable sensors are within the reach of careful design at the present.

Figure 1 illustrates a piezoresistive pressure transducer, designed to measure absolute pressure with a reference chamber built in [2]. This device has reached 3 %/ year stability after 3 months aging, at 300 mm Hg full scale range and is being used in measuring body fluid pressure with additional packaging. The disadvantages are : (1). Limited sensitivity 10 ~ 50 μV/mm Hg - Volt (2). Sensitive to differential stress. Therefore sensitive to side-way forces on touch and (3) Stability is to be improved.

To overcome these limitations capacitive pressure transducers using microelectronic technics was studies. Fig. 2 shows a photograph of such a device with a capacitive bridge on the chip. The performance is better than similar piezoresistive devices. However it needs 1/2 MHz power supply and the output impedance is high - (200 kHz).

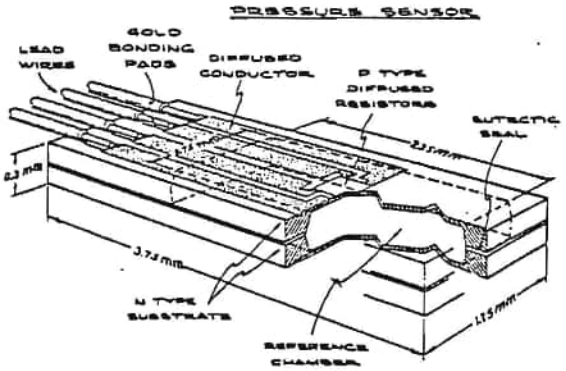


Fig. 1. Structure of a piezoresistive pressure transducer.

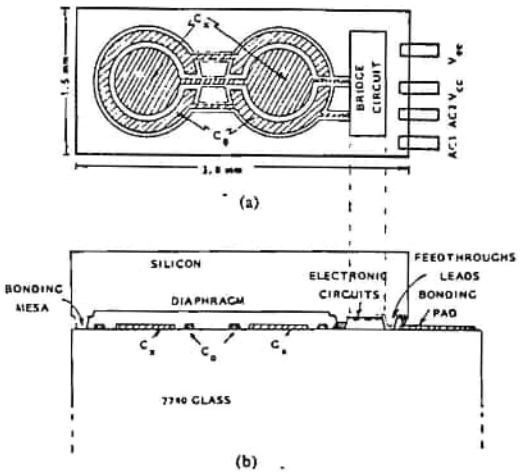
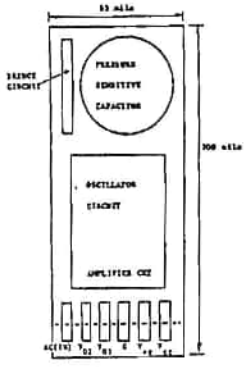


Fig. 2. Structure of the capacitive pressure transducer CP7. (a) Top view. (b) Cross section.

Fig. 3 shows a capacitive pressure transducer integrated with the 1/2 MHz oscillator and an emitter follower amplifier. This device is still being evaluated. When completed it will receive d.c., 3~5 Volt, 5~10 ma and give d.c. output of ± 200 mV corresponding to ± 300 mm/Hg (or any other range designed to operate in) at a low output impedance of 50 - 200 Ω.

This evolution in pressure sensor development is believed to be the general direction for other solid state micro sensors. Although the sensors designed now will be able to go to the last stage directlty after sufficient experiences were accumulated.



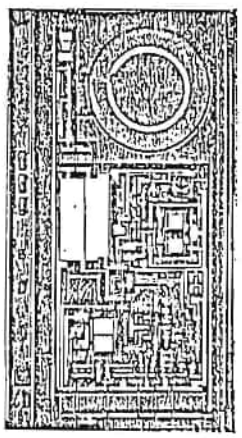


Fig. 3. Capacitive transducer with integrated circuits.

PH ION SENSITIVE FIELD EFFECT TRANSISTORS

A family of chemical sensors was explored in the last decade using MOSFET structure. They included : (1) H_2 and other gas. (2) Humility. (3) Very high impedance material processes. (4) Ion concentration in electrolytes. Fig. 4 shows the structure of an Ion Sensitive Field Effect Transistor (ISFET).

In its simplest form, it is sensitive to *p*H in the solution. By using various gate insulator or additional coating on the gate area, other sensors for K^+, Na^+, Ca^{++}, Cl^-, Br^- ... etc. have been tested.

The solid state device has many advantages : such as (1) Small , (2) Linear to H from 2~10. (3) Fast response in the order of 10~100 millisecond, (4) Low cost. The device will be usable for short term biomedical applications. However for closed loop control the problems to be solved are :
(1) Time stability of the device over long term (months to years), Need to be studied.
(2) The stable reference electrode to be developed,
(3) Temperature sensitivity and noise to be studied,
(4) Materials with good selectivity for various ions to be synthesized.

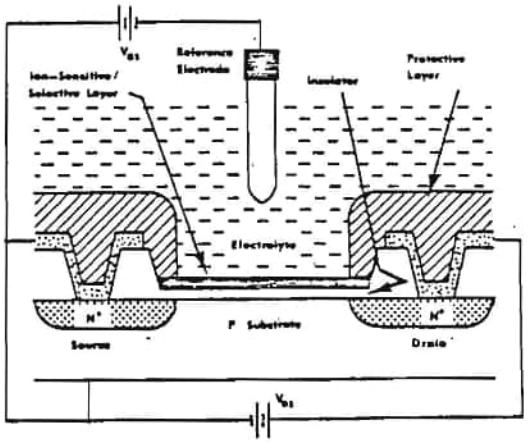


Fig. 4. Structure of ion sensitive field effect transistor.

As a first step to integrate electronic circuits on the sensor chip a 10 sensor array with multiplexing circuit on chip is designed as shown in Fig. 5. The device may have application in : (1) by provide redundancy, and using majority logic, more reliable pH measurement can be obtained to increase the life time and confidence of the device. (2) Multiple ion sensor probe can be made with the multiple sensor array.

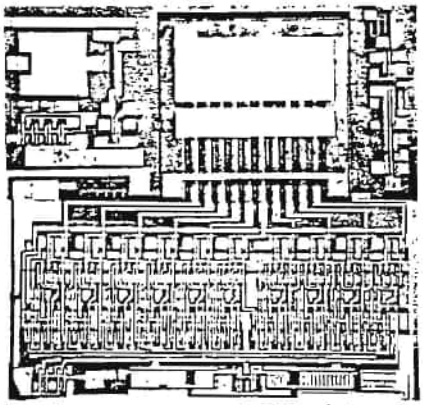
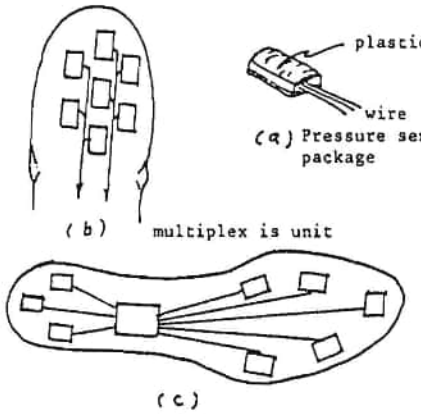


Fig. 5. Ten sensor pH FET with multiplexing circuit.

DISCUSSION

The potential of solid state microsensor close loop control of prothesis is great. For example an array of pressure sensor package property, such as shown in Fig. 6, can be used to measure force, or touch at fingertip to close the loop for hand grasp control. Some sensor can be used as "slip" sensor and for the functional stimulated walking to give the fore distribution of the foot, thus provide information for the stable standing of the patient. The pressure sensor will be useful for an automatic high blood pressure controlling system.



The pH sensor can be modified for CO_2 and will be useful in cardiovascular control such as physiologic pacer, ... etc.

However the potential itself has little value practically. The potential need to be realized by research and development by engineers and biomedical personal.

The problems of (1) New materials, (2) Fabrication technique that is compatible with the present integrated circuit technology. (3) The package techniques for biomedical applications, and (4) Theoretical understanding of the sensor behavior in biomedical environments are still to be solved.

Fig. 6. Conceptual design of pressure sensor array in protheses.
(a) Single sensor package.
(b) For finger touch sensor.
(c) For stand sensor array.

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TECHNOLOGY AND TRANSCUTANEOUS SUPPLY OF IMPLANTABLE ELECTRONIC STIMULATOR CIRCUITRY

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SUMMARY

Critical elements in the design of implantable circuits for functional electrical stimulation are longlasting hermetic packages and stable transcutaneous transmission of stimulation signal and supply power. The first question has been addressed by the development of Titanium- and ceramic packages. They both promise to provide a considerable improvement in life-time over gold-plated Kovar-packages. The ceramic package has the additional advantage that the receiver antenna coil can be located inside the package. A stable transcutaneous transmission of power and signal via two coupled coils with minimized dependence on the relative spacing of external and implanted coil is possible by employing "critical coupling" between implanted and external circuits.

INTRODUCTION

In several applications of functional electrical stimulation a configuration comprising an external stimulator/transmitter, a transcutaneous inductive link and an implantable receiver/driver circuit connected to the stimulating electrodes is used. During the development work on several versions of cochlear prostheses a number of potential problems of such a system have been addressed. This paper reports about work on alternative hermetic packages and on achieving a stable transcutaneous transmission of signal and power.

The technology used for the implantable electronic circuitry is a thin film hybrid technology employing a glass substrate, etched Nichrome resistors and naked CMOS-chips. So far it has been used to build hybrid circuits that have been part of cochlear implants for the profoundly deaf /1/, an implantable telemetry transmitter /2/ and implantable stimulators for the mobilization of paraplegic patients /3/. Development work is being done on Titanium packages and on ceramic packages. These packages will replace the commercially available gold-plated Kovar-packages which have been used up to now.

TITANIUM PACKAGE

The Titanium package comprises feedthrough-wires of Tantalum. A special glass to insulate the feedthrough-wires from the body of the package has been developed by the company Schott (Landshut, West Germany), who also developed the technological process to put the feedthroughs into the packages. The feedthroughs have been tested empploying the following methods: electron microscopy, leak testing with a helium leak-detector, application of temperature shocks and tests for mechanical stability. These tests helped to optimize the dimensions for the diameters of the feedthrough-hole and the Tantalum-wire and the Titanium

wall-thickness. The values currently used are 1,7, 0,7 and 1,2 mm.

The Titanium packages are sealed using a "parallel seam sealing"equipment at the Technical University of Vienna. Titanium lids with a thickness of 0,1 mm were found to be optimally suited for the seam sealing of Titanium. The seams have been inspected and tested. Helium leak tests for the closed packages proved their tightness with leak-rates below the limit of resolution of the leaktester (5×10^{-9} atm cm^3/s for helium bombed packages).

The problem of connecting the Tantalum feedthrough-wires to Platinum-Iridium-electrode leads and to Silver-wires, that might form the receiving antenna coil, was solved through the use of a capacitor welding technique.

CERAMIC PACKAGE

To try using ceramics as the material for implantable hermetic packages is promising because this material allows to place the receiver antenna coil inside the package.

The ceramic package which has been developed, (Figure 1), consists of bottom, frame and lid, all from Aluminumoxyd-ceramic. Glass solder is used to connect the frame to the bottom and also to connect the lid to the frame. The feedthrough-wires are thin Platinum wires which are embedded in the glass solder between bottom and frame.

