How does the timing and intensity of stimulation in home-based FES (hbFES) affect the structural recovery of lower motor neurons and muscle fibres following a complete denervation injury?

Functional Electrical Stimulation (FES) • Denervation • RISE Stimulator

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Applying home-based functional electrical stimulation (hbFES) in complete lower motor neuron (LMN) denervation injuries represents a paradigm shift in neurorehabilitation. It offers clinically significant structural recovery of muscle fibres and potential neuroregenerative effects.

At Anatomical Concepts, we work with the Stimulator RISE from Schuhfried Medizintechnik GmbH (Vienna). Clients use this key tool at home to rescue muscle tissue quality and bulk, with the aim of preventing long-term complications following a denervation injury.

This article explores how the timing of application and the optimisation of stimulation parameters can impact the structural recovery of lower motor neurons and muscle fibres after a complete denervation injury.

How we got here

In my early career, I remember being instructed that the deterioration of denervated muscle following an injury to the lower motor neurons was inevitable and rapid. The belief was that not much could be done to prevent that; and certainly not by using electrical stimulation, which would probably, I was told, only result in burns.

Ludwig Boltzmann Institute for Electrostimulation and Physical Rehabilitation in Vienna. This multinational initiative demonstrated that **home-based FES (hbFES)** could reverse atrophy in permanently denervated muscles. [1]

Key outcomes from 25 patients in the study with complete conus/cauda equina lesions were as follows:-

- **35% increase** in quadriceps cross-sectional area after 2 years of hbFES.
- **1,187% improvement** in muscle force output, enabling 25% of patients to perform FES-assisted standing.
- Ultrastructural restoration of myofibrils and T-tubule systems confirmed via electron microscopy. [2]

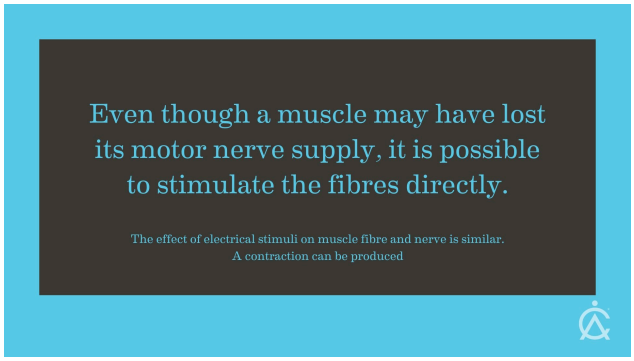
Longitudinal Muscle Biopsy Studies

Austrian teams provided the first histological evidence that hbFES induces **muscle fibre regeneration** (hyperplasia) alongside hypertrophy in chronic denervation (>2

current densities. In contrast, most stimulators designed for neuromuscular electrical stimulation (NMES) generally work with pulse widths up to 1 ms and current levels of up to 130 mA.

Mechanisms of hbFES in Denervated Muscle Recovery

hbFES circumvents LMN loss by **directly depolarising muscle fibres** through long-duration, high-amplitude pulses. For best effect, large surface area electrodes are used to reduce the current density applied to the skin and involve the most significant number of muscle fibres.



Unlike innervated muscle stimulation, which relies on intact neuromuscular junctions, denervated fibres require pulse widths typically exceeding 100 ms to overcome elevated chronaxie thresholds. These parameters induce calcium-dependent myofibrillar reorganisation, mitochondrial biogenesis, and satellite cell activation, reversing atrophy and fibrosis. Concurrently, hbFES upregulates pleiotrophin (PTN) and brain-derived neurotrophic factor (BDNF) in denervated Schwann cells, creating a pro-regenerative microenvironment. [6][7]

Temporal Factors in hbFES Efficacy

Acute/Subacute Phase (0-12 Months Post-Denervation)

Starting the application of electrical stimulation early is best. Early initiation within 6 months post-injury capitalises on residual Schwann cell neurotrophic capacity. The EU RISE trial demonstrated that hbFES started ≤ 1-year post-SCI achieved **35% quadriceps cross-sectional area (CSA) increases within 24 months**, with the ultrastructural restoration of T-tubules and sarcoplasmic reticulum. Animal models

denervation duration. Simply put, if treatment starts late, it takes much longer to produce noticeable results.

