2025Pdm3 Program and Abstracts

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Padua Days on Muscle and Mobility Medicine, March 25-29, 2025, Hotel Petrarca, Euganean Thermae, Italy: Program and Abstracts

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Abstract

Medium-sized scientific conferences held in hotels large enough to accommodate all participants increase opportunities for constructive discussion during breaks, and for evenings that bring together young and senior experts of basic sciences and clinical specialties. Time for group discussions offer opportunities for new collaborations and for jobs for young researchers. Since 1991 the Padova Muscle Days have offered collaborative opportunities that have matured into innovative multidisciplinary results to the point that it came naturally for us to underline it with a neologism now included in the title of the 2025 event: "Mobility Medicine". It is a discipline which developed naturally when we brought together fragmented areas of knowledge into one meeting. The Padua Days on Muscle and Mobility Medicine 2025 (2025Pdm3) will be hosted at the Hotel Petrarca, Euganean Thermae (Padua, Italy) from 25 to 29 March 2025. The list of unique sessions within the included program and the following Collection of Abstracts testify that it is possible to organize valid countermeasures to the inevitable tendencies towards hyper-specialization that the explosive increase in scientific progress brings. The European Journal of Translational Myology and Mobility Medicine (Ejtm3) will accept typescripts on results presented at the 2025Pdm3. Furthermore, an additional option for publication of full original Articles or Reviews is the Special "New Trends in Musculoskeletal Imaging" of the MDPI Journal Diagnostics, because diagnosis is essential to manage and follow-up neuro-metabolic- muscular- disorder and the decay of performances in aging. We hope that many will share our dreams and we make them come true at the 2025 Pdm3 Conference.

Key Words: Padua Days on Muscle and Mobility Medicine, 2025Pdm3; European Journal of Translational Myology; Ejtm3 PAGEpress Italy; MDPI (Basel) Diagnostics.

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The Padova Muscle Days (PMDs), an international meeting on skeletal muscle, began in 1985 to provide advice on Translational Myology. The interest has always been in translating the results of novel basic research into clinical trials. Indeed, function as mass of striated skeletal muscles are influenced by, and influence, central and peripheral neural disorders, diseases of the heart, lung, liver, metabolism, endocrine tissues, together with lifestyle and aging, not to say cancer. Over the course of the years, the Padova Muscle Days have offered opportunities, which have matured into innovative multidisciplinary results to the point that it became natural to underline it with a neologism now included in the title of these conferences, namely "Mobility Medicine." Mobility Medicine is a new monicker used to explicit the call to reunite knowledge currently dispersed in sub-subspecialties. The program of the five days of the Padua Days on Muscle and Mobility Medicine to be held 25-29 March 2025 (2025Pdm3) will be hosted at the Hotel Petrarca in Euganean Thermae, Padua, Italy. The program testifies that it is possible to organize valid countermeasures to the inevitable tendencies towards hyper specialization that the explosive increase in scientific progress has brought with it. Furthermore, the European Journal of Translational Myology and Mobility Medicine (Figures 1 and 2) will accept typescripts of results presented at the 2025Pdm3, as Review, Original Articles and Ejtm3 Communications. Meantime a Special Section of the MDPI (Basel) Journal *Diagnostics* will accept submissions because diagnosis is a prerequisite of prevention, management and follow-up not only of neuro- and metabolic muscular disorders, but also of the physiological unavoidable decay of the older adults, and the pathological cachexia of cancer. The Program includes oral presentations (in-person and on-line) of scientists and clinicians from Argentina, Austria, Brazil, Bulgaria, Canada, Egypt, France, Germany, Iceland, Ireland, Italy, Russia, Slovenia, Sweden, Switzerland, UK and USA. The Collection of Abstracts is included after the Program.

Here is a sole example of a topic which will be addressed at the conference: the challenges associated with physical inactivity in the elderly. Often attributed to factors such as age and concurrent medical conditions, they have far-reaching implications for well-being and independence. The lack of physical activity not only curtails autonomy, but increases the risk of extended hospitalization, leading to issues such as neuromuscular weakening, functional limitations, and substantial healthcare expenses.[1–4] It should be highlighted that physical exercise, even if performed in bed (home Full- Body In-Bed Gym) represents a highly promising option. This approach can contribute to global health promotion by enhancing cardiovascular fitness, muscle strength, flexibility, and mental well-being of old people.[5] It is a preventive, low-risk, time-saving and cost-effective strategy that can be tailored to individual needs and preferences. Indeed, community-based exercise initiatives can face various challenges, including financial constraints, difficulties in accessibility, time limitations, and a shortage of specialized guidance.[6,7] Hence, adoption of home-based physical exercise routines, is a cost-efficient alternative.