For the closure of the package the bottom carrying the fully assembled electronic circuitry, has to be kept at a low temperature while the lid is heated up to produce the solder glass joint. This is achieved by a water cooling system. No parts of the electronic circuitry get hotter than 130°C. This has been veryfied by monitoring diode voltage drop for constant current. The bottom of the package is used as the substrate for the circuitry. A common thin film system with electrolytically fortified gold conductors withstands the temperatures required. The temperature profile involves a maximum of 520°C over a duration of 10 minutes. A silver-filled two-component epoxy guarantees low contact resistance.

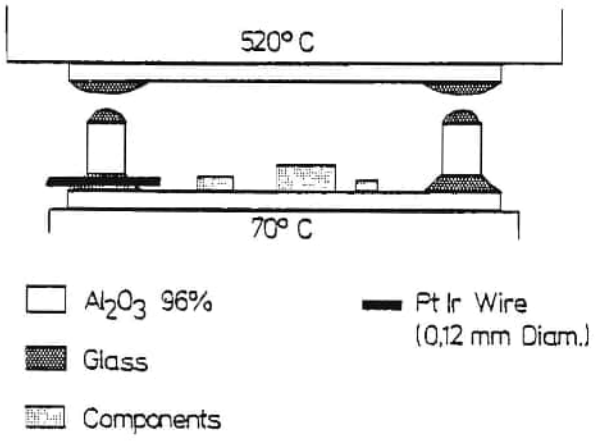


Fig.1: Ceramic package during sealing process using glass solder

A number of ceramic packages could be fabricated which are hermetic with a helium leak rate smaller than the minimum detectable leak rate. These packages prove the viability of the described technological approach. For packages that failed to be hermetic, the leak was never found to be at the feedthroughs; the reason always was in the temperature profiles for the heating and cooling.

The glass solder used for mounting the glass frame to the substrate is a devitrifying glass which is also used with ceramic packages for integrated circuits. The glass solder used for mounting the lid is a vitreous glass. It requires lower temperatures than the other glass. For both glasses the temperature profile has been optimized such that the number of small air-filled cavities within the body of the glass is minimized. This is important with respect to mechanical stability and corrosion resistance.

Tests for corrosion of the glass in warm saline solution so far did not reveal a susceptibility to corrosion that would cause concerns about not achieving extremely long life times with this sort of package.

Hermetic packages, potted in pacemaker epoxy, are immersed in warm saline solution. If they continue to hold up for 3 more months, ceramic packages of the kind described, will be used for the Vienna Cochlear Implant /4/.

TRANSCUTANEOUS SIGNAL AND POWER TRANSMISSION

One way of transcutaneously supplying implanted devices with power and/or signal is to transmit rf-power via an inductively coupled link. Previous designs have been concerned with the optimization of efficiency of the power transfer. Our work has dealt with the problem of reducing the influence of spacing variations and lateral displacements on inductive link transmission.

If the inductive link is designed in such a way that critical coupling is achieved at a convenient spacing, then is is possible to obtain a maximum of the voltage induced in the implanted coil at a certain separation between the two coils despite the steep decrease of magnetic field strength with distance. The spacing can be chosen within a comparatively wide range by selecting the proper parameters and coil geometries. In the vicinity of this maximum of the transfer function the transmission is very insensitive to distance changes and displacements as well.

The principal configuration of the transcutaneous transmission is shown in Figure 2. The power amplifier tank circuit and the tuned circuit of the implanted receiver, both of which are tuned to the carrier frequency ω_o, form a center tuned bandpass filter. G_1 represents the losses of the tank circuit and the output conductance of the rf-power amplifier, G_2, lumps together the load and the losses of the tuned receiver circuit.

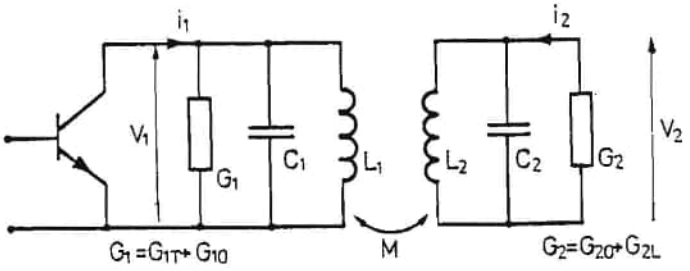


Fig.2: Schematic diagram of the inductive link for transcutaneous signal and power transmission

For a particular set of design parameters figure 3 shows the theoretical dependence of the output voltage at the secondary on spacing z together with experimental results. A maximum is obtained around which - depending on the allowable output voltage variation of the specific application- a usable distance range can be identified.

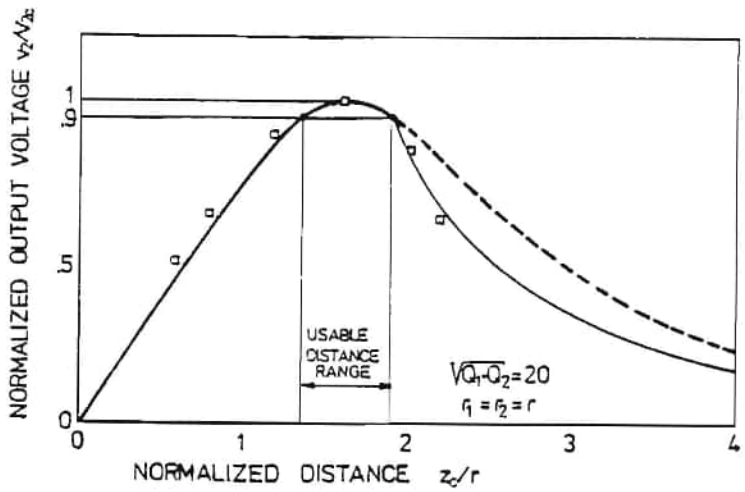


Fig.3: Normalized output voltage of the transcutaneous rf-link in dependence of spacing. Squares indicate experimental results

ACKNOWLEDGEMENT

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DESIGN- AND RELIABILITYCRITERIAS FOR AN IMPLANTABLE 16-CHANNEL STIMULATION DEVICE

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SUMMARY

In October 1982 the worldwide first implantation of a complex 16-channel stimulation devive was performed by the aim to make paraplegic patients stand up and walk a small distance with cruthes. The method of activating some groups of muscles by stimulating the inherent peripheral nerves is at full described in /1/,/2/. So, from a technical point of view the pre-conditions and reliability aspects of the technical and electronic equipment are surely a point of great importance. Therefore also the construction and developement of implant, electrodes and control-unit had to go a standardized way, though the number of production units in universitary research is very low (in our case the 0-series for human consists for example of 20 to 30 devices).

THEORETICALLY CHARACTERISTICS OF HARDWARE ASSEMBLY-SYSTEMS

An understanding of how semiconductors and other electronic parts fail is essential to improving the reliability of devices as well as that of the systems in which they are used. Such failure analysis should help identify failure modes, mechanism, and stress factors that influence degradation. A device or a hardware assembly-system can in principle fail in a catastrophic, degradation, or intermittand mode. Electrical failures are usually opens, shorts, or parameter out of specifications. The failure mechanism is the basic chemical or physical change that results in an identifiable failure mode.

Parts- or system failures can be labeled as early fall-out, stress related, and wearout. As indicated by the life characteristic curve (see fig. 1) early failures ("infant-mortality", or failure during the burn in or debugging period) occur at a high initial failure rate λ , which is the number of failures of a part per unit of time. This failure rate decreases rapidly and stabilizes at a time Tb, when the weak units have died out. Early failures are caused by many factors, including the built-in flaws of faulty workmanship, inferior materials and inadequate process controls, transportation and assembly damage, and installation and test errors. Examples of early failures are poor welds, wire bonds, or hermetic seals; poor solder joints, poor connections, dirt or contamination on surfaces or in materials; chemical impurities in metal or insulation; voids, cracks and thin spots in insulation or protective coatings.

Stress related failures exhibit a low and relatively constant failure

rate λ , and relatively constant hazard rate Z(t), which is the rate of change of the number of parts that have failed at a particular time divided by the number of parts surviving. The mean-time-between-failures (MTBF) is defined as $1/\lambda$ and is a measure of λ during the useful life-period for comparing hardware parts. The relatively constant failure and hazard rate period (between times Tb and Tw in Fig. 1) varies surely among different hardware types. For electronic devices the two most destructive stresses are excessive temperature and voltage (electrical overstress), either steady state, transient, or changing at rapid rates. Humidity (e.g. in implants), temperature cycling, vibration, thermal or mechanical shock also contribute to stress related failures.

Wearout failures occur at the end of the useful life Tw. From Tw on, the failure rate increases rapidly. Wearout failures result primarily from deterioration of the strength of a device from operation and exposition to environmental fluctuations. Such phenomena as corrosion or oxidation, insulation breakdown or leakage, ionic migration of metals, frictional wear or fatique, shrinking and cracking in plastic materials . Wearout failures are characterized by an increasing hazard rate.

The general aproach to reliability for electronic systems is to minimize early part failures by emphasizing (factory-)tests and reliability screens and to circumvent wearout failures by replacing parts prior to time Tw. But wearout failures are mainly not a factor with semiconductors, whose life characteristic curve tend to be flat after the early failure period. The useful life period, characterized by stress related failures, is the most important period and is given the most weight in the design reliability actions.

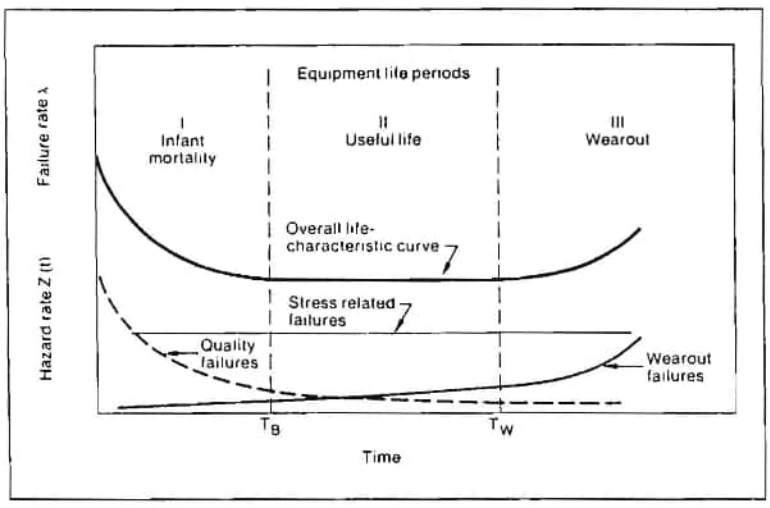


Fig. 1: Component of failure and overall life characteristic curve as plot of failure versus time (bathtub curve)

REQUIREMENTS AND TEST METHODS OF THE STIMULATION DEVICE

Resulting from the afore-mentioned generally theories it was the problem in the frame of personel and financal possibilities to optimize our device in direction of very low failure rate during the useful life, which should be itself as long as possible. The early failures should appear in the test and burn in periods, so that when the patient receive the device the hazard rate is minimized. The chose of technology of the implants was after several animal experiments and in-vitro studies with discret built devices fallen onto the thinfilm hybrid technology. Reason was the required smallnes an the very low number of units to produce. The main part of the implant (hybrid circuit) was constructed in cooperation with Technical University in the frame of a special research project. Reliability of such an implantable circuit mainly depends on the hermiticity of the encapsulation, the mechanical fixation of the hybrid chips, and the bond strength. Test methods and failure criteria are very circumstantial described in Mil.-Std. 883B. Two He-leakage test of the hybrid circuit's case assured the resistance against humidity; one after the welding of the package and the other after installing the hybrid circuit on the ready equiped receiverprint short before sealing with hysol (pacemaker resin). Another was the bond-pull test (25µm Au-wires - minimal 2,3g). Describtion of methods and failure mechanism in /3/. Essential for reaching an acceptable quality level is the visual inspection of the ready receiver circuit print including the installed hybrid circuit. The purpose is to verify that the material, design, construction, markings and workmanship are in accordance with the quality level. The apparatus used for this test is a simple light microscope with magnification of 10X to 20X. Failure criterias would be (1) visible defects or damage resulting from manufactoring, handling and testing (e.g. poor solder joints, cracked glassivated package pass-through) and (2) visible evidence of corrosion, contamination or breakage and (3) leads which are not intact and aligned in their normal location.

