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Basic design and construction of the Vienna FES implants: existing solutions and prospects for new generations of implants

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Abstract

We can distinguish 3 generations of FES implants for activation of neural structures: 1. RF-powered implants with antenna displacement dependent stimulation amplitude; 2. RF-powered implants with stabilised stimulation amplitude; and 3. battery powered implants. In Vienna an 8-channel version of the second generation type has been applied clinically to mobilisation of paraplegics and phrenic pacing. A 20-channel implant of the second generation type for mobilisation of paraplegics and an 8-channel implant of the third generation type for cardiac assist have been tested in animal studies. A device of completely new design for direct stimulation of denervated muscles is being tested in animal studies.

There is a limited choice of technologically suitable biocompatible and bioresistant materials for implants. The physical design has to be anatomically shaped without corners or edges. Electrical conductors carrying direct current (D.C.) have to be placed inside a hermetic metal case. The established sealing materials, silicone rubber and epoxy resin, do not provide hermeticity and should only embed DC-free components. For electrical connections outside the hermetic metal case welding is preferable to soldering; conductive adhesives should be avoided. It is advisable to use a hydrophobic oxide ceramic core for telemetry antenna coils embedded in sealing polymer. Cleaning of all components before sealing in resin is of the utmost importance as well as avoidance of rapid temperature changes during the curing process.

Keywords: FES; Implants; Biomaterials; Technology; Phrenic pacing; Mobilisation; Cardiac assist

1. Introduction

In general we can distinguish 3 generations of FES implants that have gained clinical relevance. Early implantable stimulators containing a very simple electronic circuit were powered and controlled via an inductive link without stabilisation measures to keep output parameters unaffected by displacement of the receiver with respect to the transmitter antenna. This construction is still in use and is acceptable if mechanical stability of the transmitter and receiver can be guaranteed, as is the case for cochlear implants [1] or in the most successful pelvic floor system, the Brindley anterior root stimulator [2]. For other applications, substantial progress awaited the second generation of FES implants, still supplied and controlled inductively but featuring stabilised output parameters. The third generation consists of battery-powered FES implants, that have gained importance in the field of cardiac pacing, are relevant to single-channel applications for dynamic myoplasty, such as cardiomyoplasty [3,4] and graciloplasty [5] and for treatment of pain, spasticity and Parkinson's disease. But for complex applications that require multiple channels and real-time control these implants are still in an early stage of development and far from clinical application. The main unsolved problem is still to achieve an acceptable battery lifetime.

The Vienna contribution to clinical FES implants is an 8-channel implantable stimulator, powered and controlled via an extra-corporal unit and an inductive link. It was applied clinically to stimulation of lower

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extremities of paraplegic patients and for phrenic nerve pacing in tetraplegic patients. Although it was implanted for the first time as early as 1982 its features still represent the state-of-the-art in clinical multi-channel implants for paralysed upper or lower extremities or respiratory support. During the years of application a number of modifications have led to improvements in the reliability and lifetime of the implant. An attempt to commercialise it failed after a few years because of high manufacturing costs and changes in legislation for medical products that made it impossible to maintain it on the market any longer. A number of these implants are still functioning satisfactorily in a group of tetraplegic patients who benefit from their use for electrophrenic respiration [6].

From this 8-channel implant 3 branches of further research originated with the following goals:

1. To develop a cheaper inductively-powered implant providing a higher number of output channels to support complex movement patterns of the lower extremity.
2. To develop a family of fully implantable battery-powered 8-channel implants for various applications based on a modular hard- and software concept.
3. To develop an inductively-powered implantable stimulator for direct stimulation of denervated muscles, an application that differs completely from known concepts all of which are restricted to stimulation of neural structures and indirect muscle activation.

The technology and application of FES implants have remained a major focus of research at the Vienna Department of Biomedical Engineering and Physics. Its growing importance is reflected in the foundation of a research group "FES implants", that is currently directed by Hermann Lanmüller and is intended to coordinate the activities in this research field. At the moment the limited research and development capacities are focused on an ECG-controlled version of the battery-powered 8-channel implant and its application to biological cardiac support in a preclinical stage of animal experiments [7,8].