In conclusion, the 2025Pdm3 will be interesting and successful like all previous Padova Days on Muscle and Mobility Medicine.[8-15]

List of acronyms

Ejtm3 - European Journal of Translational Myology and Mobility Medicine

Pdm3 - Padua Days on Muscle and Mobility Medicine
PMD – Padua Muscle Days

Acknowledgments

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Conflict of Interest

The authors disclose no conflicts of research interest.

Ethical Publication Statement

We confirm that we have read the Journal's position

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on issues involved in ethical publication and affirm that this report is consistent with those guidelines. Specifically, generative artificial intelligence has never been used in designing and writing the typescript.

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2025(Pdm3) Padua Days on Muscle and Mobility Medicine
March 25-29, 2025 – Euganean Thermae, Padua (Italy)

Hotel Petrarca, Piazza Roma 23, Montegrotto Terme (Padua) 35122 Italy

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REGISTRATION FEES: € 300 - One-Day REGISTRATION FEES: € 150 - On-Line REGISTRATION FEES: € 100 - Young Attendees: Exempt

Send Registration and Accommodation Forms to: ugo.carraro@unipd.it and petrarca@hotelpetrarca.it

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TUESDAY March 25, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

09:00 am Opening: Antonio Paoli, Greetings from Padova University

09:10 am Lecture of Jonathan Jarvis, University of Liverpool, UK: Activity, the final common path to adaptive change in muscle

09:50 am *Session I: FES for atrophying and reinnervating muscles Ines Bersch, Winfried Mayr, Chairs*

09:50 am Electrical stimulation technology, a versatile and effective tool for support of restoring and maintaining neuromuscular integrity, Winfried Mayr, Vienna Austria

10:10 am Ultrasound evidence of deceleration of denervated facial muscles atrophy through functional electrical stimulation: Johannes Krauss, Gerd Fabian Volk, et al., Department of Otorhinolaryngology, Jena University Hospital, Jena, Germany

10:30 am Electrostimulation in facial nerve palsy is safe and helpful: Giovanni Pegoraro, Fondazione Borghi Korian Brebbia (VA), Italy

10:45 am Open Coffee

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TUESDAY March 25, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

10:50 am ***Session II: FES for permanent denervated muscles, Ashraf Gorgey, Ugo Carraro, Chairs***

10:50 am Interplay between Muscle and Bone following Electrical Stimulation Exercises in Persons with SCI: Ashraf Gorgey, Richmond VA Medical Center, Richmond, VA, USA

11:20 am Tissue Composition Changes in Long-Term Denervated Muscles - Beneficial Effects of Long-Pulse Electrical Stimulation: Ines Bersch-Porada, et al., Notwill FES Center, Switzerland

11:40 am Effectiveness of FES x DDM after twenty years of permanent denervation and degeneration of human muscle: ultrasound evidence of thigh muscle contraction by surface electrical stimulation after ten years of interruption of FES x DDM, Daniele Coraci et al., Rehabilitation Unit of the Department of Neuroscience, University Padua General Hospital, Italy

12:00 am ***Session III: MED-EL Workshop on Electromedicals, Alejandro Honeyands Marti, Leonardo Boccuni, Chairs***

12:00 am Welcome and Introduction to the Med-El Workshop on Electrical Stimulation Solutions, Alejandro Honeyands Marti, Med-El Spain

12:10 am Strategies to optimize the integration of therapeutic exercise and peripheral electrical nerve stimulation: a clinical perspective, Leonardo Boccuni, Scientific Institute, IRCCS E. Medea, Conegliano, Italy

12:30 am The phenomenon of lesions of the upper and lower motoneuron in in-and extrinsic muscles of the upper limb in persons with tetraplegia – Development of a stimulation protocol to enhance functionality, Ines Bersch, Notwill FES Center, Switzerland

12:50 am Selective surface stimulation therapy for facial nerve paralysis Gerd Fabian Volk, Johannes Krauss, et al., Department of Otorhinolaryngology, Jena University Hospital, Jena, Germany

01:10 pm MED-EL Working-Lunch in the Conference Hall Paradise

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TUESDAY March 25, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

02:30 pm ***Session IV: Exercise and fasting in prevention and managements of mobility and metabolic disorders, Stephen Anton, Maria Chiara Maccarone, Chairs***

02:30 pm **Disentangling the Effects of Time Restricted Eating, Calorie Restriction and Exercise on Metabolic Health, Stephen Anton, et al., College of Medicine, University of Florida, Gainesville, FL USA**

03:00 pm **Fasting, exercise and skeletal muscle, Antonio Paoli, Department of Biomedical Sciences, University of Padova, Italy**