The very last version of the control unit consists of only 12 ICs, though in the beginning of the project an equal device needs 11 printcards (european-standard card). Generation and organisation of the information transmitted transcutanously to the implant (PCM) is done by a C-MOS microprocessor (NSC 800), so that nearly 80% of the earlier hardware (FF and shift register) changed into the software. So there is a great increase in reliability beside the advantage of reduction of size /4/. Because of the compatibility of all control units to all implants a parameter mean value control is necesary. This compatibility assures a kind of stand-by redundancy by means of a spare control unit. This test estimates the absolute maximum ratings of all time dependent transmission characteristics, like trigger levels of "high" and "low" signals in the PCM-carrier or changes in clock frequency due to the single impulses itself. So a "safe operation area" was demarcated, and by adjusting all parameters in the center all tolerances and temperature coefficient will be coverd up.

To assure a high degree of safety for the predominant used sensitive C-MOS chips a special antistatic working place for grinding and polishing the implant's surface was installed. The electrode lines which lead from the implant to the nerves are circulary coiled and

completely embedded in silicon rubber. They were tested in several deflection tests to show the threshold of material fatique (the received standard is about 4.5 million cycles of bending 90 degrees). From the point of view of view of material technology, simulated fatique tests show that the endurance limit is reached between 1 and 5 million cycles suggesting that when an electrode has sustained this value without breakage the probability of failure after that is very small /5/.

That all should not be seen especially to our stimulation device, but in all parts in engineering in health care a greater understanding of reliability designing should be aimed, because in the case of a cardiac patient with a pacemaker for example, continous proper function of the device is a matter of life and death.

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THE DEVELOPMENT OF A HYBRID PROGRAMMABLE ELECTRO-STIMULATOR FOR RESEARCH APPLICATIONS.

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SUMMARY

Present day applications of FES suggests the need for a multipurpose electro-stimulator for use as a bench-mounted research tool. Research objectives, together with the corresponding design criteria of the stimulator system, are given. The use of the complete system is described in its application to evaluate waveforms and parameters used in transcuyaneous electro-stimulation as we feel that contradictions surrounding a practical stimulus need setting to rest once-and-for-all.

INTRODUCTION

The Strathclyde Programmable Electro Muscle Stimulator (SPEMS) has been developed to suppport the electro-stimulation research currently underway at the Bioengineering Unit. Primarily, research interests are directed towards three areas:-

1. Parameter, waveform and electrode evaluations.

2. Therapy research.

3. Closed-loop control.

Choice of transcutaneous waveform and stimulation parameters not only influence the type of neuromuscular response (effectiveness) but also the cutaneous sensations experienced by the subject (abnoxiousness). This is not only so with 'normals' but also with subjects posessing neurological disorders. Their response may not only be a sensation but also a reflex. Studies of high level modalities, such a pain, using different forms of electro-stimulation, is not new (von Helmholz H., 1851). Physiologists, aswell as psychologists, have postulated theories concerning pain mediators within the skin and mechanisms of sensory input for over a century (Tschiriew S. & Dewatteville A., 1879). Since then, current, voltage, power, waveform and frequency have, at one time or another, been recommended as basic to pain. In 1955 Lilly et al suggested that a zero net current flow, biphasic waveform produced no detectable tissue damage within neurological tissue. This initiated a contoversy which lasted not only through the development of the first peroneal stimulator, but up to the present day (Vodovnik L., et al, 1981). The basic parameters for effective transcutaneous stimulation have been well researched and it remains for effectiveness and pain to be correlated.

The use of electro-stimulation in physiotherapy is a well proven application of FES requiring little review. A few applications within therapy research are just being realised. Those of interest to our research include the

treatment of spasticity, biofeedback therapy, reduction of adhesions following microsurgery and muscle restrengthening in both geriatric and spinal cord injured.

Problems surrounding closed-loop control of joints has been well documented. (Stanic U, et al, 1974). Muscle fatigue, electrode movement, price, size, cosmesis and position transducer problems were all stated as preventing a position controller from being clinically viable. Recently, CMOS microprocessors and new types of goniometric devices have paved the way to overcoming at least some of the earlier problems. Closed-loop systems have been utilised in descrete function systems, such as the one developed by Borisov et al (1976) for correcting knee extension prior to weightbearing. Intramuscular stimulation has also been used to overcome these problems (Crago P.E., et al, 1980).

METHOD AND EQUIPMENT DESIGN.

To conduct the evaluations under the most objective conditions possible, a double-blind assessment is considered to be appropriate using full computer control to enable a complex protocol. This would also satisfy the criteria for both closed-loop control evaluation and therapy research; where feedback to the stimulator is vital. The electronic design of the stimulator can be summarised into three blocks of circuitary:-

1. Waveform generator.

2. Output stages.

3. Digital interface to microcomputer.

The waveform generator has been built around a selection of commercially available waveform synthesis ICs developed for use by the electromusic industry. They are all voltage controlled thus facilitating digital control. Three types of IC are implemented to synthesise most waveforms of conceivable interest in transcutaneous electro-stimulation. The VCOs produce sinusoidal, pulsed, triangular and sawtooth waveforms and enable control of frequency and mark/space ratio. VCAs allow intermodulation of VCOs and also enable amplitude modulation control giving the option for exponential, aswell as linear operation. The final waveform can be shaped within a complex envelope consisting of four possible segments, each with control of shape and time.

The output stage consists of amplifiers for both monophasic and biphasic current stimulation together with power and safety circuitary. All patient connected circuits are ground isolated with opto-isolation of signal inputs and control outputs. A DC/DC converter provides high voltage while limiting current in both mono- and biphasic modes. Design is to the safety standards set down by the European Commission and BS5724.

Digital interface to a BBC microcomputer has been realised using three sections each dealing with a different function:-

1. Simulation of potentiometer control is conducted through twenty 8-bit D/As.

2. A multiplexed 12-bit A/D converter reads back values from the potentiometers.

3. Twenty CMOS analogue switches set up the various modes of synthesis and output.

Hence, the complete hardware allows analogue, digital and hybrid control. The latter is important during waveform evaluation when complex software does not overcome the complexity in setting up waveforms. In this application the waveforms are built up using an oscillascope and analogue control. Programming the computer for each waveform is performed by instructing it to read the set values on each potentiometer after switching out analogue control.

The software is responsible for conducting a double-blind evaluation while maintaining a pseudo-objective assessment of pain. A visual linear scale is used to represent the level of pain. It is set by the subject and its value is read by the microcomputer via. an A/D input. Effectiveness is taken as isometric joint moment measured using a ring force transducer; also interfaced to the microcomputer, after signal conditioning, using an A/D input. Evaluation is performed on the quadriceps area after ensuring regulation of hip and knee angles with a specially constructed bench/chair.

The software is also responsible for evaluation protocol, twice choosing each waveform and repeating in a block organisation relating to a preset step increase in joint moment obtained. This ensures a low level of anxiety response from the subject who is already familiar with sensations during transcutaneous electro-stimulation.

CONCLUSIONS

The stimulator design has reached all its research objectives and is presently involved in the evaluation of waveforms used for transcutaneous electro-stimulation. Any positive results can easily be implemented in present day portable microprocessor controlled stimulators using available CMOS voltage controlled waveform synthesiser ICs.

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PROGRAMMABLE MULTICHANNEL STIMULATION SYSTEM UTILIZING MULTIPOLAR ELECTRODES

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1. INTRODUCTION

A programmable 10-channel nerve stimulation system for supplementing or replacing lost functions in disabled individuals is described. The stimulator instrument comprises an external transmitter controlled by a microprocessor, and an implantable receiver with six monopolar and four bipolar electrode channels.

2. SYSTEM DESIGN

The stimulator programmer is equipped with all the controls to produce the stimulus parameters for the transmitter control unit (Fig. 1). STIGRAM-bus allows data and control transfer between these two units.

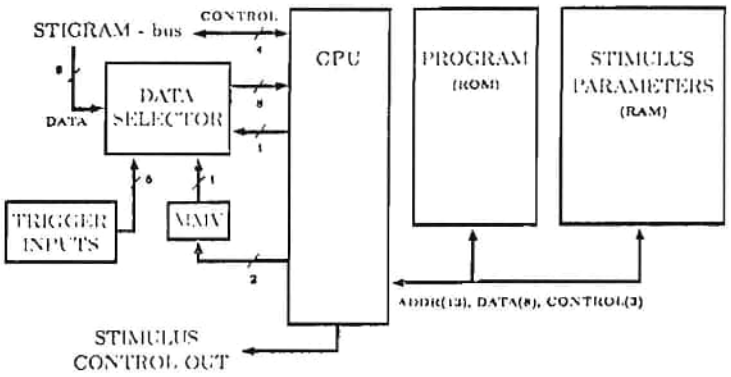


Fig. 1.

Power consumption minimizing has an essential role in designing portable instrumentation. The battery current drain may be influenced by hardware considerations and in systems utilizing processors by means of software, also. The transmitter control unit hardware has been implemented using CMOS-technology throughout. The software employs effectively the CMOS-processor power-saving modes, called WAIT and STOP. With all channels active the total current drain of the control unit is in order of one mA only.

The receiver unit picks up its stimulus energy and information via a single, pulse width modulated rf link, Talonen *et al.*, (1983). The information signal also includes a sychronization pulse. All stimulation channels have the same stimulus pulse frequency. The receiver unit has four independent bipolar alternating biphasic constant current channels. In each of these channels cathodal and anodal stimulus pulse amplitudes can be adjusted separately. The other six channels are monopolar cathodal biphasic constant current channels with a common anode electrode.

3. OPERATION

The developement of stimulus functions for individual channels is three-phasic:

1) finding the nerve excitation threshold level,

2) editing (i.e. manipulating) the envelope of the stimulus current pulse train and

3) defining the triggering source.

In the first mode, a single stimulus current pulse with user-defined amplitude and duration is generated. The operator gets the feedback information for finding the optimal threshold in form of muscle response.

In the curve editing mode the operator is able to implement and test the designed stimulus current envelope. Finding the optimal envelope is usually an experimental procedure and versatile editing functions has been accomplished to easily change or re-create the envelope. An oscilloscope is used to visualize the form of pulse train envelope (Fig. 2).

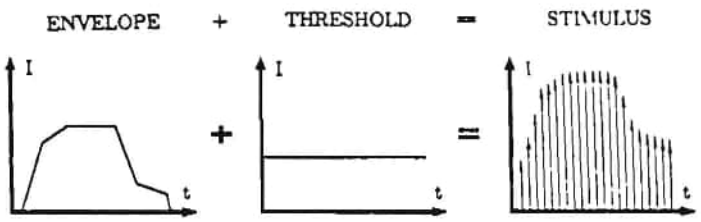


Fig. 2.