2. Principles of construction

Inside the human body we have to deal with a highly corrosive chemically and electrochemically aggressive electrolytic medium and mechanically stressful conditions. Conversely the organism reacts sensitively to incorporated foreign bodies and corrosion products. The choice of materials that are both biocompatible and bioresistant is limited and is further reduced by technological limitations. In addition the mechanical properties needed to resist mechanical stress on the one hand and to avoid tissue damage on the other play an important part in the design of all kinds of implant.

For the construction of an FES-implant some important rules have to be considered:

1. All surfaces have to be of proven biomaterials that do not cause excessive tissue reactions even in the presence of slight inflammation of the adjacent tissue. The surfaces must not deliver material to the tissue interface or react chemically with resulting corrosion products. These attributes are provided by certain plastic materials, metals and ceramic materials.
2. The mechanical design of the implant has to be kept small in size and weight. Its surface has to be shaped as far as possible to the assigned anatomical site and it must not present corners and edges that could cause pressure damage of the adjacent tissue.
3. All electrical conductors carrying direct current (DC) have to be sealed hermetically; consequently all electrical conductors that are exposed to moisture have to be kept DC-free. This requirement applies especially to the electrode outputs and the electrodes themselves, which directly interface with an electrolytic medium and are in danger of being destroyed rapidly by electrochemical corrosion if loaded with DC [9].
4. Antenna coils for transmission of energy and/or for data transmission have to be positioned inside a hermetic capsule or if that is not possible constructed in a manner that avoids both leakage current and change of electrical capacity between different windings of the coil. The coil is usually part of a resonant circuit that is susceptible to detuning or loss of efficiency.
5. Special care has to be taken when connecting metal parts. They must not differ excessively in electrochemical contact voltage. Electrochemically equivalent materials are to be preferred, alloys should be avoided if possible and welding techniques are preferable to soldering techniques. For soldering, acid-free flux and careful removal of residues are required. Conductive adhesive is not recommended if it is to be exposed to moisture.
6. Plastic materials, including the usual medical grade silicone and epoxy polymers, do not provide hermeticity. DC-loaded parts of the electric circuit have to be enclosed in a metal or ceramic case as mentioned in 3. Metals that can be used to enclose implant electronics are made of the reactive metals titanium, tantalum or niobium with glass-to-metal-seals made from sodium-free borosilicate glass. Stainless steel is not suitable, because the alloy is decomposed during the welding process that seals the case. For data transmission with a limited data rate it is possible to position the antenna coil inside a metal case. The carrier frequency is a compromise between the shielding factor of the case and the required data rate; realistically

it is in kHz rather than MHz. To power an implant circuit via an RF-carrier the antenna has to be placed outside, and distant to, the metal case to achieve an acceptable efficiency. An alternative is to choose a ceramic case, but these are difficult to seal hermetically at temperatures low enough not to destroy the enclosed electronic circuit.

7. The usual strategy of combining a hermetic case with some external components embedded in a polymer requires additional care to avoid or at least to elongate leakage paths as far as possible. They originate normally where the electrodes penetrate the surface, and inside the implant they follow all the surfaces of embedded components.
8. Finally it is important to carefully clean all surfaces before embedding them to avoid residual ions that cause corrosion as soon as they come into contact with moisture. The mould with the as yet liquid sealing compound has to be evacuated at the very beginning of the curing process to remove air bubbles, and the rest of the curing procedure has to be done under nitrogen of high purity. Rapid temperature changes have to be avoided during polymerisation to prevent inhomogeneities, strain and cracks within the cured material.

In the author's view these are the most important rules for constructing implantable stimulators that are to have a lifetime of more than 10 years. The following describes their application to different practical solutions, that were developed and applied or at least tested in vivo in Vienna.

3. Devices

3.1. The RF-powered, RF-controlled 8-channel implant

This implant consists of a resonant circuit to receive the pulse-code-modulated (PCM) carrier, a power management circuit, decoding logic, a current source, electrode switches, output capacitors for DC decoupling and finally electrode connectors (Fig. 1A, Fig. 3). All components are embedded in Hysol (medical grade epoxy). The receiver antenna is a 3-turn coil made from a 0.8 mm silver-plated copper wire, coiled on a ceramic ring with grooves that separate the turns to avoid the leakage currents mentioned above and changes of dielectric properties with penetration of moisture. All other components with the exception of the electrode connectors are integrated in two thin-film hybrid circuits that are placed inside two hermetically sealed gold-plated standard Kovar cases (Isotronics, USA) measuring 1″ by 1″. The 8 decoupling capacitors are mounted on a hybrid substrate of their own and are in a separate case because of their size. The rest of the electronic circuit fits into another case of equal size.

