Editorial

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The Ejtm Specials "*The long-term denervated muscle*"

The first Issue of the Journal of Translational Myology/Basic Applied Myology Vol. 24 (1), 2014 belongs to the *Ejtm Specials on* "*The long-term denervated muscle".* It is dedicated to pioneers and followers of biology, physiology, pathology, therapy and rehabilitation of the permanent denervated muscle, in particular to the physical approaches for the diagnosis and treatments in those cases in which the hope for reinnervation is very poor or lost. Although some study may be found in the literature of the Nineteenth Century,[1] it was in the 1940s that the study of events occurring in denervated muscle fibers emerged as a topic distinct from the more clinical relevant studies of nerve regeneration and muscle reinnervation.[2-4] During the following twenty years, the reports increased in numbers year after year. Finally in 1962 the book edited by Ernest Gutmann summarized previous knowledge from biology to rehabilitation by electrical stimulation and opened the modern era of "*The Denervated Muscle*".[5]

Three pioneers of the modern studies are contributing to the Ejtm Specials and/or lectured at the 2014Spring PaduaMuscleDays: 1. Bruce M. Carlson, co-author of several papers with Ernest Gutmann on regeneration of transplanted muscles, opens the Ejtm Specials with the review "*The biology of long-term denervated skeletal muscle*".[6] He offers to researches the basic concepts and the results to understand problems and actual or future solutions that continue to nurture Translational Myology; 2. Terje Lømo was the first in 1972 to electrically stimulate denervated rat muscle to test the hypothesis that induced activity modifies muscle properties and indeed he demonstrated that it suppress one of the hallmarks of muscle fiber denervation, i.e., ACh sensitivity spreading from the synaptic area to the whole sarcolemma.[7] Prior to 1972, it was believed that neurotrophic factors, not related to excitatory impulse transmission, played a role in spontaneous fibrillation, another functional marker of muscle denervation, whose appearance is inversely related to the length of the degenerating nerve stump. Lømo and co-workers demonstrated, instead, that chronic electrical stimulation of denervated rat muscles caused ACh-sensitivity to disappear from denervated muscles already ACh supersensitive. Further, he showed that the passive electrical properties and the contractile characteristics that distinguish fast and slow fiber types are under the control of the patterns of activity.[8,9] In a report at the First Abano Terme Meeting on Rehabilitation (1985), here reprinted,[10] Lømo et al. defended his hypothesis against the criticisms of authoritative neuroscientists. In his Commentary,[11] he states now "*While reports favoring the existence of neurotrophic factors were numerous before 2000, they have now essentially disappeared from the literature, including original research papers, textbooks and handbooks, which suggest that the hypothesis is no longer arguable. Thus, the results that I presented in our paper in 1985 seem to have held up rather well*". Terje Lømo is much more recognized for an important discovery, namely long term potentiation, the phenomenon that brief activation of synapses in the brain can lead to very long-lasting increases in their efficiency of transmission, a property now generally seen as essential for the ability to learn and remember.[12]

We hope that the Ejtm Specials on long term denervated muscle, rising again the interest of scientists (Terje Lømo, included) and clinicians on rehabilitation of denervated muscle may add to his merits the pioneering evidence that activity, anyhow imposed, strongly modulate trophism and characteristics of denervated muscles; 3. Clara Franzini-Armstrong lectured at the 2014Spring PaduaMuscleDays on "*Structure-function relationships in skeletal muscles. Lessons from ultrastructure*".[13] She remembered to us that "*Muscle fibers have a stereotyped organization of contractile myofibrils and membrane systems best defined by their ultrastructure. The sliding filament model (in 1945) established currently accepted principles of most cell motility"*. Her many contributions to the study of the muscle membrane systems and ability to attract young brilliant scientists to electron microscopy are well known and demonstrated also by two speakers of the 2014Spring PaduaMuscleDays, Feliciano Protasi and Simona Boncompagni of Chieti University.[14,15] They have been and are strongly contributing to the success of h-b FES for permanently denervated muscles.[16] We would like to add to the Clara's many merits, the pioneering electron microscopy study in the field of muscle denervation: her 1963 article *"An electron microscope study of denervation atrophy in red and white skeletal muscle fibers".*[17]

Standing on the shoulders of these giants, we are contributing to the Ejtm Specials three articles that describe history and results of an application of the concepts and discoveries of Bruce M. Carlson, Terje Lømo and Clara Franzini-Armstrong, namely the Vienna Rehabilitation Strategy by home-based Functional Electrical Stimulation (h-b FES) for permanently denervated muscles (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"*.[18] Analytical tools and devices, designed and implemented to diagnose, treat and follow up the *Conus Cauda* complete syndrome that paralyze large muscles of human legs are also described.[18] Among the new analytical tools, Gargiulo P, Helgason T, Ramon C, Jónsson H jr, Carraro U describes "*CT and MRI assessment and characterization using segmentation and 3D modeling techniques: applications to muscle, bone and brain*".[19] Recently, a multi-disciplinary team of the Interdepartmental Research Center of Myology of the University of Padua is applying the Vienna principles to the apparently easier cases of peripheral incomplete denervation of limbs. To support the project, denervated muscle fibrillation analyses are revisited in the article of Pond A, Marcante A, Zanato R, Martino L, Stramare R, Vindigni V, Zampieri S, Kern H, Masiero S, Piccione F "*History, mechanisms and clinical value of fibrillation analyses in muscle denervation and reinnervation by Single Fiber Electromiography and Dynamic Echomyography*".[20] Further, in collaboration with his international partners, Dr. Kern is now extending the benefits of h-b FES to those subjects, which for different reasons suffer the consequences of muscle weakness, from the mild but unrelenting process of aging,[21-24] to the devastating fast progression of muscle cachexia in cancer patients.[25,26]

The collection of Abstracts of the 2014Spring PaduaMuscleDays, the majority concerning neuromodulation of long-term denervated muscles, closes the first of issues of the *Ejtm Specials on the long-term denervated muscle*.[27] The Helmut Kern's Habilitation Thesis (1995, in German) opens the Ejtm-BAM volume 24(2), 2014.[28]

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