# Functional Electrical Stimulation (FES) of Denervated Muscles: Existing and Prospective Technological Solutions

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**Abstract**

Recent experimental and clinical work gives strong evidence that functional electrical stimulation (FES) is a powerful tool for regeneration, functional restoration and maintenance of denervated musculature, a fact that for various reasons was not recognized in the past.

On reason was the lack of associated technology that in comparison to existing FES equipment for nerve stimulation has to meet various completely different demands. Most of the few existing stimulators for denervated muscles provided by industry or published in conjunction with scientific studies are not sufficient for muscle restoration and maintenance due to their limited range of electrical parameters obviously with respect to the presently too restrictive EU regulations for stimulation devices.

In order to be effective a stimulator for activation of denervated skeletal muscles via surface electrodes requires biphasic long-duration impulses with a pulse width between 10 and 300ms and amplitudes of up to ± 100 V respectively ± 250 mA. These demands rise safety issues in the design and application of both the stimulator and the electrodes. In Vienna a sufficiently working prototype equipment was developed and clinically tested.

The alternative of an implantable stimulation system is not jet available for clinical application, but an experimental prototype system was tested in an experimental study on sheep for up to 18 months. Stimuli of similar pulse width are required, but - due to the direct electrode attachment to the muscle - with less amplitude. Specific solutions are needed in conjunction with power supply, end stage and electrode design to induce a suitable electrical field while avoiding tissue damage.

**Key words**: denervated muscle, FES, implant, mobilisation, muscle maintenance, muscle restoration, paraplegic patients, RISE, surface electrode, technology.

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Practically all established clinical FES applications are based on direct excitation of neural structures and - in case of muscle functions - indirect activation of the muscles. For reactivation of denervated and especially denervated degenerated muscles (DDM) the technical demands are completely different. Due to the absence of the neuromuscular junction and decomposition of motor units, muscular contractions can only be elicited by depolarizing the cellular membrane of each single muscle fibre.

There are few published studies that demonstrate in both animal and clinical experiments that functional reactivation of denervated muscles by FES is possible in principle and in the long-term even in case of severe degeneration [4, 8, 9]. This means that two important conditions are given: first remaining excitable structures in the DDM and second a sustained myogenetic capacity, that both improve in reaction to enhanced activity. Lomo et.al. [6] have demonstrated in a fundamental study on rats, that electrical stimulation is able to restore the electrical and electrochemical conditions of the muscle membrane from various degrees of degeneration to normal conditions not only once but repeatedly. In parallel they were able to show a similar restoration of muscle force and twitch characteristic. Carraro et al. [2] have demonstrated also in a study on rats a low but sustained residual myogenetic activity in the denervated untreated muscle and a substantial increase of this activity after severe injury of the muscle. Similar myogenetic events were observed by the same research group in paraplegic patients with denervated lower extremities that had performed an intensive FES training of their quadriceps muscles.

All those experiments give strong evidence that FES is a powerful tool for regeneration, functional restoration and maintenance of denervated musculature. The technique obviously has the potential to serve as a novel rehabilitation method for patients with muscle denervations of various origins and especially after injury of the cauda equina. To work out a firm scientific basis for the later application is the main goal of the European project RISE, "Use of electrical stimulation to restore standing in paraplegics with long-term denervated degenerated muscles".

### Excitability of the Denervated Muscle

The electrical membrane sensitivity strongly depends on the state of degeneration or recovery of the muscle cell, but in any case it is much lower than the sensitivity of a nerve cell. It requires impulse durations between 10 and 150 ms and after severe degeneration even more to elicit a depolarisation event in the muscle membrane at one location along the muscle fibre followed by formation of action potentials that travel in both directions towards the ends of the fibres. Consequently also the amplitude values are significantly higher than in nerve stimulation. The recruitment of a sufficient fibre population is depending on a homogeneously distributed electrical field more or less concentrated on the target muscle. The later condition is essential to minimize unwanted co-contractions of adjacent other muscles and excitation of neural structures in the adjacent tissue. Useful impulse shapes are biphasic rectangular or in selected cases ramp shaped impulses. The rectangular form is more efficient in recruiting muscle fibres, the ramp shape provides the important advantage of reducing the excitation of neural structures in the immediate neighbourhood of the muscle. A severe problem that inhibits the application of FES on denervated muscles lies in the current EU regulations for stimulators that limit the output energy to 300 mJ per impulse. This is by far not enough to elicit functionally usable contractions in denervated muscles via surface electrodes, unless these muscles are very small and not severely degenerated.