The design and manufacture meet most of the design rules described above: the antenna is protected against detuning by the hydrophobic oxide ceramic material and is connected directly to the first hybrid case. All DC-loaded components lie inside the case. The electrode outputs run via short separated wires to the second case containing the decoupling capacitors and finally to the connectors. The internal connections are soldered using pure colophonium as an acid-free flux. The entire circuit is cleaned before sealing in Hysol by a sequence of 3 cleaning cycles in isopropanol followed by 3 washing cycles in deionised water. The mould is cooled during curing of the epoxy and the implant is tempered subsequently over a period of three days. The whole manufacturing process is carried out under clean-room conditions. Functionally each single output impulse is defined in real time by a series of pulse trains containing information about constant-current (CC) amplitude, pulse width, impulse frequency, target electrodes, and polarity. The current amplitude range covers 0–4 mA with 8 bit resolution (256 steps); impulse duration varies between 0.1 and 1.2 ms, and the upper limit of the frequency range is 200 Hz when two nerves are stimulated simultaneously. The direct-current decoupled electrode outputs are programmable as anode or cathode, or switched off from impulse to impulse. In this way the stimulator can be adapted for conventional mono- or bipolar stimulation as well as for the more complex Carousel [6] and Sequence stimulation [10] for which recruitment changes from impulse train to impulse train, or from impulse to impulse, respectively.

The final version has proved to be stable for more than 8 years without signs of developing technical problems. Older versions had to be changed relatively frequently after periods of between 1 and 7 years because of technical failures, most of them associated with detuning of the receiver antenna or failure of components directly embedded in the Hysol resin such as diodes from a DC-loaded voltage-limiter circuit.

The first clinical implantation was performed in 1982, when two of the implants were used to regain hip and knee extension in a paraplegic patient. Altogether 4 patients received this type of implant. Standing up, moderate walking in swing-through and four-point gait, and propulsion of a special tricycle were achieved [11]. Between 1983 and 1992, 23 patients with complete ventilatory insufficiency of various etiologies were treated with the 8-channel implant for stimulation of both phrenic nerves to regain physiological respiration (Fig. 2) [6]. To date, the longest application has already lasted more than 16 years; although the patient suffers from a complete C1/C2 lesion he lives permanently at home, has a closed tracheostomy and is able to speak naturally.