03:30 pm **Full-Body In-Bed Gym advancements for elderly subjects (30min), Maria Chiara Maccarone et al., Department of Neuroscience, Rehabilitation Unit, Padua University, Italy**

04:00 pm Open Coffee

04:05 pm ***Session V: Maintaining compliance in rehabilitation, Richard L. Lieber, Jan Fridén, Chairs***

04:05 pm **Lecture of Jan Fridén, University of Gothenburg, Gothenburg, Sweden: Restoring upper extremity motor function in tetraplegia using muscle and nerve transfers**

04:45 pm **Differential lower motoneuron damage patterns of potential donor and recipient nerves for upper extremity nerve transfers in tetraplegia, Ines Bersch-Porada et al., Notwill FES Center, Switzerland**

05:00 pm **Specific Tension of Human Muscle - Direct and Indirect Approaches Richard L. Lieber, Northwestern University, Chicago, IL, USA**

05:30 pm **Muscle-muscle cross-talk during unilateral electrical/mechanical stimulation, Lars Larsson, Department of Clinical Sciences, SLU, Uppsala, Sweden**

06:00 pm **Mechanisms of action of hyperbaric oxygen therapy, Gerardo Bosco, University of Padua, Italy**

06:30 pm **Transient hyperoxia after exercise-until-exhaustion to mitigate aging muscle decay: a new mechanism for training addiction over time? Ugo Carraro, University of Padua, Italy**

06:45 pm **Conference Hall Paradise: A glass of Prosecco before dinner: A well-known compliance (addiction) mechanism**

07:30 pm Dinner

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WEDNESDAY March 26, 2025 Villa Pollini, Luvigliano, Euganean Hills (Padua) Italy

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08:30 AM Complimentary Bus from Hotel Petrarca to Villa Pollini, Luvigliano di Torreglia (Padua) Italy

09:00 am	***Session VI: Pathogenesis, regeneration and therapy in sarcomeric muscle diseases, H Lee Sweeney, Daniela Tavian****, Chairs*
09:00 am	**Lecture of H. Lee Sweeney, University of Florida, Gainesville, FL, USA, New insights leading to improved designs of micro-dystrophins for use in AAV vectors.**
09:40 am	**Proteomic profiling of the dystrophin complexome in skeletal muscle, Kay Ohlendieck, Maynooth University, National University of Ireland**
10:00 am	**Lipotoxicity and lipophagy in NLSDM: mechanisms and treatments, Sara Missaglia, Daniela Tavian, Catholic University of the Sacred Heart, Milan, Italy**
10:20 am	**Pharmacological Treatment through HiPSC-based Drug Repurposing for ultrarare congenital myopathies, Edoardo Malfatti, Paris Est University, Creteil, France**
10:40 am	**Remodeling of neuromuscular junction in dystrophic sarcomeric muscles, Gabriele Siciliano, University of Pisa, Italy**
10.55 am	**Development of a 3D muscle tissue model of Pompe disease, Francesca Torri et al., University of Pisa, Italy**
11:10 am	Coffee break
11:20 am	**Multifactorial Systemic factors affecting spinal muscular atrophy patients' health, Piera Smeriglio, Sorbonne Université, INSERM, Myology Institute, Paris, France**
11:40 am	**Reversion of RNA toxicity and muscle dysfunction in Myotonic Dystrophy, Denis Furling, Sorbonne Université, INSERM, Myology Institute, Paris, France**
12:00 am	**Effects of age and sex in human muscle secretome, Barbara Crisol, et al., Sorbonne Université, INSERM, Myology Institute, Paris, France**
12:20 am	**Transcriptomic characterization of Type II SMA muscle to understand the variability in phenotypes and treatment response, Fiorella Grandi, Sorbonne Université, INSERM, Myology Institute, Paris, France**
12:40 am	**Cell specific loss of MBNL: implication for Myotonic Dystrophy skeletal muscle homeostasis, Frédérique Rau, Sorbonne Université, INSERM, Myology Institute, Paris, France**
13:00.pm	Standing Lunch

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WEDNESDAY March 26, 2025 Villa Pollini, Luvigliano, Euganean Hills (Padua) Italy

02:00 pm ***Session VII: Skeletal muscle adaptations to exercise and disuse, David Hood, Anna Picca, Christiaan Leeuwenburgh, Chairs***

02:00 pm **Introductory words (by Zoom): Christiaan Leeuwenburgh, Florida University, US**

02:10 pm **Role of the lysosome in maintaining muscle health across the lifespan, David Hood, Toronto, Canada**

02:40 pm **The role of AMPK in the neuromuscular system, Vladimir Ljubicic (Hamilton, Canada)**