Although being referred as "phase-3", the operator may define the triggering sources for any channel anytime. The main trigger sources are: the very beginning of stimulation cycle, the user-defined delay from the beginning of the cycle and six external inputs from peripheral sensors. Certain combinations of these may also be utilized.

"Toggle"-function exhibits a single stimulation cycle with all channels active. This allows the operator to compare the total achieved response with the one wanted. If these do not agree, the editing mode may be invoked and changes can be made. When the total stimulus function has reached its final form, the system can be switched to stimulate continuously.

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CLINICAL FOLLOW-UP OF FRESH LIMB FRACTURES UNDER THE INFLUENCE OF DYNAMIC INTERFERENTIAL CURRENT (DIC)

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SUMMARY

In accident surgery patients treated with intermittent dynamic interferential current (DIC) for soft tissue swelling (traumatic or post-operative), both clinical and roentgenologic findings in concomitant fresh fractures suggested an accelerated healing process of these bone insults. - The effect of DIC on regenerating bone tissue was verified quantitatively and qualitatively in an experimental sheep model. - Clinical and experimental results led to a new concept for the practical management and DIC therapy of fresh fractures, stressing the importance of adequately timing the onset and stop of treatment. Optimal application of DIC shortens post-traumatic hospitalization and improves the patient's rehabilitation in his social and occupational environments.

MATERIALS AND METHODS

The potential influence of dynamic interferential current on the regular course of reparative osteogenesis in freshly injured bone was studied in an experimental model of standardized reproducible design. Six-months-old pure bred Blackhead sheep of 37.6 kg mean body weight were anesthetized with Nembutal under aseptic conditions; surgical osteotomy of radius and ulna in one foreleg across the diaphysis was performed with an oscillating saw. Scraping the radius shaft without removing the periost produced a paradigmatic lesion which impaired the intramedullary, cortical and periostal supply to the bone and periosseous soft tissue. The distal fragment was more strongly affected than the proximal one.

The 1.6 mm gap in the compacta between the two fragments was bridged and maintained in position with a 4-hole-AO-plate. Absence of interfragmental compression intentionally provided a "factor of mechanical disturbance" (1) preventing the "mechanically stable conditions" required for primary bone healing (2). The operated leg was splinted with an open plaster tutor fixed by circular adhesive tapes. Waking from anesthesia the animals were free to move and stand on their legs which further impaired the biomechanical conditions for unimpeded bone healing. Since DIC in living tissue has not been demonstrated, so far, in reproducible form, we had to verify whether this kind of current exists in vivo, and to make sure that the reparatory process in the osteotomy gap could be exposed intentionally to a dynamic field of interferential current.

Dynamic interferential current is produced by superposition of two separately ineffective sinus currents of slightly different medium frequency - e.g. 4000 and 4100 Hz - released by two pairs of electrodes upon the skin. The electrodes are fixed to ensure a "crossing"

of the two currents. The difference in frequency suitable for therapeutic use ranges from 0 to 100 Hz. We selected a difference of 90 to 100 Hz which is said to posses a certain sedative quality (3). In a total of 34 operated sheep, two groups of 12 animals received for 6 weeks, three 10 min. applications per week of 12 mA or 60 mA DIC, respectively. The remaining 10 animals were left untreated as controls. All animals were regularly monitored clinically and roentgenologically at every DIC application. During the whole 16 week assay one animal of each group was killed and dissected after 13, 15, 17, 21, 25, and 28 days, and then 5, 6, 7, 12, and 16 weeks. In the essential phases of bone regeneration several clinical, roentgenological, macroscopical, histological and chemical parameters were assessed to evaluate its progress.

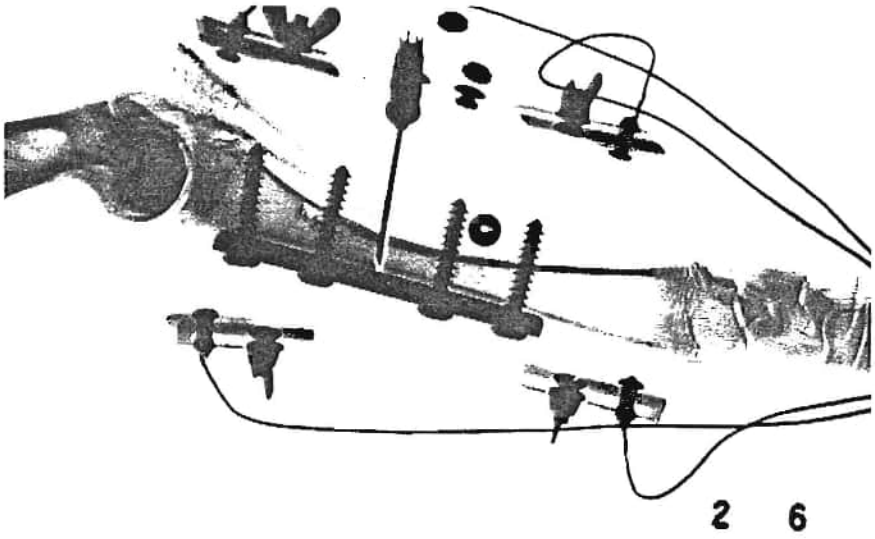


Fig.1: Intraoperative roentgen demonstration of the experimental set-up in sheep: The osteotomy gap is bridged by a 4-hole-AO-plate; DIC-electrodes are fixed on the skin; a bipolar microelectrode (Termistor) is inserted into the osteotomy gap exclusively for measuring the endogenous DIC field, and removed before closing the skin.

RESULTS

The highest intensity of the unfocused field of endogenous interferential current was found in the osteotomized zone itself. Neither the inhomogeneity of tissue nor the metal implants exerted a measurable influence on the field pattern of DIC. The implants showed no electrolytic alterations.

Clinically, the DIC-treated animals were able to use the operated limbs about 7 to 10 days earlier than the controls, which agrees with similar observations in man. Roentgenographs taken of the animals at scheduled intervals, suggested an accelerated stabilization of the fracture on account of the higher density of mineralization in the regenerating callus. Histologic findings, supported by macroscopical, analytical and biochemical parameters, were in agreement with these observations (4).

The macroscopical comparison of necropsy specimens revealed no evidence of patho-anatomical changes; there were no signs of ectopic calcification nor of cellular damage.

In DIC-treated animals bone fracture healing was manifested in a more harmonious microarchitecture with regular trabecular profiles of thick spongiosa trabecles and a clear radial array with more horizontal connections. Comparing histomorphologic and radiologic findings, however, failed to yield any definitive statement about the osseous reconstruction of the osteotomy gap.

In chemical analysis the influence of current intensity was documented by higher mineral density, reduction of Mg/Ca and CO_2 molar ratio, and increase of Ca/P ratio when the matrix had reached mineralization (5). In parallel, increased collagen synthesis was verified by means of higher hydroxyproline levels.

These experimental data may substantiate the clinical concept of therapeutic procedure, based so far merely on empirical observations. Repeated electron microscopical investigations have shown that the metals used are not undergoing any changes, and that there was no clinical evidence of increased or intensified metallosis in the surrounding soft tissues.



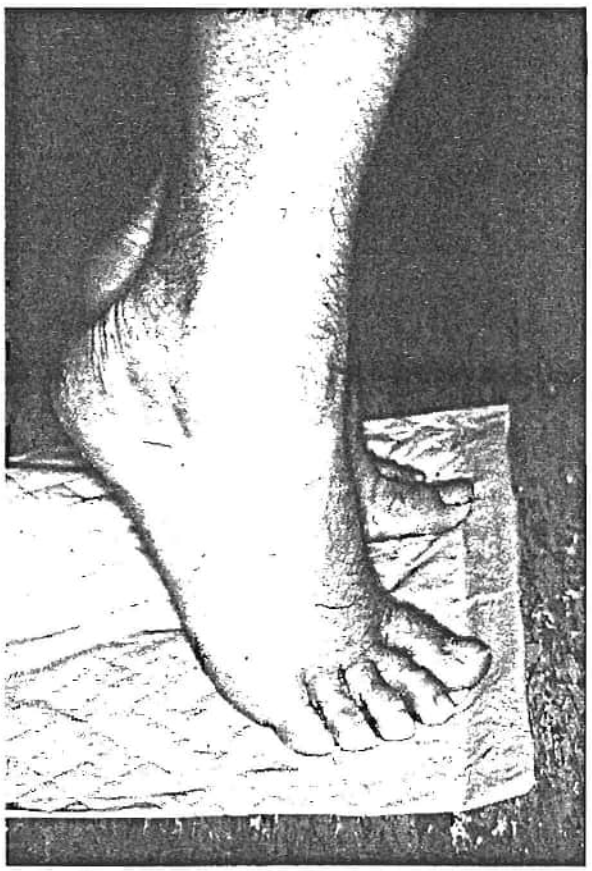


Fig.2: Fresh closed fracture of right hallux (male, 45 yrs): The foot is immobilized in a plaster boot, DIC applied by electrodes fixed on wet viscose bags.
Fig.3: The same patient 3 weeks later, after 12 DIC applications.

Judging from the accumulated data the most effective period for DIC application is between the days 7 to 35 after surgery and pp. wound healing. We performed daily treatments of 20 min duration with 12 mA and a difference of 90-100 Hz.

This protocol has now been applied to several hundreds of accident surgical patients. Statistical evaluation by independent observers have verified osseous consolidation about two weeks earlier than in a matched untreated collective, without complications in the follow-up period. No pseudarthroses were observed in patients treated with DIC.

DISCUSSION

New methods for positively influencing bone reconstruction will be effective only if they serve to "speed healing" (6), and to improve safety and quality of the process.

In 1970 NIKOLOVA (7) had inferred from clinical observations that interferential current combined with phototherapy might facilitate the "more rapid regeneration of bone tissue". Considering the clinical, roentgenological, macroscopical, histomorphological and chemical parameters documented in our study, the inference appears justified that the influence of DIC favors and accelerates the endogenous reactions triggering the regeneration of freshly traumatized bone.

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MORPHOLOGY OF CALLUS FORMATION AFTER INTERMITTENT STIMULATION WITH DYNAMIC INTERFERENTIAL CURRENT (DIC)

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SUMMARY

Intermittent application of dynamic interferential current (DIC) to sheep undergoing transversal radius osteotomy, accelerates endogenous reparative reactions to the bone defect. Although normal patterns of periostal, cortical and endosteal callus formation are principally preserved the quality of provisory callus filling and formation of fiber callus is improved under the influence of DIC. The phase of uncoordinated apposition is shortened, which leads to earlier formation of definitive callus and lamellar bone.

MATERIALS AND METHODS

Radius and ulna with surrounding soft tissue were fixed in formalin. Longitudinal and transversal bone sections were performed in the area of experimental transversal osteotomy; after decalcifcation with RDO paraffin sections of 7µ were stained with HE, Azan, PAS, Goldner, and Ladewig. Details of the experimental design are described by LAABS (1).

RESULTS

Morphologic patterns of the reactive formation of periostal, cortical, and endosteal callus were principally preserved in the sheep treated with DIC in general analogy to the untreated controls. Qualitatively, the process was the same in the distal and proximal part of the osteotomy except for a marked delay in the distal end. The periostal and endosteal vascular systems contributed evenly to bone regeneration. When an osseous bridge had formed over the osteotomy, superfluous callus was resorbed.