The main advantages of this generation of implants is

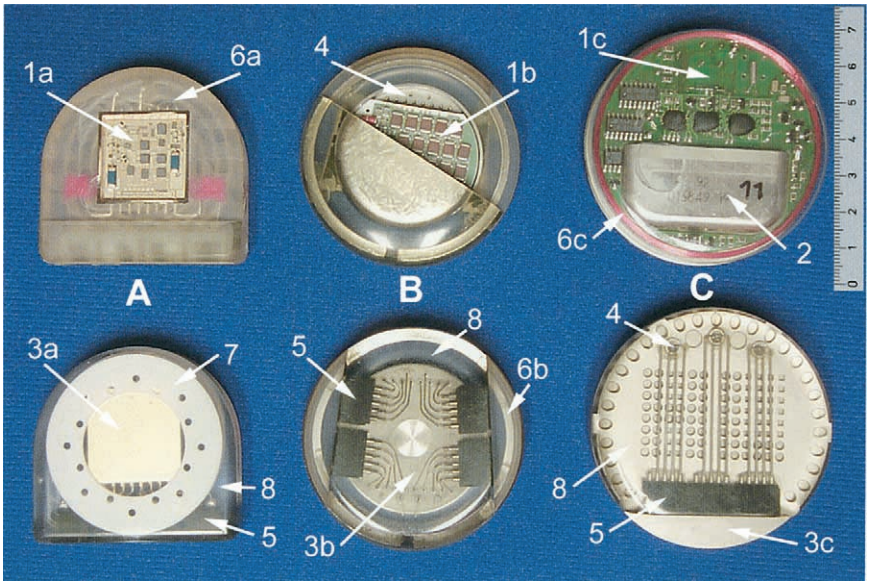

Fig. 1. Technology of three generations of Vienna implants: (A) RF-powered 8-channel implant (upper view shows an older version); (B) RF-powered 20-channel implant; (C) Battery powered 8-channel implant. The main components are: (1a) thin-film hybrid; (1b) thick-film hybrid; (1c) SMT board; (2) Lithium thionyl chloride battery; (3a) Kovar case; (3b) niobium case; (3c) titanium case; (4) Glass to metal feedthrough seals; (5) Electrode connectors; (6a) 3-turn antenna (older version), (6b) single turn antenna; (6c) antenna coil inside the titanium case; (7) Oxide ceramic core (current version); (8) Hysol. The three views at the bottom represent the reverse sides of the devices at the top, part of the internal views is exposed (scale numbering in cm).

that devices are not dependent on limited battery capacity and provide flexible on-line access to each single stimulation impulse for open- and closed-loop control. The main disadvantage is the need to carry external devices and cables whenever the stimulation is in use. The 8-channel implant is hand made and extremely costly to manufacture. In particular, construction of the thin-film hybrid circuit consumes about 40 h of highly specialised hand work under clean-room conditions. To retain the advantages but to avoid the disadvantages of the 8-channel thin-film implant the following two types of implants were developed.

3.2. The RF-powered, RF-controlled 20-channel implant

The functional principles of this implant are similar but the technology is modified in various ways (Fig. 1B, Fig. 3). First of all the number of electrode outputs is increased to 20, primarily to provide additional channels for the lower extremity application and to improve gait by adding flexion functions.

Secondly the costly thin-film circuit was replaced by a much cheaper thick-film version manufactured by a co-operating industrial partner. To keep to a similar size as the older implant, despite the enhanced number of channels and less integrated technology, two gate-array circuits were developed and bonded to the hybrid.

Thirdly a special niobium case was developed that not only seals hermetically all electrical components except the antenna and electrode connectors but is directly exposed to the tissue to serve as a common anode for monopolar cathodic stimulation. The case consists of a base plate carrying the hybrid circuit and 24 feedthroughs made from 0.3 mm tantalum wire embedded in borosilicate glass and a deep-drawn dome-shaped lid that is welded to the base plate in a helium atmosphere with a pulsed Neodyn YAG laser.

Last but not least, the antenna coil was replaced by a single turn antenna that is made from niobium and that avoids the detuning problems described. One turn is not enough to obtain sufficient voltage from the parallel resonant circuit to power the implant, so a voltage cascade was included in the hybrid circuit.

The technical output parameters are similar to those of the 8-channel thin-film implant. Owing to technological limitations the output configurations are less flexible. Whereas the 8-channel version allows an absolutely free choice of output configurations over all 8 outputs, for the 20-channel version this choice is restricted to 5 electrode outputs within 4 electrode groups. As an alternative the implant allows a monopolar mode, in which all electrodes can be used as single cathodes against the niobium case as common anode. This mode has to be pre-programmed during manufacturing. It is possible to build mixed versions with both bipolar and monopolar electrode groups.

This implant is not currently in clinical use. Two animal studies have been performed on sheep, one to test long-term stability and biocompatibility of the technical components (6 sheep, 26 weeks), the other to test the reproducibility of selected muscle functions, especially