03:00 pm **The importance of Ca^{2+} signalling in skeletal muscle adaptations to exercise, Nicolas Place (Lausanne, Switzerland)**

03:20 pm **Molecular mechanisms of muscle adaptations: role of PGC-1a, Christoph Handschin (Basel, Switzerland)**

03:40 pm **Mitochondria-derived vesicles in physical frailty and sarcopenia, Anna Picca, Department of Medicine and Surgery, LUM University, Italy**

04:00 pm **Testosterone depletion and intracellular calcium in skeletal muscle, Agnese De Mario et al., Department of Biomedical Sciences, University of Padua, Italy**

04:20 pm Coffee Break

04:30 pm ***Session VIII: Managements of cancer cachexia, Sandra Zampieri, Dario Coletti, Chairs***

04:30 pm **Effects of exercise and chemotherapy in cancer cachexia, James Carson, Huffines Institute for Sports Medicine & Human Performance, Texas A&M University, USA**

05:00 pm **(ZOOM) Oxytocin treatment reduces cancer cachexia in a pre-clinical model, Dario Coletti, Sapienza University, Rome, Italy**

05:00 pm **RAGE activity at myofiber level sustains cancer cachexia, Guglielmo Sorci, University of Perugia, Italy**

05:40 pm **(ZOOM) Silencing tumor-muscle crosstalk, Marilia Seelander, University of Sao Paulo, Brazil**

06:00 pm **Impact of sarcopenic myosteatosis on patients with esophagogastric cancer (25min), Elisa Sefora Pierobon, DiSCOG,University of Padua, Italy**

06:20 pm **Lecture of Massimo Ganassi, Involvement of Satellite cells in the pathogenesis of Neuromuscular disorders, Molecular Biophysics, King's College London *and* Genetic Therapy Accelerator Centre, University College London, UK**

07:10 pm Complimentary Bus from Villa Pollini, Luvigliano to Hotel Petrarca, Montegrotto Terme

07:30 pm Dinner

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THURSDAY March 27, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

09:00 am *Session IX: Neuromuscular plasticity to disuse and ageing,*

Elena Monti, Marco Narici, Chairs

09:00 am Morphological and Functional Instability of the NMJ with Chronic Inactivity in Humans, Marco Narici, Department of Biomedical Sciences, University of Padova, Italy

09:30 am Reduction of daily steps alters whole body and muscle oxidative metabolisms without affecting mitochondrial dynamics and function, Roberto Bottinelli, Pavia University, Italy

10:00 am Oxidative Metabolism and Mitochondrial Function: Adaptations to Disuse in Humans, Bruno Grassi, University of Udine, Italy

10.30 am Human Motor Unit Remodelling with Chronic Inactivity, Giuseppe De Vito, Department of Biomedical Sciences, University of Padova, Italy

11:00 am Open Coffee

11.00 am Circulating Factors Associated with Extremes of Physical Function in Octogenarians, Russell Hepple, Physical Therapy and Muscle Biology, University of Florida, USA

11:30 am A transcriptomic and spatial proteomic atlas of human aging and sarcopenia, Elena Monti, Department of Microbiology and Immunology, Stanford University (CA), USA

12.00 am Muscle Gene Expression and Physiological Adaptations to Overloading Following Disuse in Humans, Martino Franchi, Department of Biomedical Sciences, Padova University, Italy

12:30 a.am Lunch

02:00 pm *Session X_a: Exercise and exerkines, Elisabhet Barton, Bert Blaauw, Chairs*

02:00 pm Adaptations of the Extracellular Matrix to Overloading in Children with Cerebral Palsy, Richard Lieber, Northwestern University, Chicago, IL, USA

02:30 pm Loss of Calpain 3 perturbs junctional sarcoplasmic reticulum protein stability at rest and following exercise, Elisabeth Barton, Myology Institute; University of Florida, Gainesville, Florida, USA

03:00 pm Over-Expression of the ERG1A Potassium Channel in C2C12 Myotubes Modulates Sodium Current Amplitude, but not Nav1.4 Gene Expression (25min), Amber L. Pond, Anatomy, Southern Illinois University School of Medicine, Carbondale, IL., USA

03.30 pm Nerve Activity Inhibits mTORC1-dependent Protein Synthesis in Skeletal Muscle, Bert Blaaw, et al. Department of Biomedical Sciences, University of Padova, Italy

04:00 pm Reduced ATP turnover during hibernation in relaxed skeletal muscle of brown bear, Leonardo Nogara, Department of Biomedical Sciences, University of Padova, Italy