### A Surface Electrode Based Stimulation System for Clinical Use

During the past 15 years various clinical trials on patients with permanent complete denervation of the lower extremities were performed in Vienna. The work was carried out using non-invasive equipment with surface electrodes and different stimulator prototypes. The electrical parameters and training strategies were determined more or less by trial and error and very specific for the individual patients. The patients started the FES training between 1 and 30 years after denervation and consequently the state of degeneration differed in a wide range. Generally biphasic rectangular constant voltage (CV) impulses where used. The pulse width was varied between more than 150 ms in case of severe degeneration down to 40 ms with progress of training and muscle regeneration. In average a minimal amount of training of once 60 minutes or twice 30 minutes per day and muscle group was applied to restore and maintain the muscle function.

The study clearly showed that restoration and functional use of denervated muscles with FES is possible and muscle functions can be maintained on the long-term [4]. Up to present seven patients were able to regain active standing up using their own muscle power. Other patients have achieved various states of improvements of their muscle conditions to near normal contraction characteristic and growing but still to low muscle force for standing-up manoeuvres. The training procedures where very long-lasting, minimally 2 to 3 years till the first standing up, and had to be modified frequently, when the expected improvements where lacking. Many technical and physiological questions have remained open and call for a systematic scientific analysis [5].

The applied stimulator in its recent development state [3] (Fig. 1) is a dual-channel stimulator that is capable of delivering charge balanced biphasic or monophasic CV impulses with amplitudes of up to ± 80 V on an output load down to 300 Ω. To guarantee optimal patient safety the system is powered by rechargeable batteries, all output lines are decoupled via capacitors and patients´ access to adjust the parameters is reduced to an absolute minimum. The patient has access to up to nine pre-programmed stimulation sequences and to adjustment of the intensity in a limited amplitude range. All other parameters can only be adjusted by authorised personnel via laptop or PDA (Personal Digital Assistant) computer using an IrDa link. In addition to the rectangular impulses various alternative impulse shapes can be programmed to serve individual demands in case of incomplete or discomplete lesions. The pulse width is adjustable between 10 and 300 ms, the interpulse interval down to zero to allow optimal parameter adjustment in relation to the actual conditioning state of the muscle. The device records a compliance protocol containing date and time of use, chosen programs and intensity level. The surface electrodes are either conductive silicon-rubber types applied via a wet sponge layer or attached directly using electrode gel, or self adhesive hydro gel electrodes. The choice depends on skin condition and muscle training state respectively required electrical parameters. To minimise current density and optimise the electrical field distribution pairs of large electrodes with 200 to 250 $cm^2$ for the quadriceps muscles and 100 $cm^2$ for the hamstrings are essential. Accurate electrode application with equally distributed contact pressure and perfect electrode condition are indispensable to guarantee save operation of the system and avoid skin burn.

Actually the dual-channel stimulator is a bench version and the electrodes are attached one by one [3]. The next development step is a 4-channel belt version of the stimulator and garments with integrated electrodes and cables, both to simplify donning and doff-

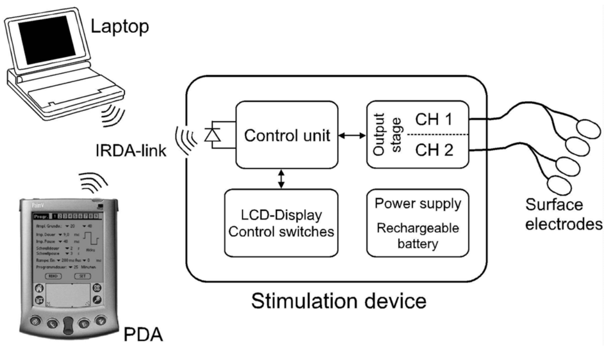


*Figure 1. Schematic diagram of the surface electrode based 2-channel stimulator for denervated musculature, details in [3].*

ing of the equipment and to make its permanent use more reliable and attractive.