Treatment with DIC considerably accelerated the process of osteogenetic regeneration, manifested first on the 13th day after surgery. All morphologic criteria then visible in the tissue components involved in the regenerative process, could only be observed 5 to 7 days later in the controls. The earlier manifestation of morphologic phases in DIC-treated animals could be documented in the progress of osteogenesis up to the 47th day after surgery. For instance, the trabecular profile of subperiostal callus in DIC-treated animals on day 13 resembled that of controls on day 19. Lacunar transformation of Havers' channels in the proximal fragments observed in DIC-animals on day 13 was considerably more advanced than in controls on day 17. Mineralization of collagenous bundles in the distal part of the osteotomy as seen in DIC- animals on day 34, corresponded approximately to that of controls on day 40.

Under the influence of DIC, both provisory filling callus and fibrous callus were improved in quality, as manifested in a higher degree of cellular activity. This led to an earlier formation of equally improved definitive callus (Fig.2) with thick trabecular profiles and a close internal texture of regenerated lamellar bone.

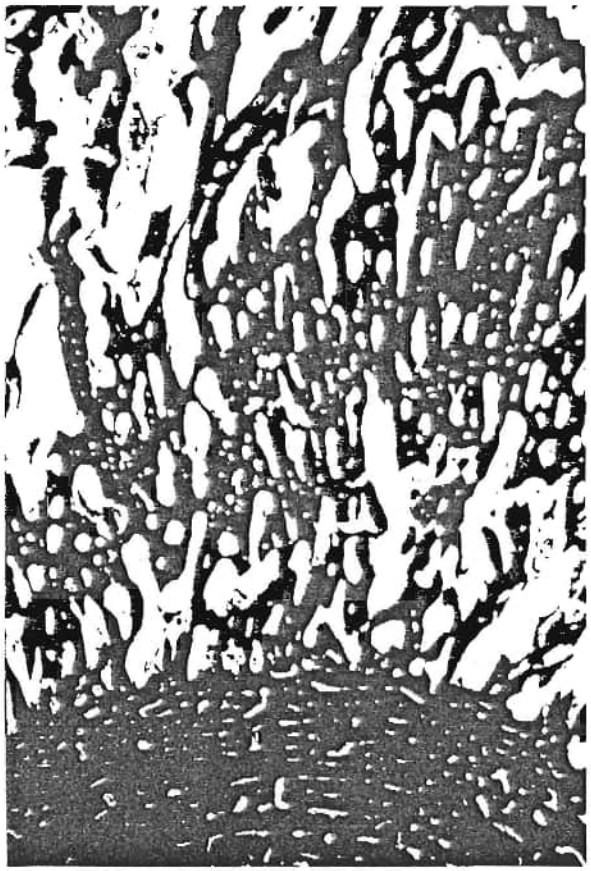


Fig.1

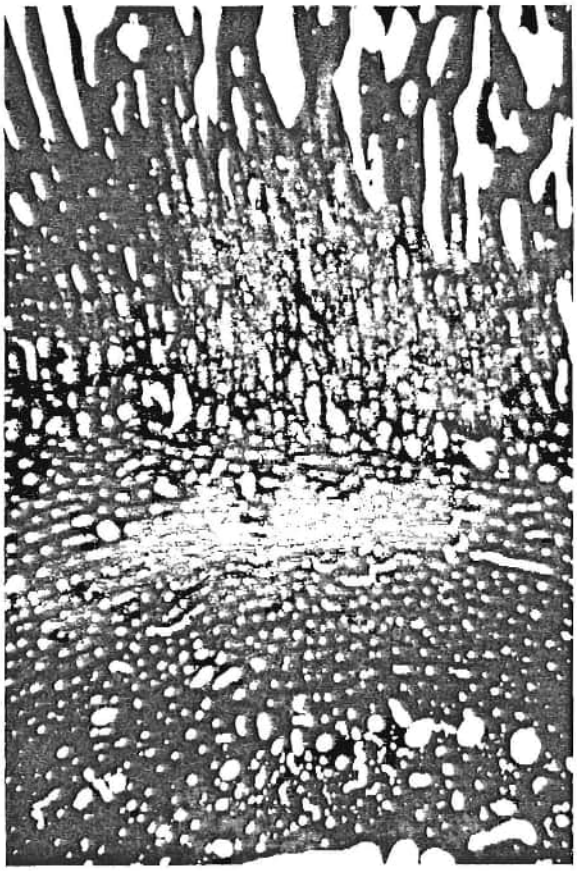


Fig.2

Fig.1: Control animal, 40th day after surgery. Transversal section through the inner callus area of the radius shows a coarse meshwork of regenerated trabecles, some of them in contact with the basic lamella of the radius.
Fig.2: DIC-animal (after 16 treatments with 12 mA DIC), 40th day after surgery. Corresponding transversal section through callus of the radius shows tight meshwork of dense lamellar bone in complete contact with the basic lamella of the radius.

DISCUSSION

Correlation of a wide spectrum of histologic findings yielded first that in the experimental set-up chosen DIC-treatment provoked no disturbance of osteogenesis under biological aspects. The treatment rather promoted an improved microarchitecture of the osseous callus by favoring endogenous reactions to the experimentally induced bone defect. Similar results have been published by GÜTTLER and KLEDITSCH

(2) who also recorded (by X-ray monitoring) accelerated and intensified callus formation in rabbits under stimulation by interferential currents induced via invasively implanted electrodes.

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Stimulation of Fibroblast Proliferation by Means of Electrical Current

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With interferential current cell proliferation can be promoted. The maximum proliferative effect occurs at a current intensity of 5 - 9 mA. More than 10 - 14 mA current damages the cells. Intermittent stimulation was found to produce a better effect than continuous current.

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ENHANCED OSTEONEOGENESIS BY DYNAMIC INTERFERENTIAL CURRENT; PART: 1 x)

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SUMMARY

Alkaline phosphatase activity is a marker enzyme for the initiative phase of hard tissue formation of collagenrich tissues, e.g. enchondral ossification, ossification processes during osteosarcoma growth, mineralizing tibia tendons of avians and bone healing. This markerenzyme was taken to study the influence of dynamic interferential current (DIC) during the process of osteoneogenesis on osteotomized long bones of sheep. It could be shown, that the DIC stimulates cellular activity resulting in an increased production of alkaline phosphatase activity. Consequently, the calcification rate is increased, resulting in an enhanced bone healing.

MATERIAL AND METHODS

Clinical data, methods of work-up and materials used are reported in the literature (1, 2, 3, 4).

RESULTS AND DISCUSSION

Biomineralisation of collageneous tissues is initiated by the formation of a calcifiable matrix, followed by a subsequent enrichment of the mineral forming elements, resulting in a mineral deposition at the right locations. The first mineral deposition is transformed in a later stage to the final hard tissue, e.g. bone, with its specific biomechanical functions. Although several of the single reactions and steps of hard tissue formation are known, the whole continuous mechanism is still unclear. One of the open questions is the role of an alkaline phosphatase activity, occurring during hard tissue formation, mainly during the stage of Ca and P enrichment and first mineralization. The mineralization process can be influenced by inhibitors of alkaline phosphatase e.g. phosphonates, EDTA, SH-reagents. With regard to an activation of calcification a positive effect of electromagnetic fields is reported in the literature (5). However most of these data reported are not based on quantitative chemical analyses but referred to the behaviour of patients after treatment with electromagnetic fields. Even radiographic studies seem often to be too insensitive for an objective interpretation. Thus the aim of our studies was to find out whether the alkaline phosphatase activity represents a good parameter to give an objective status of a certain phase of calcification and secondly whether the calcification can be activated by electromagnetic fields. For these studies we have chosen the so-called Dynamic Interferential Current (DIC) (details see: 4).

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x) Supported by the Deutsche Forschungsgemeinschaft

Alkaline phosphatase in enchondral ossification

Topological analyses of porcine epiphyseal growth plates have shown, that the calcification of cartilage is indicated by a high alkaline phosphatase activity (1). In these areas of the growth plate, where cell degeneration and first deposits of mineral can be recognized, the alkaline phosphatase activity is about 1o times higher than in normal cancellous bone. Parallel with maximal alkaline phosphatase activity maximal amounts of phosphoesters, calcium and magnesium were extractable under mild physiological conditions, suggesting a high rate of incorporation and/or a high turnover. These findings are confirmed by studies of Reddi et al. (6) demonstrating that the incorporation of ^{45}Ca is very high during this phase of matrix induced enchondral calcification. Thus, the alkaline phosphatase activity correlates with the enrichment of Ca and P and so results in the first mineral depositions.

Alkaline phosphatase in osteosarcomas

Recent studies of different human osteosarcomas (2) have shown, that in those areas of bone tumors where ossification takes place, alkaline phosphatase activity is highest during the stages of initiation of calcification. Although these collagenrich calcifying systems are pathologic hard tissue formations, it is interesting that even here the alkaline phosphatase activity indicates the initiative phase of a calcification.

Alkaline phosphatase activity in mineralizing tibia tendons of avians

Mineralizing turkey tibia tendon is an excellent model to study hard tissue formation (3). The tibia tendons of young turkeys remain uncalcified during the first 1o weeks after hatching. First signs of initiation of calcification can be observed at about 11 weeks after hatching, indicated by the occurrence of an alkaline phosphatase activity. During this process of hard tissue formation a mineralization front occurs, growing within 1o weeks towards the proximal muscle connection of the tendons. The hydroxyproline content of the tendons remains constant. Thus hydroxyproline as a marker for collagen can be taken as an internal standard. Consequently the alkaline phosphatase activity is related to the corresponding hydroxyproline content. Maximal values of alkaline phosphatase activity per µg hydroxyproline were always found at the calcification front, indicating the initiation of calcification.

Alkaline phosphatase activity in bone healing and the influence of dynamic interferential current (DIC)

Summarizing these findings it is obvious that the different types of hard tissue formation of collagenrich tissues reveal that alkaline phosphatase activity reflects the phase of the enrichment of the mineralforming components and early calcification. Thus, the enzymatic activity was taken as a parameter to study the influence of dynamic interferential current (DIC) during bone healing of osteotomized long bones of sheep (4). One group of animals was treated with 6o mA DIC, another group with 12 mA DIC and a third group remained untreated for control.