Patients starting hbFES 3-5 years post-injury required 12-24 months to achieve tetanic contractions, with hamstring CSA increasing only 15% versus 75% quadriceps growth.

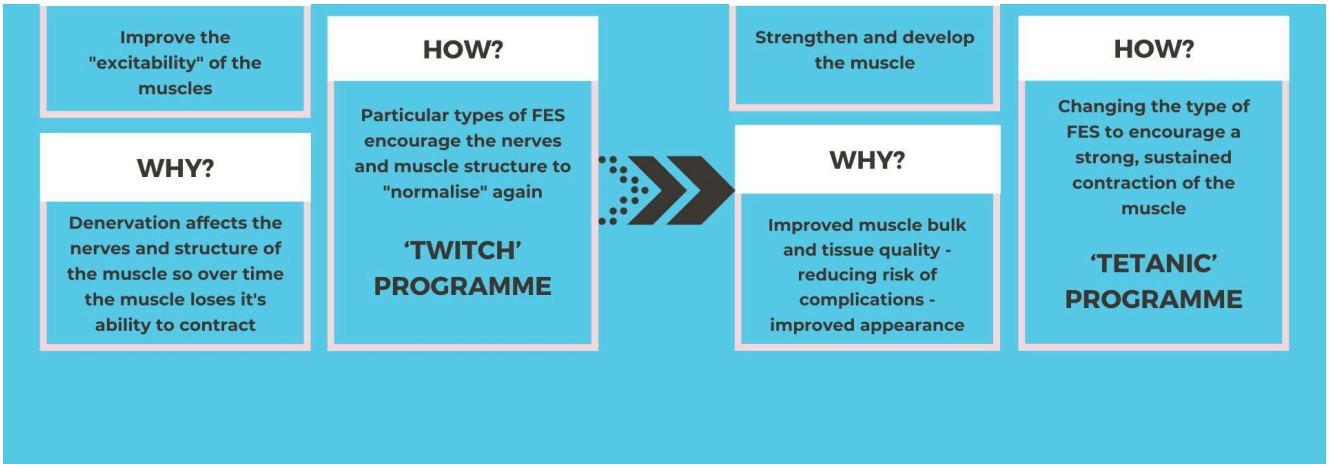
Beyond 5 years, fat infiltration can exceed 50%, necessitating adjunct therapies like testosterone to potentiate hbFES effects. Nevertheless, chronic cases still show epidermal thickening (27% increase) and capillary network restoration after 2 years of daily stimulation. [8]

Intensity Modulation and Parameter Optimisation

Pulse Characteristics

The pulse waveform used as first choice is rectangular and biphasic in form and current controlled. Pulse are delivered in modulated bursts so that periods of muscle contraction are followed by a period of muscle relaxation. The pulse widths, current amplitude and burst intervals are adjustable. In outline, these are typical pulse characteristics. We will look at application protocols in a section below.

- **Width:** 100-200 ms pulses (vs. 0.2-0.5 ms for innervated muscle) directly activate sarcolemmal L-type calcium channels. As excitability improves, a gradual reduction to 40-50 ms occurs. [9][10]
- **Amplitude:** 200-250 mA surface currents overcome subcutaneous fat resistance, achieving current densities >15 mA/cm² for deep fibre recruitment.
- **Frequency**: 20-30 Hz induces tetanic fusion without fatigue, versus >1 and ≤ 10 Hz during early twitch-phase training.



Session Dynamics

Training requires a significant time commitment, especially in the early stages of hbFES. We always discuss this factor with potential clients.