04:30 pm Open Coffee

04:30 pm Exercise-driven remodeling of Mitochondria and Sarcotubular System:a muscle strategy to improve function and resistance to fatigue, Feliciano Protasi, Chieti University, Italy

05:00 pm Extracellular matrix alteration and force transmission in older humans: A finite element analysis, Lorenzo Marcucci, DBS, University of Padova, Italy

05:20 pm How does the acute response to exercise depend on prior activity? Jack Edmondson, University of Liverpool, UK

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THURSDAY March 27, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

05:40 pm *Session X_b: Exercise and exerkines, Daniela Tavian, Bert Blaauw, Chairs*

05:40 pm Plasma and Salivary Irisin Response to Resistance Training: A Comparative Study, Luigi Marano et al., University Cattolica-Milan, Italy

06:00 pm Effects of superimposed electromyostimulation during cycling on plasma irisin levels, Ester Tommasini et al., Università Cattolica, Milan, Italy

06:20 pm The effects of pedaling exercise with superimposed adaptive functional electrical stimulation (AFESK) on the physiological and perceptual responses to exercise and performance in healthy humans: a training study, Andrea Bosio et al., MAPEI Sport, Olgiate Olona, Varese, Italy

06:40 pm Improved Irisin and Mental Well-being in Breast Cancer Survivors Following 8 Weeks of Aerobic Exercise, Denise Vagnini et al., Università Cattolica-Milan, Italy

07:00 pm Increased serum levels of adiponectin upon a single bout of exhaustive exercise in amateur athletes, Martegani Eleonora, Università Cattolica-Milan, Italy

07:00 pm Characterization of a knock-in mouse model carrying a human mutation (D44N/+ in Calsequestrin-1) associated to Tubular Aggregate Myopathy. Laura Pietrangelo et al., Chieti/Pescara University, Italy

07:30 pm Dinner

FRIDAY March 28, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

09:00 am *Session XI Hyaluronans, glycosylated proteins and fibrosis in mobility disorders, Elena Barbieri, Giovanni Abatangelo, Chairs*

09:00 am Hyaluronans and Glycosylated Proteins in Mobility Medicine Elena Barbieri, University of Urbino, Italy

09:20 am Intra-articular injections with Carboxymethyl-Chitosan in patients affected by knee osteoarthritis nonresponders to hyaluronic acid: a pilot study, Nicola Manocchio et al., Physical and Rehabilitation Medicine, Clinical Sciences and Translational Medicine Department, University of Rome Tor Vergata, Italy

09:40 am Conservative treatment of Achilles tendinopathy with infiltrative hyaluronans, Piero Sestili, University of Urbino, Italy

10:00 am Blue turmeric: a novel food targeting inflammatory molecular networks, Michela Battistelli, University of Urbino, Italy

10:15 am A Novel Fascial Mapping of Muscle Spindles Distribution: Insights from Murine Model Study, YunFeng Sun, Carla Stecco, Department of Neuroscience, Padua University, Italy

10:30 am The impact of MACO stroke on forelimb ECM in mice, XiaoXiao Zhao, et al., Department of Neuroscience, Padua University, Italy

10:45 am Open Coffee

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FRIDAY March 28, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

10:50 am SESSION XII: Hydrotherapies in mobility disorders, Philippe Perrin, Stefano Masiero, Chairs

10:50 am **Meteorological, chronobiological and thermal factors impacting postural control in knee osteoarthritis, Philippe Perrin, et al., University of Lorraine, Nancy, France**

11:20 am **Eustachian tube dysfunction: possibile role of crenotherapy, Alessandro Martini, University of Padua, Italy.**

11:50 am **"AQTOX Study": a single blind controlled pilot study on aquatic therapy after spasticity treatment with botulinum toxin injection, Andrea Marcante, UOC Functional Recovery and Rehabilitation Unit, ULSS8 Berica, Lonigo (Vicenza), Italy**

12:10 pm **Method of pelvic symmetry recovery in musculoskeletal disorders, Kirill V. Terentev,** et al., **National Medical and Surgical Center named after N.I. Pirogov, Moscow, Russia**

12:30 pm **Lunch**

02:00 pm ***SESSION XIII: Rehabilitation approaches in mobility disorders, Ugo Carraro, Stefano Masiero, Chairs***

02:00 pm **Rehabilitation approach to recover post-stroke diaphragm dysfunction, Elena Yu. Starkova, et al., Moscow, Russia**

02:20 pm **Repetitive Peripheral Magnetic Stimulation to recover balance function in hemiparetic patients, Tatyana Chernyavskaya, et al. Moscow, Russia**