Fig. 1 shows the results obtained for the different groups in the second, third and fifth week after operation. The maximum of alkaline phosphatase activity for each group was found in the third week p.o. indicating that the calcification is initiated in this time range. Comparing the three different groups, it is obvious, that the group treated with 6o mA DIC shows in the third week p.o. enzymatic activities being about 7 times higher than the control group; and in the group treated with 12 mA DIC the activity is about two times higher

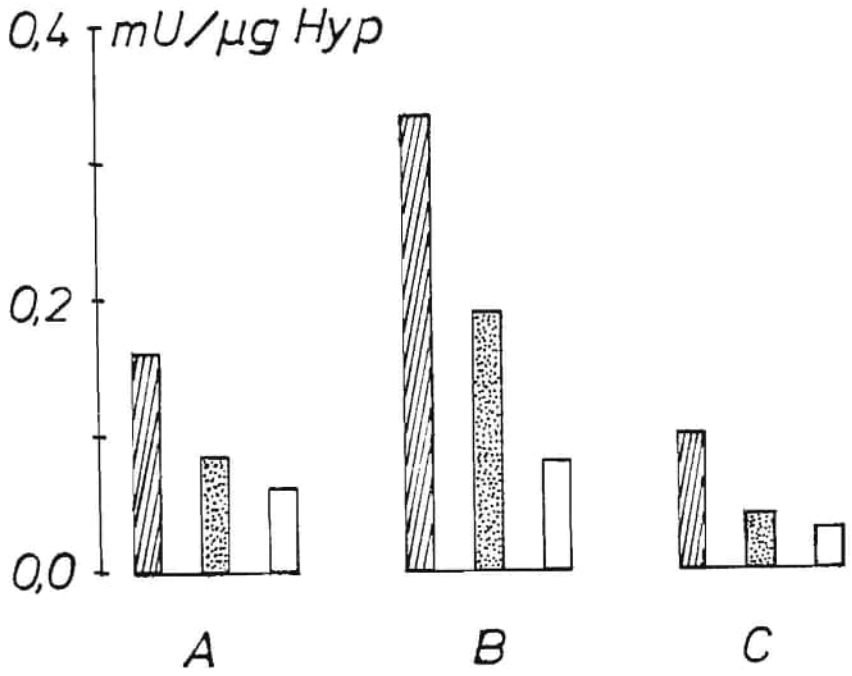


Fig. 1: Alkaline phosphatase activity extracted from the osteotomy cleft; average of the values obtained in: A (2nd week after operation); B (3rd week after operation); C (5th week after operation); ▨ treated with 60 mA DIC; ▩ treated with 12 mA DIC; ☐ untreated control

than in the control group. 16 weeks after operation all groups have reached the same final value of about 0.01 mU/µg Hyp. Analogous results were found for the extracted phosphoesters.

These results reveal that the date of onset of calcification is not influenced by DIC since the maximum for the alkaline phosphatase activity for each group lies in the same time range. That means there is no time shift in the beginning of calcification after treatment with DIC when compared with the control group. However, the DIC causes an activation with regard to cellular activity, resulting in more enzyme production and phosphoesters. Furthermore it could be demonstrated that the stimulation of cell activity is dependent on the dosis of the applied DIC. In summary the DIC application yields in more alkaline phosphatase activity; therefore a higher calcification rate is to be expected, resulting in an enhanced bone healing.

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ENHANCED OSTEONEOGENESIS BY DYNAMIC INTERFERENTIAL CURRENT, PART. 2 x)

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SUMMARY

The aim of these studies was to clarify the influence of dynamic interferential current (DIC) of bone healing after osteotomy. Measurements of the calcium, magnesium, carbonate, and phosphorus levels in the newly forming bone tissue documented full mineralization in the DIC treated animals at a much earlier date than in the untreated controls. Comparing the data of the DIC treated bones with the untreated controls, a characteristic chronological apppearance of trace elements, e.g. Cu, Cd, Fe, Pb, and Zn happens significantly earlier and is often even higher, reflecting an enhanced bone healing.

MATERIAL AND METHODS

To analyse the influence of DIC on bone healing the two bones of the right foreleg of 34 black headed sheep were osteotomized in the middle of the shaft. The diaphysis of the radius was deperiostalized and instable fixed with a 4-hole AO-plate leaving a cleft of at least 1.5 mm width. 24 sheep were treated 3 times per week for ten minutes with DIC, one group with 12 mA and the other with 6o mA. The other sheep remained for control. The experiment lasted for 16 weeks /see: 4/. One animal of each group was killed, starting on the 13th day, and continuing in a certain time sequence.

Samples for analyses were taken from the callus on top surrounding of the osteotomy cleft. For the chemical analyses the samples of the callus were homogenized; and the contents of Ca, K, Mg, Na, CO_2, and P were determined by a modified method according to /6/. The trace elements were determined, after pressure combustion with HNO_3 in PTFE vessels, by anodic stripping voltammetry according to /9/, and/or by AAS, respectively.

RESULTS

The full carrying capacity of the operated legs of the animals treated with DIC was reached about one week earlier than that of those of the control group /3/. The histological results showed a corresponding earlier bridging over the osteotomy cleft /13/.

Bone healing starts with the formation of a bone matrix, consisting mainly of collageneous material. It becomes calcified in a later stage, as described in part 1. The beginning of mineralization is connected with a maximal alkaline phosphatase (APase) activity, indicating the first Ca-enrichment.

The Ca contents of the callus of the animals treated with 12 mA DIC

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increase earlier than those of the controls, rising in a continuous way. The Ca and P contents of the 12 mA DIC treated animals, 6 weeks post operationem, were 18.5 ± o.32% resp. 8.5 ± o.32%, corresponding nearly to the values of "fully" mineralized bone (Ca and P values of the corresponding controls: 7.45 ± o.37% resp. 3.4 ± o.31%). After 7 weeks, the Ca and P contents of the fully mineralized callus of the 12 mA DIC treated animal was 2o.1 ± o.5% resp. 9.2 ± o.51% and that of the control 13.2 ± o.51% resp. 6.1 ± o.45%. The fully mineralization of the callus of the animals treated with 6o mA DIC (a superdosis) was already reached after 27 days, with 19.o ± o.13% Ca and 9.5 ± o.2o% P (number of experiments for all measurements = 1o). After 16 weeks, the end of the experiments, the Ca and P contents (21.5% Ca and 1o.1% P) were the same for all three groups.

The Mg and carbonate contents (measured as CO_2) increase with advancing mineralization in a characteristic manner, for the callus as well as for other collagen rich hard tissue /7, 8/. The molar Mg/Ca and CO_2/Ca ratios are highest in the prestage of mineralization and decrease with its progression /7/. The sequence of changes of the molar ratios for normal callus mineralization is described elsewhere /7/. The same is found in the DIC treated animals, however it appears 1-2 weeks earlier.

The carbonate values of the maturating definitive callus in form of the lamellar bone are highest, with 1.7 ± o.15% for the control animals in the 7th week, with 2.2 ± o.12% for the 12 mA DIC treated animals in the 6th week and 2.8 ± o.23% for the 6o mA DIC treated ones in the 3rd week. Corresponding carbonate values (2.8%) were found in the primary spongiosa of the epiphyseal growth plate of domestic pigs /8/. In the adjacent remodeling zone the carbonate values decrease to 1-2%. Corresponding CO_2 values were found in the nearly decomposed definitive callus, 16 weeks post operationem (controls: 2.o ± o.2o%; 12 mA DIC: 1.4 ± o.o7%; 6o mA DIC: 1.o ± o.o9%).

A further indication of elevated cell activity caused by the DIC is reflected by the highest K (and Na) values in the callus during osteotomy healing; the highest K values being o.9 ± o.o8% (Na: 1.1 ± o.o1%) for the 6o mA DIC animals on day 13, K = 1.1 ± o.1o% (Na: 1.3 ± o.13%) for the 12 mA DIC animals on day 15 and K = o.5 ± o.o1% (Na: 1.o ± o.o6%) for the controls on day 2o. At the end of the experiments after 16 weeks the K (∿o.15%) and Na values (∿o.6%) are nearly the same for the 3 groups.

The difference in the time scale of callus differentiation between the 3 groups can also be observed by the vascularization, reflected by the Fe content, being 42o ± 11o ppm for the controls, 55o ± 14o ppm for the 12 mA treated and 1ooo ± 25o ppm for the 6o mA treated animals, until 3 weeks post operationem (4 animals for each group).

Further, the highest Cu values appear during the most intensive phase of callus formation with 15.5 ± 1.5 ppm for the controls up to the 5th week. These values appear already in the 2nd to 3rd week for the 12 mA DIC treated animals. They decrease down to 1.o ± o.1 ppm for the 12 mA DIC treated animals in the 5th week and to 1.5 ± o.1 ppm in the definitive callus of the controls in the 7th week; the callus mineralization is completed. Cu is connected with enzymes representing high cell activity and it has an important function in collagen synthesis /5/.

Zn is also an important trace element increasing with the degree of mineralization (controls: 52 ± 3.o ppm in the 3rd, 85 ± 3.o ppm in the 7th and 111 ± 2.5 ppm in the 16th week at the end of the experiments). The accelerated bone formation by the application of 12 mA DIC leads to a Zn increase, reaching the 1o5 ± 7.o ppm of the fully mineralized callus already in the 7th week. The Zn content decreases with definitive callus decomposition. The different Zn contents can be correlated with

the different degrees of maturation and remodeling.

The slope for the Pb contents are independent of the DIC. For callus of the controls the Pb values increase from 8 ppm (2nd week) to 15.o ± 1.o ppm (5th week) (for the DIC treated animals: 13.5 ± 1.4 ppm). In the 7th week p.o. a minimum for the Pb contents of 3.o ± o.2 ppm was found. Afterwards the Pb content is slightly increasing parallel with the decomposition of callus (16 weeks).

The Cd contents reach highest values during the most intense phase of the formation of the fibrous callus (controls: 2.o ± o.2 ppm in the 5th week). In the mineralized callus of the DIC treated animals these values are already reached two weeks earlier (1.9 ± o.2 ppm). These values decrease already at an earlier stage in the DIC treated group than in the control to the minimum values of less than o.1 ppm in the decomposing callus corresponding to those of the mature bone.

For an interpretation of a possible function of Zn and Cd in vitro activation studies with a purified hard tissue APase were carried out with differing Zn/Cd ratios, the elements being chosen in those concentrations found in vivo. Lowest APase activity was observed with the highest Zn concentrations, Cd showed no effect. When both ions are present the inhibition effect of Zn is decreased with an increasing concentration of Cd /9, 11/.

DISCUSSION

Bone healing under the influence of electromagnetic fields is an important but unsolved field of hard tissue research /1/. While several groups have applied magnetic fields of very different modification we have applied the non invasive method using DIC, whose field strength had been measured in the osteotomy cleft /3/. Chemical analyses of the callus were carried out to clarify whether the DIC shows a positive effect or an unphysiological influence on callus formation. It was found on the one hand that the contents of elements such as Ca, P, Mg, and of certain trace elements found in the chronology of callus formation could be correlated with their topological distribution in the growth plate reflecting also different stages of hard tissue formation. As an example, the Zn distribution in the growth plate, showing a broad maximum reaching from the zone of primary mineralization to the zone of bone remodeling, can be correlated with its chronological appearance in the callus /1o/. Further the maximum of the Zn distribution in the growth plate correlates with that of the distribution of an acid phosphatase /8/, so that an influence of this element on this enzyme might exist. Further, Zn is known to be a cofactor of the carbonic anhydrase, regulating the carbonate status. This enzyme has been demonstrated histochemically in the zone of primary calcification /2/.

A maximum of Pb could be found in the growth plate and in the mineralizing callus of these experiments for the stage of intense formation of fiber callus. A simple accumulation can be excluded since the Pb content is decreased in the mature bone. According to /12/ Pb is essential for bone formation. A corresponding increase of Cd with the beginning mineralization and its decrease with the bone maturation as well as the in vitro experiments of Cd and Zn with the purified APase might lead to the conclusion that Cd can also act as a regulating trace element during hard tissue formation.

Summarizing the chemical results and correlating them with the clinical and histological findings the conclusion can be drwan that the application of the DIC accelerates the osteoneogenesis. Pathological effects could not be observed; furthermore the different parameters of the osteoneogenesis when compared with those of enchondral ossification, reveal clearly the controlled mechanism of the different steps of hard tissue formation.