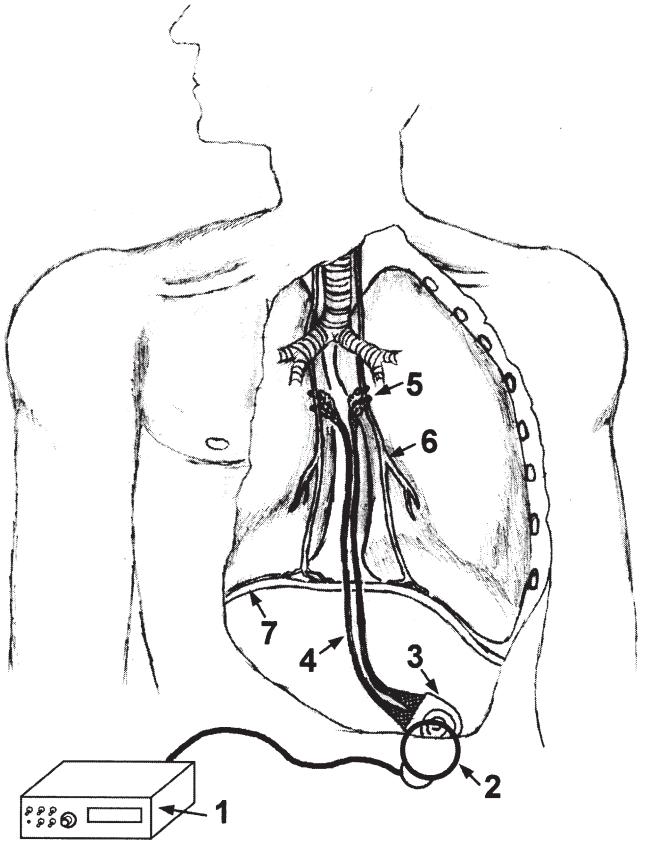

Fig. 2. The phrenic pacer, designed to elicit respiratory movements of the diaphragm in cases of high level injury to the cervical spinal cord or central hypoventilatory apnoea (Ondine's curse). (1) External supply and control unit; (2) Transmitter; (3) 8-channel implant; (4) Electrode leads; (5) Epineural electrodes; (6) Phrenic nerve; (7) Diaphragm.

flexion functions, under epineural stimulation at different sites along the peripheral nerves (3 sheep, 26 weeks) ([12,13]).

3.3. The battery-powered 8-channel implant

This type of device is representative of a forthcoming innovative generation of FES implants, characterised by a substantial degree of independence of external components, except for a programming device to set parameters via a telemetric link, and substantially automatic operation (Fig. 1C, Fig. 3).

The electronic circuit is manufactured in surface mount technology (SMT), which is cheaper and more amenable to design adaptations than the hybrid technologies. Another economical aspect is the strictly modular hard- and software concept that allows one basic device to be used for a variety of applications. The differences lie in specific parts of the microcontroller software and in different amplifier modules that can be added to access different control signals if required. The entire electronic circuit, including the telemetry antenna coil and battery, is contained within a hermetic titanium case. The only external parts, the connectors for stimulation and recording electrodes, are embedded in Hysol. The case consists again of a dome-shaped lid that is welded to a base plate carrying the feedthroughs and the electronic circuit. The 4 wire feedthrough-seals are commercially available (Schott, Germany) and are fixed to the base plate by laser welding. This effects a further economy compared to the 20-channel niobium case, in which the feedthrough seals are integrated directly into the base plate in a very costly procedure. In contrast to the other implants, only part of the base plate is covered with Hysol; the rest of the case surface is directly exposed to the tissue and serves as a reference electrode. The adhesion of the Hysol resin to the titanium surface of the case is not sufficient for reliable fixation. It is essential to embed part of the case in the resin. To meet this requirement we weld a shaped perforated titanium sheet to the base plate. The electrical specifications correspond to those of the 8-channel thin-film implant except for a lower maximum frequency of 50 Hz. In addition the implant features pre-programmed burst/pause timing for open-loop applications or to provide programmable burst duration and phase synchronised to the ECG for cardiac assist applications. A prototype version with two EMG recording inputs is also available. The calculated lifetime for chronic applications such as graciloplasty, phrenic pacing or cardiac assist lies between 3 and 5 years, depending on parameter settings and the stimulation strategy used. To achieve this lifetime from a conventional lithium thionyl chloride heart pacemaker battery (Wilson Greatbatch, NY, USA) of 3 Ah capacity, extreme power-saving solutions had to be worked out in both hardware and software. One important example is a patented energy saving end-stage (Lanmüller, Austrian patent Nr. A382/99). Another example is the load-shift-keying technique for the 100 kHz telemetry link, which does not require a current supply from the implant battery [7,14].