## An Implantable Stimulation System for Experimental Use

An implantable system for reactivation of denervated muscles potentially offers a number of advantages. It could be much more comfortable in daily handling than a surface electrode based system, provide a much higher selectivity in activating single muscles and avoid pain in applications where sensitivity is partly or completely intact. On the other hand many specific technological problems have to be solved in comparison to the usual implants for neural stimulation that make the development of this type of implant a complex task. Again long duration impulses between 10 and 150 ms have to be delivered in contrast to 0.1 to 1 ms for nerve stimulation. Consequently the charge flow across the electrode tissue interface is by far greater making it difficult to design a biocompatible and corrosion resistant electrode that is sufficiently flexible and mechanically resistant for long-term use. Alternative solutions are also required for the electronic circuitry, especially for the power supply and output stages, that have to deliver up 1500 fold the power of nerve stimulators, or for the decoupling capacitors, that have to guarantee charge balance for up to 1500 times longer impulses. All those constraints may explain, that no implantable equipment is available at least for clinical use.

One prototype solution was designed and tested in Vienna [7] (Fig. 2) that originated from a project aiming in development of an implantable solution for chronic bilateral recurrent nerve lesions. The animal study on sheep was dedicated to development of technological means including synchronisation with respiration, stimulation and training parameters for the denervated crycoarytenoid muscles, and a long-term feasibility study focused on the muscle condition under chronic stimulation. Implanted stainless steel (316L) electrodes and biphasic ramp-shaped constant current (CC) impulses with 30 ms per phase and a frequency of 10 Hz where applied. The results were encouraging [1, 9]. Respiration synchronous stimulation could be demonstrated for periods of up to 18

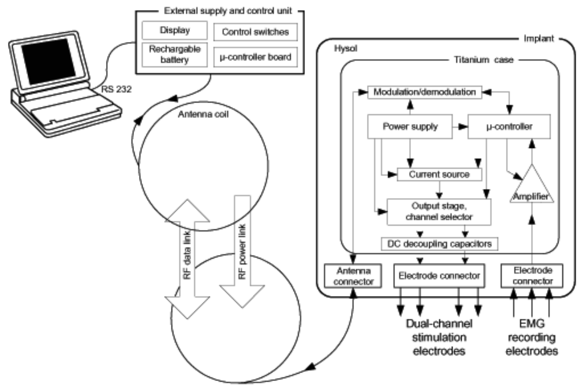


*Figure 2. Schematic diagram of the RF-powered 2-channel implant for denervated muscles, details in [7].*

months under full maintenance of the muscle function. The histological and biochemical investigations showed a transformation to a dominatingly slow type muscle with lack of atrophy and areas showing even hypertrophy, whereas now major signs of muscle damage where observed. The electrodes remained stable throughout the long observation period. The ramp-shaped impulses showed excellent selectivity in eliciting muscle contractions whilst avoiding the excitation of sensible and motor nerves in the surrounding tissue.

In conclusion the study demonstrated that it is possible to design and operate long-term stable implantable systems for FES of denervated muscles, which in addition to the specific application in the larynx may support various new therapeutic approaches.

## The EU-project RISE

Based on the above mentioned work a consortium was formed to apply for funding of the project RISE by the European Community within the 5th Framework Programme. The consortium consists of ten European partner institutions from Vienna, Liverpool, Padova, Ljubljana, Hamburg, Tuebingen and Heidelberg, and additional six subcontractors from Austria and Germany. Nine out of the sixteen are spinal cord injury centres. The proposal was favourably evaluated and the project started with November 1, 2001. The duration is four years. The work is coordinated by the corresponding author of this paper.

Within RISE a novel clinical rehabilitation method for patients suffering from long-term flaccid paraplegia (denervated degenerated muscles - DDM) with no chance of recovery of the nervous system, will be developed. It will restore their muscle fibres and mass, muscle function (tetanic contractions, weight bearing) and thus their ability to rise ('standing up') and maintain a standing posture ('standing'). Based on the results of animal experiments on rabbit and pig and initial clinical trials the associated technology will be developed and an application for modification of EU-standards is planned. It will provide European industry with a novel product. The method addresses the needs of about twenty new patients per million EU inhabitants per year.

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