02:40 pm **Taopatch nanotechnology integrated into hearing aids, improves the parameters of the balance in hearing-impaired subjects, Andrea Fabris, Giuseppe Messina, etal., Department of Human Sciences and Promotion of the Quality of Life, San Raffaele University, Rome, Italy; and PLab Research Institute, Palermo, Italy**

03:00 pm **Adolescent idiopathic scoliosis treatment through the PosturalSpine® D'Amanti Method and the Chêneau brace. A case study, Alfredo D'Amanti, Giuseppe Messina, et al., School of Specialization in Physical and Rehabilitation Medicine, University of Florence, Italy, Department of Human Sciences and Promotion of the Quality of Life, San Raffaele University, Rome, Italy; and PLab Research Institute, Palermo, Italy**

03:20 pm **Nanotechnology and athletic performance: Taopatch and athletic excellence, Andrea Pagliaro, Patrizia Proia, Giuseppe Messina, et al., Department of Human Sciences and Promotion of the Quality of Life, San Raffaele University, Rome, Italy; and PLab Research Institute, Palermo, Italy**

03:40 pm **Application of mindfulness techniques in the treatment of stress and eating disorders in the patients with type 1 diabetes. The need to reconnect mind and body, Marina Terenteva, et al., Moscow Regional Research Clinical Institute named after MF Vladimirsky, Moscow, Russia**

04:00 pm **Biodental engineering in research and innovation of dental implants (byZOOM), Sarkis Sozkes, Tekirdag Namik Kemal University, Turkey**

04:20 pm **Conclusive Remarks, Stefano Masiero, University of Padova, Italy**

04:40 pm Coffee Break

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FRIDAY March 28, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

05:00 pm SESSION XIV: Healthcare digitalization, AI and muscle imaging for Mobility Medicine, Paolo Gargiulo, Daniele Coraci, Chairs

05:00 pm 3D and virtual reality techniques for planning, training and education of complex anatomical disorders, Paolo Gargiulo, University of Reikjavik, Iceland

05.20 pm Virtual Muscle Histology: towards an AI characterization in healthy and pathological condition, Riccardo Forni, Reykjavik University, Iceland

05:40 pm 3D printed patient specific anatomy of cartilage tissue. Gianmarco Dolino and Damiano Coato, Reykjavik University, Iceland

06:00 pm Cohort studies using 3D-CT are needed to assess whether "home Gym-Bed" exercises are beneficial against sarcopenia, Daniele Coraci, Department of Neuroscience, Rehabilitation Unit, Padua University, Italy

06:20 pm Innovative approaches in Adolescent Idiopathic Scoliosis: from neurophysiology to Artificial Intelligence, Maria Chiara Maccarone et al., Department of Neuroscience, Rehabilitation Unit, Padua University, Italy

06:40 am Quantitative 3D-CT Imaging for Sarcopenia Mitigation and Muscle Symmetry Restoration in an Elderly Subject: A Longitudinal Case Study (2014-2024), Marco Quadrelli, et al., Synlab Euganea Medica Padua and Neaple, Italy

07:00 am Conclusive Remarks, Aldo Morra, SynLab, Euganea Medica, Padua and SynLab, Naple, Italy

07:30 pm Dinner

09:30 pm Second Meeting of the International Board of the A&C M-C Foundation for Translational Myology and Mobility Medicine (A&C M-C Foundation for TM3)

10:00 pm Good Night to all at the Bar of the Hotel Petrarca with a glass of Euganean Hills wine

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FRIDAY MARCH 28, 2025

Conference Hall Grazia, Hotel Petrarca, Euganean Thermae (Padua) Italy

09:00 am ***SESSION XV: Masterclass on Muscle Rehabilitation in Dentistry***

Claudia Dellavia, Elena P. Ivanova, *Chairs*

09:00 am **Innovative methods for the diagnosis and treatment of craniomandibular disorders, Elena P. Ivanova, Moscow, Russia; Frank Saxler, Cologne, Germany**

09:20 am **Bruxism and oral mucosa: new relationships to investigate? Mariana Dimova-Gabrovski, University of Sofia, Bulgaria**

09:40 **Biodental engineering in research and innovation of dental implants (by ZOOM), Sarkis Sozkes, Tekirdag Namik Kemal University, Turkey**

10:00 am **New perspectives in the myofascial pain treatment. Francesca Lenci, University of Naples Federico II, Naples, Italy**

10:20 am **Morpho-functional safety of the stomatognathic system during sports performance: indications of the Italian Society of Sports Dentistry. Alessandro Beraldi, Milan, Italy**

10:40 am **The masticatory muscles sEMG reliability in TMD patients; preliminary results. Paola Tessera, University of Pavia, Italy**

11:00 am Coffee break

11:20 am **US Imaging of masseter-parotid district. Dolaji Heinin, et al., University of Milan, Italy**