Parallel to accelerated in-vitro tests, in-vivo tests consisted of bilateral conditioning of the latissimus dorsi muscle in 4 sheep for a total of 16 months. The implant is currently undergoing tests in goats, where it is being used to condition the latissimus dorsi muscle preparatory to formation of a skeletal muscle ventricle for cardiac counterpulsation in parallel to the descending aorta [15].

3.4. The RF-powered and EMG-controlled 2-channel implant for denervated muscles

This is the most innovative implant of the Vienna series, but is still in an early stage of development (Fig. 3, Fig. 4). It was developed for a very specific application: the therapy of bilateral recurrent nerve paresis. Reactivation of respiration-synchronous glottal opening by the denervated posterior crycoarytenoid muscle calls for a

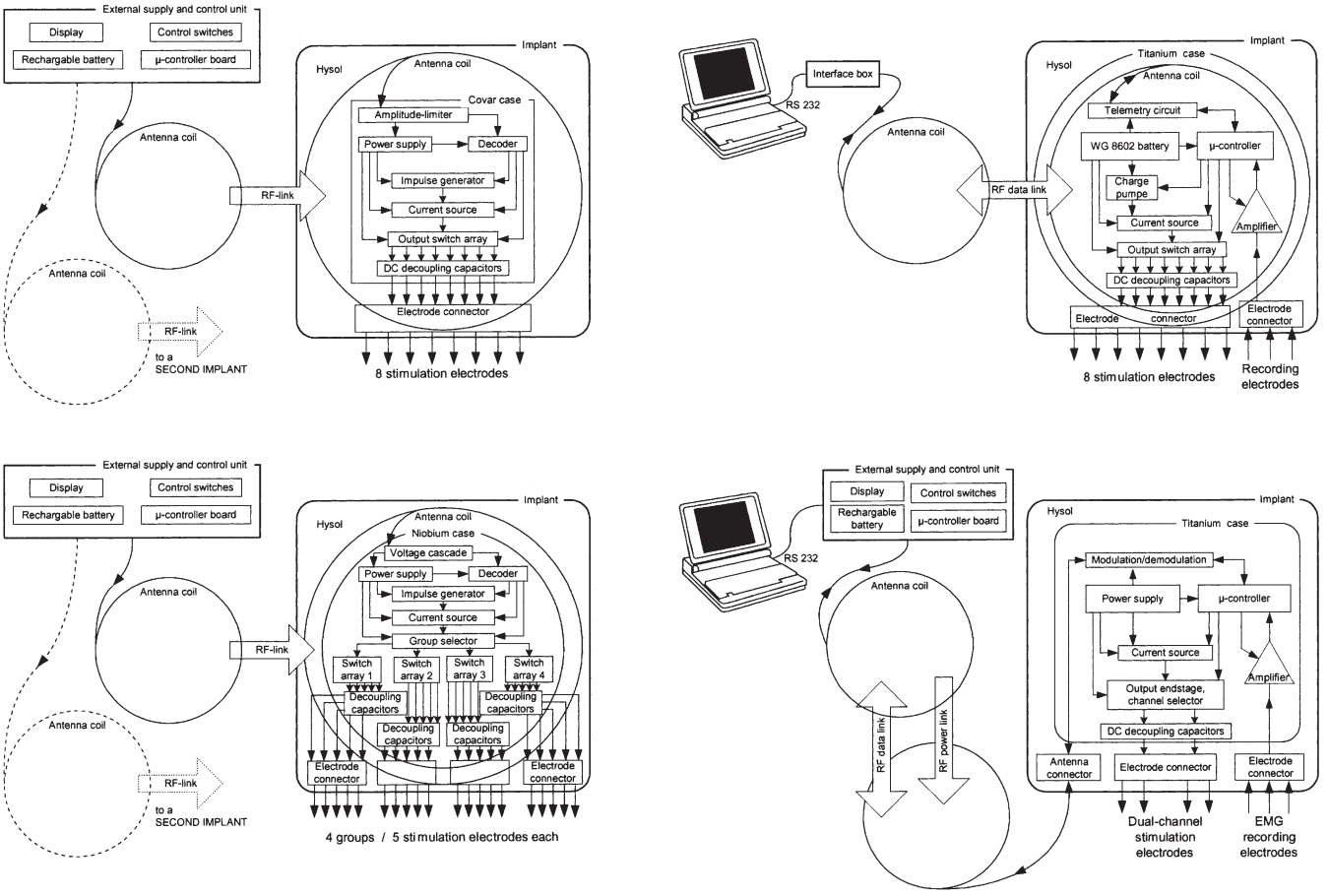

Fig. 3. Schematic diagram of all 4 Vienna implants: Left side: RF-powered 8-channel and 20-channel implant, Right side: Battery powered 8-channel implant and RF-powered 2-channel implant for denervated muscles.