Daily 30-60 minute sessions (5 days/week) maintain excitation-contraction coupling proteins. The Vienna Protocol escalates stimulation from single twitches (first 3 months) to loaded contractions (≥ 6 months), increasing ankle weights by 0.5 kg weekly as strength improves[11]. MRI T2 mapping shows this progression correlates with 24% CSA gains/year in early adopters versus 7% in chronic groups .

Structural Reorganization of Muscle Fibers

Myofibrillar Architecture

Post-hbFES biopsies reveal myofibril density increases from 45% to 82% of normal, with Z-disc realignment and troponin-T redistribution. Electron microscopy confirms triadic structure restoration, enabling calcium-induced contraction. These changes underpin the 1187% force output improvement observed in RISE participants.

Co-Activation Phenomena

overlapping motor units.

- **Mechanical Coupling:** Quadriceps contractions stretch adjacent muscles, activating stretch-sensitive ion channels.
- **Trophic Cross-Talk**: IGF-1 released during contraction diffuses to neighboring tissues. [12]

Large wet sponge and carbon rubber electrodes cover much of the quadriceps to give large field spread

Lower Motor Neuron Plasticity

While hbFES primarily targets muscle, emerging evidence suggests indirect LMN effects:

- Neurotrophic Signaling: Stimulated muscles secrete GDNF and CNTF, rescuing 30% of axotomized motor neurons in rat models.
- Axonal Guidance: FES-induced IL-6 gradients guide regenerating axons toward reinnervation sites, as shown by tracer studies in continuous pelvic nerve stimulation protocols.
- Synaptic Reconnection: In complete conus medullaris injuries, 24-month hbFES enabled partial NMJ reformation, with electromyography showing nascent motor unit potentials. [13]

Clinical Protocols and Future Directions

Staged Application Guidelines

As an example, the application of hbFES might progress as follows. Initially, the aim is to rebuild the structure of the tissue via twitch phase training. As soon as possible, tetanic contractions should be aimed for with functional training representing the

Years 1- 2: Functional training (e.g., stand-assist) using 30 Hz bursts.

Adjunct Therapies

Testosterone: Augments hbFES-induced hypertrophy by 37% via androgen receptor-mediated mTOR activation. [8]

Stem Cells: IPSC-derived motor neurons transplanted post-hbFES show 3x higher engraftment rates in rodent models.

Conclusion

Sometimes, the general public thinks that progress in medical science is often rapid. I wish it were true. The French physician Duchenne, after all, worked with electrical stimulation in the 1870's with paraplegics. He used electrical stimulation as a therapeutic intervention and a diagnostic approach. You would think that progress could have been faster. Even 50 years ago I was being discouraged from applying electrical stimulation to denervated muscle.

hbFES has transformed denervation management from palliative care to active recovery. Clients can rescue the muscle bulk and tissue quality by using products such as the RISE Stimulator.

Timing dictates molecular responsiveness—early intervention leverages intact Schwann cell networks, while chronic applications require intensity escalation.

Although early intervention after an injury is always best, even those many years post-injury should be allowed to try as the risks are low and the potential benefits are high.

The process involves a commitment to 30 minutes of application per muscle group 5 days per week, starting with a low-frequency, long pulse width protocol that seems to make the muscle twitch. This normalises muscle tissue, making it more excitable. As soon as a tetanic contraction can be achieved, this is introduced to build strength. The

a strong tritch or tetanic contraction as necessary within the protocol.

With 75% of patients achieving standing capacity after 2 years, these protocols redefine neurotrauma rehabilitation ceilings. Future integration with neuromodulation and regenerative therapies promises further LMN repair, moving beyond muscle rescue to proper neurological restoration.