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INDICATIONS FOR ELECTROSTIMULATION IN THE TREATMENT OF PSEUDOARTHROSES

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SUMMARY

Five congenital and 78 acquired nonunions of bone were stimulated using an invasive device. The unit delivered a constant but pulsed right-angled current of positive polarity measuring 20 to 25 µAmps (voltage of 750 mV) and a frequency of 20 Hz. The power pack encapsulated in epoxy resin was implanted at the time of operative fragment stabilization. The cathode was inserted at the site of the nonunion gap. After two to 12 months, all but 3 of the acquired nonunions and two of the congenital pseudarthroses healed. In 2 unsuccessful cases, the bone ends were totally necrotic, 3 cases required reimplantation because of broken wires of the battery. Two cases failed owing to purulent infection. Electrostimulation is an adjuvant treatment to fragment stabilization in hyporeactive and hypovascular or congenital pseudarthroses. Electrical stimuli may be assumed to simulate conditions which are essential for bone healing.

INTRODUCTION

Surgical treatment of delayed unions or nonunions of bone was done in the last century with the intention to stimulate bone formation by various methods. This concept was made more precized in the last 20 to 30 years, realizing the necessity of fragment stabilization.

Since then, stabilization of the fragments, with or without compression, is considered to be the chief principle in the treatment of fractures and pseudarthroses. In hypertrophic reactive pseudarthroses fragment stabilizing is the method of choice. Bone, augmentation done as autologous bone grafting, is thought to be indicated only in hypovascular or avascular types of pseudarthroses or in bony defects.

In addition, for more than 20 years orthopaedic surgeons have been trying to stimulate new bone formation by use of electrical currents.

This is based on the fact that bone formation and bone healing can be explained as the result of electric processes.

The relationship between the function of bone and its form is well known since Wolff (1) first proposed the law of transformation of bone with respect to mechanical stresses. Mechanical stress and genetic determination both affect the shape and function of embryonic bone. A direct mechanical effect that changes the function of bone cells and the form of bone may be a change in hydrostatic pressure. An indirect effect, electrical energy converted from mechanical energy, is believed to change the electrical environment of mesenchymal cells.

METHOD

Based on fact that human bone is rhythmically loaded by muscle contractions as during walking (at a frequency of approximately one Hz) we developed a stimulator which delivers a constant but pulsed right angled current of positive polarity.

The electrical stimulator consists of two parts. The first part contains the batteries with a primary working potential of 3 V, decreasing in time to 2.3 V. In respect to battery type and capacity, an operating duration of six to 24 months is possible.

The second, the electronic part, is composed of a multivibrator, a Schmitt-trigger, a stabilizer, a current limiter, and a disconnector. Thereby the effective current is constant over 90 per cent of the reaction time in a range of 20 to 25 µAmp.

Considering a resistor capacity of the bone to be in the range of 3.3 to 19.3 KOhm with an average of 9.6 KOhm and a secondary voltage of 750 V, a secondary current results with an intensity of 20 to 25 µAmp.

It is of importance that the maximum of the effective potential in the bone does not exceed 1.35 V -the electrolysis point of water.

The unit is as large as a small finger and epoxy encapsulated and the electrodes are built of stainless steel for the cathode and of platinum-iridium (relation 1:9) for the anode. In positioning the cathode one can influence the site but not the amount of callus formation.

MATERIAL

Previous Animal Studies

In our animal experiments, done in mongrel dogs, the first reaction to electrical stimuli in the undamaged medullary canal was a dilation of the existing vessels followed by the opening of resting vessels. This process was more pronounced in the region of the active cathode than around the anode or inactive electrodes. Thereafter an excrescence of the mesenchyme developed in the marrow cavity and bone trabeculae were laid down.

Accordingly, the initial phase was dominated by a high vascularity resulting in an angiofibromatosis. This area was called the mantle zone. During the intermediary phase in the intermediate zone, the initial bone formation was remodeled into a spongiosclerotic tissue. During the terminal phase the woven bone in the inner zone remodels into lamellar and mature bone. Its structures were directed parallel to the long axis of the bone.

Using the Texture-Analysis System in quantitating the new bone formation, we measured the areas covered with newly formed bone around the electrodes. There was a distinct differentiation between the stimulated and control side. In the electrically activated femur, statistically significantly more bone was formed. The p-value was less than 0.005. Comparing the sites at which the electrodes were inserted, the analysis demonstrated that most bone was formed around the cathode; the next highest amount was counted in the region where the anode was inserted; minor formation took place around the distally implanted inactive electrode, and even less at the proximal inactive site. The p-value again was statistically significant at the level of 0.05. The new bone formation was time dependent: the longer the period of stimulation, the larger was the amount of newly formed bone. Bone formation in these experiments was limited by the width

of the medullary canal.

In other experiments, the effect of electricity on bone fractures (surgically produced as osteotomies of the ulna and femur) and pseudarthroses (obtained by segmental bone resection of the ulna and temporary interposition of a teflon disc to produce obliteration of the medullary cavity) was evaluated. In all experiments, a characteristic callus tissue was formed which may be called electrocallus:

1) The callus was dominated by an increased vascularity;
2) The newly formed tissue structures were mainly oriented parallel to the long axis of the bone;
3) The calcium precipitation was increased. This type of mineralization is bonded to the cells as well as precipitated onto extracellular stroma;
4) Remodeling of the woven bone callus to lamellar structures was accelerated.

A significant acceleration in healing of osteotomies as a model of fracture healing was not achieved either in the non stabilized or in the stabilized osteotomies. The healing period of stimulated hyporeactive pseudarthroses, however, was shortened by one-quarter of the normal healing time.

Therefore, one can assume that in bone lesions with sufficient blood supply, as in normal fractures, an acceleration of bone formation by means of electrical stimuli does not occur. This holds true also for the common reactive and hypertrophic pseudarthroses.

In contrast, in poorly reactive pseudarthroses an acceleration of bone formation with electricity can be achieved (Zichner (2)).

Transferring the experimental results and especially the morphology of the electrical callus, to the application in human beings, it may be possible to apply this type of tissue reaction achieved by electrical stimulation to humans. Therefore, our indication for use of electrostimulation is to influence

1. hypo- or avascular (so called poorly reactive or hypotrophic) pseudarthroses and defects
2. situations as found in elongation osteotomies, and after comminuted fractures and
3. congenital pseudarthroses.

TREATMENT IN MEN

Following these criteria we treated 83 patients by means of electrical stimulation. At the beginning it was prerequisite that at least two unsuccessful operative procedures preceded the electrical treatment in each patient. An osteosynthesis was performed simultaneously with implanting the electrical stimulator. Other surgical interventions such as freshening the pseudarthrosis, autologous bone grafting, and decortication were not done. The cathode was put around the pseudarthrosis or passed through drill holes crossing the nonunion, forming a figure eight. The anode was placed into the medullary cavity through a special drill hole approximately 2 cm above the pseudarthrosis.

In 92 % of our patients we achieved a bony bridging and healing of the pseudarthroses in a period of three to six months. In one young patient, who suffered a pathological fracture of a transplanted mother's fibular graft for bridging a defect of a congenital osteomyelitis to replace the tibia, we failed initially. However, one year later, after resorption of the necrotic bone areas, we transplanted the ipsilateral fibula and stimulated the bone. Solid bony healing occurred after three months. In 5 cases we did not succeed because of breakage of the cathodal wire. 2 cases became infected.

DISCUSSION

In our opinion, a general application of electrostimulation in bone surgery is not indicated. In the more numerous and common hypertrophic nonunions, stabilization of the fragments by means of internal or external fixation is successful. Electrical stimulus is no substitute for fragment stabilization. It is, however, promising in special indications, e.g., in the treatment of hypo- and avascular nonunions. In these special conditions, either congenital or acquired, electrical potentials effect callus formation. It is presupposed that at the place of implantation, a tissue component presides that is capable of forming bone. Thus, we can discuss whether electrostimulation may replace autologous bone grafting.

We define electrostimulation as an adjuvant and additive treatment to fragment stabilization. It is possible to render a nonreactive pseudarthrosis to a reactive one and to create the conditions necessary for bone healing.

Some authors suggest that most of the patients treated by electrostimulation have been young and the same results may not hold up in older patients because of hypovascularization of the tissue. However, in recent studies we were able to successfully treat eight patients, all of whom were older than 50 years of age (the oldest being 85).

We prefer the invasive unit for electrostimulation, because our aim is to achieve a stable osteosynthesis, thereby allowing early physical therapy and avoidance of "fracture disease." We saw only one temporary Sudeck syndrome in the treatment of a scaphoid nonunion.

Electrostimulation will not be successful in totally necrotic bone, as evidenced in two scaphoid bone nonunions in our series.

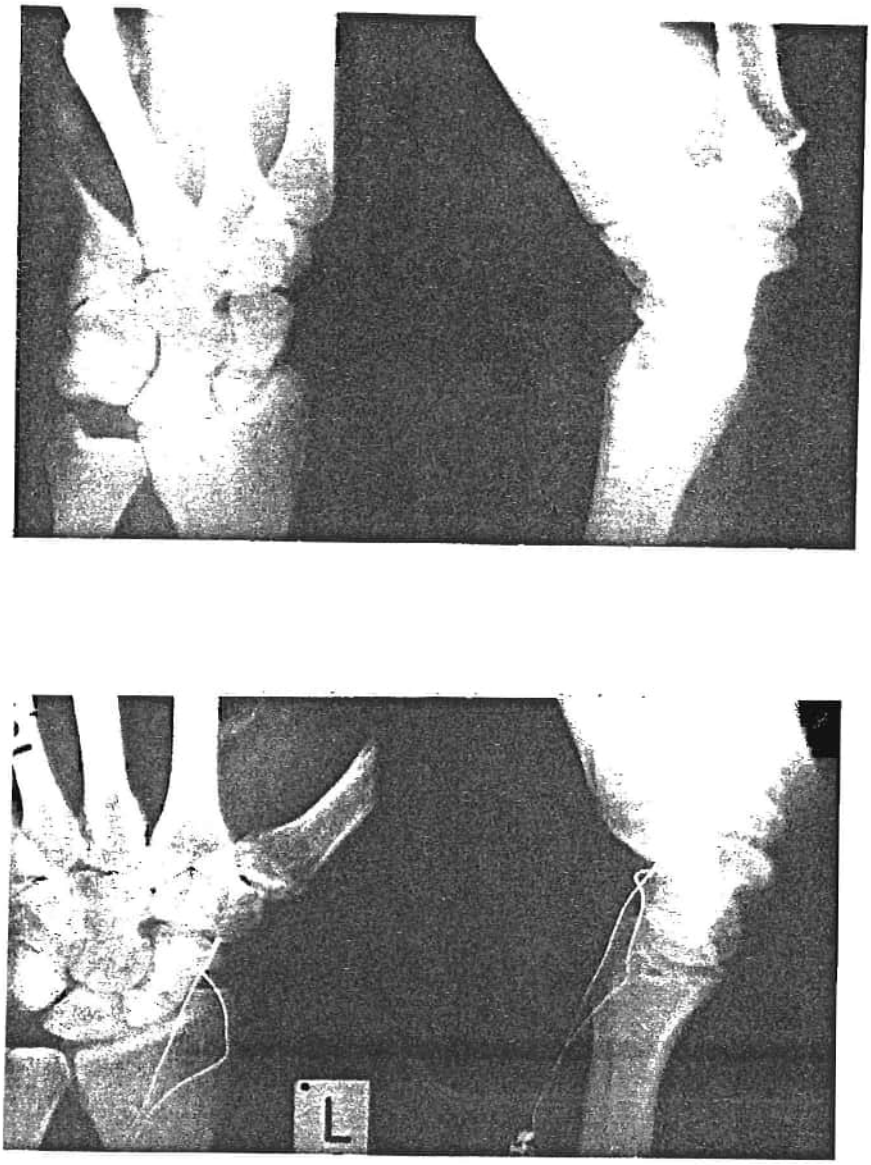
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Electrical stimulation of a scaphoidal nonunion.
Above: before stimulation.
Below: 2 months after stimulation: the gap is almost bridged by boney tissue.