dual-channel stimulator for direct muscle stimulation and a reliable control source to synchronize glottal opening with inspiration—in our experiments diaphragm EMG. A series of long-term animal experiments has demonstrated the basis for the development of this implant [16,17].

The electronic circuit consists of an EMG amplifier and a signal conditioning stage, a micro-controller, a telemetry link for energy supply and programming, and two constant-current end stages. It is realised in SMT on a printed circuit board. Owing to the extremely high power consumption of the implant, which has to deliver very long impulses, the antenna coil is not integrated directly into the implant, but is coated with Silastic so that it can be placed separately, connected to the implant via a cable. The rest of the circuitry is encapsulated in a titanium case consisting of two deep-drawn shells and a plate carrying three 4-wire feedthrough seals. The feedthrough wires are connected directly to connectors for recording and stimulation electrodes and the antenna coil.

The end stage is capable of delivering biphasic ramp-shaped impulses with a pulse width up to 150 ms. The long pulse width is needed to activate denervated muscles, the ramp-shaped impulses make use of accommodation of neural structures and avoid activation of adjacent neural structures. Denervated muscles react on much lower intensities of these particular stimuli than intact nerves.

Prototypes of the miniaturised circuit with implanted electrodes and percutaneous leads were tested in sheep for periods of up to 18 months of bilateral respiration-synchronous activation of the crycoarytenoid muscle.

4. Discussion

Clearly the present state-of-the-art implants—RF-powered and controlled multi-channel and battery-powered single-channel—are interim solutions that have limited practical relevance. RF-powered implants require external devices and cables to be set up and this makes it unattractive for most applications in the long term. Under these circumstances compliance can only be expected from a proportion of patients. With regard to paralysed lower extremities, for example, surface-electrode based solutions provide similar gait quality and require similar donning and doffing efforts, but avoid the