Literature

[1] Mödlin M, Forstner C, Hofer C, Mayr W, Richter W, Carraro U, Protasi F, Kern H. Electrical stimulation of denervated muscles: first results of a clinical study. Artif Organs. 2005 Mar;29(3):203-6. doi: 10.1111/j.1525-1594.2005.29035.x. PMID: 15725217. https://pubmed.ncbi.nlm.nih.gov/15725217/

[2] Kern H, Carraro U, Adami N, et al. Home-Based Functional Electrical Stimulation Rescues Permanently Denervated Muscles in Paraplegic Patients With Complete Lower Motor Neuron Lesion. Neurorehabilitation and Neural Repair. 2010;24(8):709-721. doi:10.1177/1545968310366129 https://journals.sagepub.com/doi/abs/10.1177/1545968310366129

[3] Kern H, Carraro U. Home-Based Functional Electrical Stimulation for Long-Term Denervated Human Muscle: History, Basics, Results and Perspectives of the Vienna Rehabilitation Strategy. Eur J Transl Myol. 2014 Mar 27;24(1):3296. doi: 10.4081/ejtm.2014.3296. PMID: 26913127; PMCID: PMC4749003.

[4] Kern Helmut , Barberi Laura , Löfler Stefan , Sbardella Simona , Burggraf Samantha , Fruhmann Hannah , Carraro Ugo , Mosole Simone , Sarabon Nejc , Vogelauer Michael , Mayr Winfried , Krenn Matthias , Cvecka Jan , Romanello Vanina , Pietrangelo Laura , Protasi Feliciano , Sandri Marco , Zampieri Sandra , Musaro Antonio. Electrical Stimulation Counteracts Muscle Decline in Seniors. Frontiers in Aging Neuroscience VOL 6, 2014. DOI=10.3389/fnagi.2014.00189. ISSN=1663-4365 https://www.frontiersin.org/journals/agingneuroscience/articles/10.3389/fnagi.2014.00189

neurons. Proc Natl Acad Sci U S A. 2007 Mar 13;104(11):4664-9. doi: 10.1073/pnas.0603243104. Epub 2007 Mar 5. PMID: 17360581; PMCID: PMC1838658.

[7] Gordon T. The role of neurotrophic factors in nerve regeneration. Neurosurg Focus. 2009 Feb;26(2):E3. doi: 10.3171/FOC.2009.26.2.E3. PMID: 19228105.

[8] Gorgey AS, Khalil RE, Alrubaye M, et al Testosterone and long pulse width stimulation (TLPS) for denervated muscles after spinal cord injury: a study protocol of randomised clinical trial. BMJ Open 2022;**12:**e064748. doi: 10.1136/bmjopen-2022-064748.
https://bmjopen.bmj.com/content/12/10/e064748

[9] Chandrasekaran S, Davis J, Bersch I, Goldberg G, Gorgey AS. Electrical stimulation and denervated muscles after spinal cord injury. Neural Regen Res. 2020 Aug;15(8):1397-1407. doi: 10.4103/1673-5374.274326. PMID: 31997798; PMCID: PMC7059583.

[10] Bersch, I and Fridén, J. Upper and lower motor neuron lesions in tetraplegia: implications for surgical nerve transfer to restore hand function. Journal of Applied Physiology 2020 129:5, 1214-1219
https://journals.physiology.org/doi/abs/10.1152/japplphysiol.00529.2020

[11] Kern H, Hofer C, Strohhofer M, Mayr W, Richter W, Stöhr H. Standing up with denervated muscles in humans using functional electrical stimulation. Artif Organs. 1999 May;23(5):447-52. doi: 10.1046/j.1525-1594.1999.06376.x. PMID: 10378940.
https://pubmed.ncbi.nlm.nih.gov/10378940/

[12] Bazarek SF, Krenn MJ, Shah SB, Mandeville RM, Brown JM. Novel Technologies to Address the Lower Motor Neuron Injury and Augment Reconstruction in Spinal Cord Injury. *Cells*. 2024; 13(14):1231. https://doi.org/10.3390/cells13141231
https://www.mdpi.com/2073-4409/13/14/1231

[13] Possover, M., Forman, A. Recovery of supraspinal control of leg movement in a chronic complete flaccid paraplegic man after continuous low-frequency pelvic nerve

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