ELECTRICAL STIMULATION OF BONE GROWTH USING THE 'VIENNA STIMULATOR'

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INTRODUCTION

Ever since Fukada and Yasuda [1] showed in 1957 that bone has piezoelectric properties, i.e. that it generates electrical potentials in response to mechanical stresses, several research teams have tried to accelerate the repair of bone defects by stimulation with electrical currents. It is, however, difficult to draw any definitive conclusions on the usefulness of the concept because the methods employed varied widely. In fact, some groups reported that positive effects were altogether absent [2].

STATING THE PROBLEM

In a first series of experiments using the 'Osteostim' stimulator by Telectronics we found it impossible to say whether and for how long post implantation the stimulator was functional. This prompted us to develop an implantable telemetric unit for monitoring the function of the implanted stimulator and measuring the stimulating current throughout the duration of the experiment. This had already been done by Güttler [3] for external stimulation.

For our first series in which the 'Frankfurt bone stimulator' developed by Zichner and Happel [4] was used we devised a small self-sustained telemetric unit to be coupled to the anodic circuit. For a later experimental series a telemetric unit for integration in the stimulator appeared to be desirable.

SOLVING THE PROBLEM

Design of the self-sustained telemetric unit

The 'Frankfurt bone stimulator' is a pulsed direct current source of approximately 20 µA and a pulse frequency of about 35 Hz. Figure 1 shows the blockcircuit diagram of the telemetric unit and its interfaces with the stimulator.

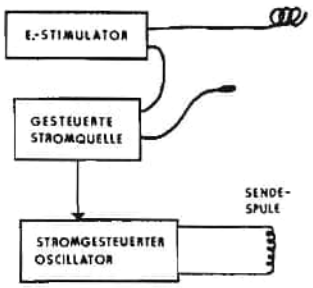


Fig.1

Controlled by an anodic current, the power source in itself controls an oscillator. The frequency shift of the transmitter coil signal versus the intrinsic frequency of the transmitter is proportionate to the anodic current. In addition, it serves as a basis for computing the pulse interval ratio and the cycle frequency of the pulsed stimulator.

The transmitter is encapsulated in Araldite and has a size of about 20 x 12 x 8 mm. The receiver consists of a measuring unit which should be positioned at a maximal distance of 2 cm above the transmitter. In addition, it features an amplifier (Fig.2). The measuring unit contains the receiver coils, a low noise preamplifier and a display (LED) which only lights up if a sufficiently large signal is received (capture range).

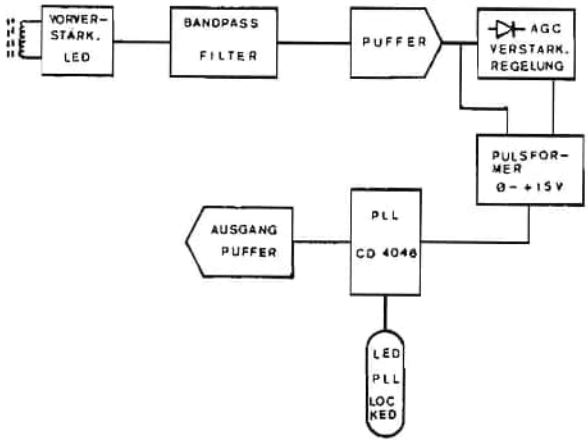


Fig.2

An analogous display is available on the front plate of the amplifier unit. The signal from the pre-amplifier successively passes a band-pass filter, a buffer, an automatic sensitivity control and a pulse-shaping unit.

A demodulator (PLL) generates a DC potential with superposed AC voltage. The mean DC potential reflects the receiver frequency (receiver range), while the amplitude of the superposed AC voltage is proportionate to the anodic current of the stimulator.

Integrated telemetric unit (Fig.3)

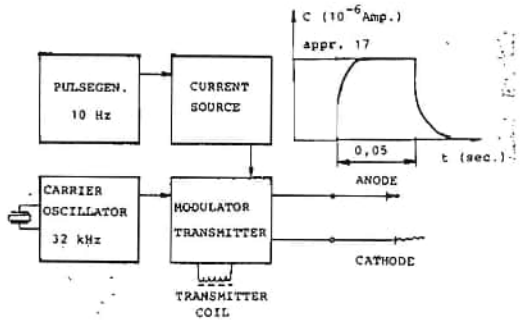


Fig.3

The stimulator contains a pulse generator (pulse duty factor 1:1) and a current limitor for the stimulator current. The telemetric unit consists of a 32 kHz carrier frequency oscillator and a stimulator current controlled modulator as well as a transmitter unit. Compared to the self-sustained telemetric transmitter the integrated telemetric unit offers some important advantages: The total volume of the stimulator including the integrated telemetric unit is about 70 % of that for the two separate units. Owing to the special design simple testing for the presence of the carrier frequency will show whether the system is functional. The additional power required by the integrated telemetric unit is approximately 3.5 µA. This can easily be supplied by a battery make of adequately high capacity. The useful life of the stimulator plus integrated telemetric unit is better than 9 months for stimulating currents of 15 µA. The receiver (Fig.4) picks up the emitted signal (Fig.5) via a tuned receiver circuit.

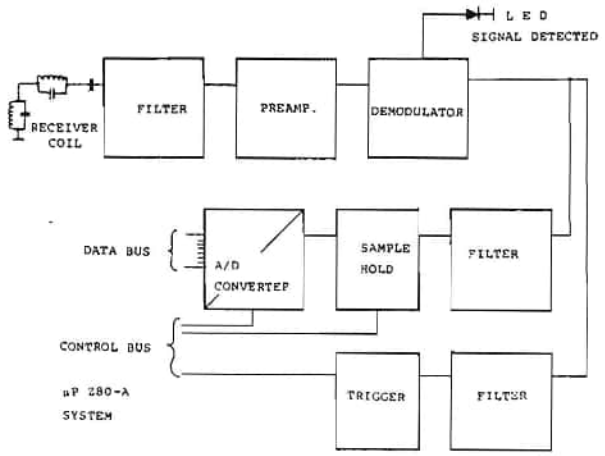


Fig.4

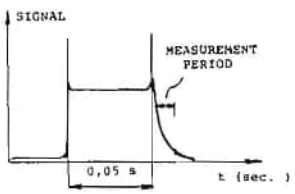


Fig.5

Noise from line or other electromagnetic sources is filtered out by a steep-slope filter. A demodulator further processes the signal for subsequent analysis. It also indicates optically whether the carrier frequency was recognized ('carrier frequency on'). Signal analysis proper is done on a microcomputer console (Z 80 A) which, allowing for the requisite correction factors after stimulator code input, also provides readings of the pulsed current levels.

RESULTS

In a first series of experiments the self-sustained telemetric transmitter was tested in 11 sheep dog mongrels. Of these 6 were fitted with the stimulator, while 5 had a dummy implant.
Both the radius and ulna of the right fore-limb were exposed and 4 AO cortical bone screws were put in place for transfixation in the mid-thirds of the two bones. Then a diaphyseal cylinder of 1 cm was resected from the radius between the distal and the proximal pairs of screws and the resultant defect was packed with a cortico-cancellous bone mix. In addition, the cathode end was coiled up to form a spiral and wrapped around the bone graft (Fig.6).

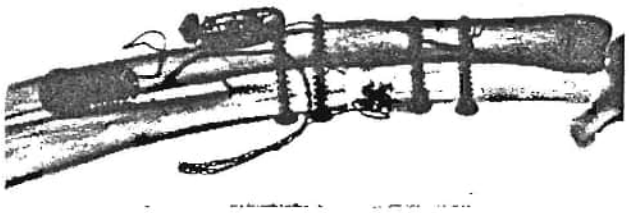


Fig.6

The anode was implanted in the extensor muscles and the transmitter or a dummy of identical size were positioned between the proximal bellies of the forelimb extensors. After closing the wound in layers the extremity was supplied with a Baycast dressing for 14 days.
The postoperative follow-up period varied from 1 to 6 months.

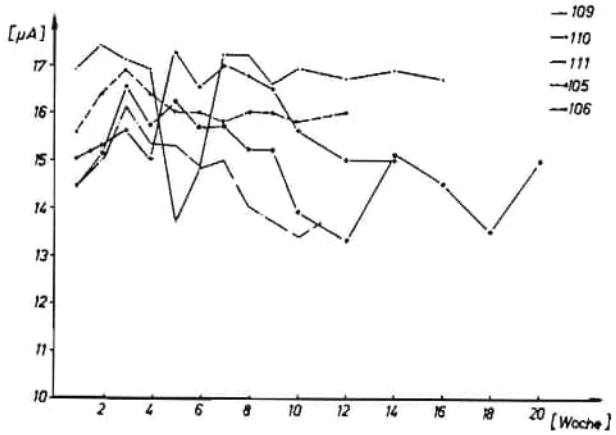


Fig.7

Figure 7 shows the current readings throughout the duration of the experiment. It is of interest to note the current rise during the first 3 weeks. Inspite of some variation the current was not found to drop substantially below baseline throughout the experiment so that, under the experimental conditions described, the stimulator can be regarded as fully functional throughout the test period. However, there was no evidence of accelerated bone repair. This is likely to be due to the poor stability at the site of the bone defect. To overcome this problem the dog humerus was chosen as a model for a follow-up series of experiments with the integrated telemetric unit. The Animals (sheep dog mongrels with a body weight of 25 to 30 kg) were placed in the left lateral position. The humerus was exposed and, in its mid-sigment, a bone defect extending over 2 x 1 cm was produced. The bone were stabilized with an osteosynthesis plate of plastic material. Distal and proximal to the bone defect a pair of screws was inserted for fixation of the plate. Defects were packed with a homologous cancellous bone graft.

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EXPERIENCES WITH FUNCTIONAL ELECTRICAL STIMULATION OF PERONEAL NERVE IN THE REHABILITATION OF HEMIPARETIC PATIENTS

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SUMMARY

Since 1981 the authors have been using the equipments for functional electrical stimulation of hemiparetic patients having peroneal paresis

MATERIAL AND METHODS

The equipments, used by us, were developed by the Institute for Rehabilitation of the Disabled in Ljubljana.

The type of FESPA PO-10 and AM-5 equipments have been used in 53 cases:

- cerebrovascular disease in 18 cases
- craniocerebral trauma in 22 cases
- brain tumors in 9 cases
- neurologic systemic disease / sclerosis multiplex / in 4 cases

RESULTS

Among of 53 cases :

- in 1 case the patient / having cerebrovascular disease / refused the treatment
- in 1 case we had to interrupt the treatment because of allergy
- in 19 cases we were able to leave off stimulation on the average after 2-month-period having a good gait pattern without any orthesis
- in 12 cases theperoneus paresis was reduced, and later the patients had to wear other orthesis
- in 16 cases the peroneus paresis were not reduced, but the stimulation made easier the mobilisation, the gait.
- in 4 cases after initial successes we gave up the treatment because of progression of disease

DISCUSSION

However we have relatively few cases aim of film wos to demonstrate the application method in our hospital

EXPERIENCES WITH FUNCTIONAL ELECTRICAL STIMULATION OF PERONEAL NERVE IN THE REHABILITATION OF HEMIPARETIC PATIENTS

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