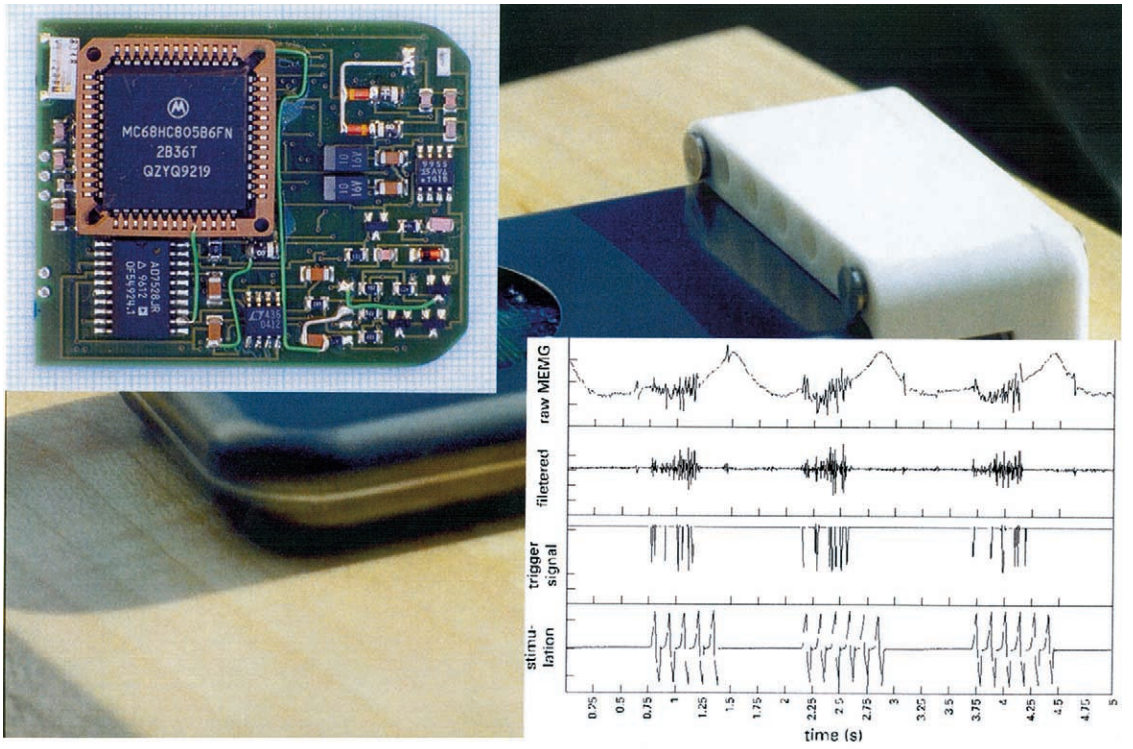

Fig. 4. Prototype version of the RF-powered EMG-controlled 2-channel implant for denervated muscles: Left side: SMD-circuit, Right side: Recorded and processed diaphragm EMG and stimulation impulse, Background: Hermetic titanium case and connector unit made from oxide ceramic.

risks associated with an operation (and possible reoperation in the event of technical failure). On the other hand the functional performance of state-of-the-art battery implants is limited except for cardiac pacing applications. These have requirements that are fundamentally different to all other neuroprostheses, where in general more than one channel and real-time control features are required.

The Vienna applications rely on small ring-shaped (0.8 mm-diameter) stainless steel electrodes that are sutured to the epineurium (epineural electrodes). These have proved to be reliable in the long term and biocompatible in both animal and clinical use [18–20]. They allow substantial selective recruitment of nerve fibre groups if 4 electrodes are attached to one nerve and combinations of electrodes are changed from stimulation burst to stimulation burst (Carousel stimulation), and this reduces problems of muscular fatigue in continuous applications such as phrenic pacing [6]. Experience of mobilising paraplegic patients using the same principle has shown that the facility for modifying recruitment is beneficial for optimising movement patterns as well as managing electrode problems such as dislocations or breaks [11].

Evidently, multi-channel solutions have the potential for providing both reduction of fatigue in continuous applications and improved control of movement and flexibility in complex functional applications, as well as a degree of redundancy in the event of electrode problems. For this reason we see battery-powered multichannel implants as the ideal solution for many applications. To give some examples, simple free-running versions would greatly enhance the comfort and performance of phrenic pacing or graciloplasty, EMG-controlled versions could be the basis for a vocal-cord-controlled phrenic pacer, a fully implantable upper extremity neuroprosthesis or a fully implantable automatic foot-drop assist device, and ECG controlled versions could improve fatigue management in cardiac assist applications. All these applications could be performed with essentially similar implants adapted to the specific requirements via software and recording amplifier modules. The classical packaging techniques from older implant generations are familiar and still valid for the new implant generation. Battery technology and power-saving electronic circuits and micro-controllers have reached a stage of development that enables us to realise this new generation of implants. At the same time SMT provides an accessible alternative to expensive hybrid technologies and makes prototyping and manufacturing of small series easier and cheaper.

The stimulation of denervated muscles is a completely new and challenging field. All existing systems are based on stimulation of neural structures. In the case of muscle denervation the membrane of every single muscle fibre has to be depolarised. Though this is possible, the mem-

brane of a muscle cell is much less excitable than the membrane of a nerve cell so direct muscle stimulation requires long duration impulses, between 10 ms and 150 ms instead of durations between 0.1 ms and 1 ms that are typically required for nerve cells. This has consequences for the design of the implant, in particular for the end stage and for the telemetry link, which must transfer enough energy to power this end stage. A second requirement for muscle stimulation is an electrode geometry that induces an homogenous electrical field in the muscle but affects adjacent neural tissue as little as possible. The implant we have developed meets the requirements of a special application and a very small muscle. Our experiments have shown that the task of functionally reactivating denervated muscles can be solved in principle and in the long term. We see a promising future for this type of implant, especially for drop-foot assist, for lower extremities of paraplegic patients, and for denervation in the upper extremity.

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