11:40 am **sEMG in patients with parotitis induced by masseter muscle hypertrophy, Massimiliano Vella. University of Milan, Italy**

12:00 am **Lectio magistralis: Differential diagnosis of salivary gland and surrounding muscle disorders: a handbook for dentists, Pasquale Capaccio, University of Milan, Italy**

12:50 am **Discussion**

01:00.pm Working Lunch

02:00 pm ***SESSION XVI: Masterclass on Muscle Rehabilitation in Dentistry Roberto Rongo, Riccardo Rosati, Chairs***

02:00 pm **Functional Anatomy Research Center (FARC) history and results. Claudia Dellavia, University of Milan, Italy**

02:30 pm **Maintenance and restoration of masticatory muscle function in everyday dentistry, Piero Simeone, Rome, Italy**

05:30pm **Functional and non-functional parafunctions: what role in TMDs? Rosaria Bucci and Roberto Rongo, University of Naples Federico II, Naples, Italy.**

06:30 pm **Standardized electromyographic examination of the masticatory muscles: technical and clinical suggestions to reduce the learning curve. Riccardo Rosati, University of Milan, Milan, Italy**

06:30 pm **Conclusive Remarks and Greetings, Riccardo Rosati, Milan, Italy**

07:00 pm Dinner

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SATURDAY MARCH 29, 2025

Conference Hall Paradise, Hotel Petrarca, Euganean Thermae (Padua) Italy

09:00 am	***SESSION XVII: Ludwig Boltzam Institute Workshop on Rehabilitation,***
	Vincent Grote, Ugo Carraro, Chairs
09:00 am	**The impact of exercise and nutrition therapy on measures for sarcopenia in patients with rheumatoid arthritis: A systematic review, Barbara Strasser et al., Ludwig Boltzmann Institute for Rehabilitation Research, Vienna, Austria**
09:20 am	**Performance score T2D – a new way to look at rehabilitation outcomes of post COVID patients. Vincent Grote, et al, Ludwig Boltzmann Institute for Rehabilitation Research, Vienna, Austria**
09:40 am	**Which factors influence the success of rehabilitation? - A mixed-methods study on patients and healthcare professionals, Vincent Grote et al., Ludwig Boltzmann Institute for Rehabilitation Research, Vienna, Austria**
10:00 am	**Effectiveness of a digital intervention to promote physical activity after oncological rehabilitation in breast cancer patients: a protocol for a randomized controlled trial, Spela Matko et al., Ludwig Boltzmann Institute for Rehabilitation Research, Vienna, Austria**
10:20 am	Coffee break
10:20 am	**SESSION XVIII: Therapies in Gastroenterology, Fabrizio Cardin, Ugo Carraro, Chairs**
10:20 am	**Gastrointestinal Disorders and Neurological Diseases, Fabrizio Cardin MD, former Gastroenterology Specialist in Padua Hospital-University Company, Italy**
10:40 am	**Sacral Neuromodulation for bowel dysfunction, Giacomo Sarzo, Padua, Italy**
11:00 am	**Surgical treatment for constipation, Giacomo Sarzo, Padua, Italy**
11:20 am	**Safety and Efficacy of Intermuscular Tunnelling prior selective miotomy in a young patient affected by type 2 Achalasia, Alessandro Gubbiotti, Gastroenterology and Digestive Endoscopy Unit, Sant' Antonio Hospital, Padua, Italy.**
11.40 am	**Esophageal motility disorders: from diagnosis to treatment, Luca Provenzano, O.U. General Surgery 1 - Padova University Hospital, Department of Surgical, Oncological and Gastroenterological Sciences, Padua, Italy**
12:00 am	**Chemokines as potential biomarkers and therapeutic targets for intestinal motility disorders in IBD, Igor Maev et al., the Russian University of Medicine, Moscow, Russia**
12:15 am	**Gut microbiome - SCFA - motility disorders dynamic system as the target for correction, Igor Maev et al., the Russian University of Medicine, Moscow, Russia**
12:30 am	**Final Remarks: Ugo Carraro, University of Padova, Padua, Italy**
12:40 am	**Ugo Carraro: Arrivederci, Auf Wiedersehen, Au revoir, Goodbye to the 2026Pdm3, Euganean Thermae (Padua), Italy**
13:00.am	**Lunch at the Trattoria Da Nicola, Montegrotto Terme (Padua), Italy**

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SATURDAY MARCH 29, 2025

Conference Hall Grazia, Hotel Petrarca, Euganean Thermae (Padua) Italy

09:30 am ZOOM SESSION: Therapy & Rehabilitation in Mobility Disorders,

Elena P. Ivanova, Igor Reverchuck, Chairs

09:30 am	Neurophenomenological interview as a method of studying psychosomatic balancing in the process of adaptation to learning, (by ZOOM), Victoria V. Kostyrkina, et al., Immanuel Kant Baltic Federal University, Kaliningrad, Russia
09:40 am	Prognosis of movement disorders in the early recovery period of ischemic stroke on the background of anticoagulant therapy (by ZOOM), Georgy Avakyan, Minh Duc Tranas, Albina N. Yasamanova, Neurology, Neurosurgery and Medical Genetics, Faculty of General Medicine, Pirogov Russian National Research Medical University, Moscow, Russia
09:50 am	Neurokinetics of emotional motor components of behavior in adolescents in norm and pathology (by ZOOM), Igor Reverchuk, BioInstitute for Somatomental Health, Samarkand State Medical University of the Republic of Uzbekistan
10:00 am	Can the microclimatic conditions of a terrainkur influence the results of treatment in patients with arterial hypertension and overweight? (by Zoom) Irina A. Grishechkina, Anatoliy D. Fesyun, Tatyana A. Knyazeva, Maxim Yu. Yakovlev, Mikhail V. Nikitin, National Medical Research Center for Rehabilitation and Balneology, Moscow, and Sechenov University, Moscow, Russia
10.10 am	The paradigm of somatic intelligence in neurorehabilitation (by ZOOM), Igor Reverchuk, BioInstitute for Somatomental Health, Samarkand State Medical University of the Republic of Uzbekistan
10:20 am	The Effect of Calcium and Vitamin D3 on Calcium Homeostasis and Falls Incidence in Patients with Osteoporosis Undergoing Medical Rehabilitation (by ZOOM), Larisa Marchenkova, Anatoliy Fesyun, National Medical Research Center for Rehabilitation and Balneology, Moscow, Russia
10:30 am	Effectiveness of the Pelvic Floor Muscles Electrotherapy and Magnetic Stimulation in Preconception Programs for Women of Reproductive Age, Natalia Kotenko, Anatoliy Fesyun (by ZOOM), National Medical Research Center for Rehabilitation and Balneology, Moscow, Russia
10:40 am	Effectiveness of a Rehabilitation Programme for Patients with Post-Thrombotic Syndrome including Robotic Biofeedback Training of the Calf Muscle Venous Pump (by ZOOM), Tatyana Apkhanova, et al., National Medical Research Center for Rehabilitation and Balneology, Moscow, Russia
10:50 am	Prognosis of movement disorders in patients with cardioembolic stroke on the background of anticoagulant therapy, (by ZOOM) Georgy Avakyan, Minh Duc Tran, Albina N. Yasamanova, Neurology, Neurosurgery and Medical Genetics Department, Institute of Neuroscience and Neurotechnology, Pirogov Russian National Research Medical University, Moscow, Russia
11:00 am	Functional asymmetry and interhemispheric interactions as predictors of mental and somatic disorders (by ZOOM), Reverchuk IV, Aryamkina OL, Kuzmina IO, Kugaevskaya T, Melnikova DO, Safiullina LR, Bioinstitute for Somatopsychic Health, Kaliningrad, Russia Surgut State University, Surgut, Russia.
11:10 am	Final Remarks: Ugo Carraro, University of Padova, Padua, Italy

12:40 am Ugo Carraro: Arrivederci, Auf Wiedersehen, Au revoir, Goodbye to the 2026Pdm3, Euganean Thermae (Padua), Italy

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COLLECTION OF ABSTRACTS

2025Pdm3 March 25 - Abstract 001

Activity, the final common path in muscle adaptation

Jonathan Jarvis, Stanley Salmons

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E-mail: J.C.Jarvis@ljmu.ac.uk

Activity drives adaptation

Stanley Salmons was the first to use autonomous miniature electronic stimulators to modify activity in skeletal muscles to investigate the mechanisms of muscle adaptation that had been known for centuries in the realm of muscle training and had been highlighted by experiments on cross re-innervation.

His circumstances do not permit him to attend PMD 2025 as he had intended. I will cover some of his seminal work, showing that adult 'terminally differentiated' muscle fibres can indeed respond to changes in activity by re-expression of their genome, and that activity itself and the cellular consequences of that activity, is the primary causal aspect of the fast-to-slow and slow-to-fast changes associated with cross re-innervation and increases in accustomed activity achieved by neuromuscular stimulation or exercise interventions, or periods of disuse.

Adaptation is a graded re-expression of the genome

The molecular signature of the exercise response can be considered at many levels, from the earliest changes in metabolites, to intracellular shuttling of signalling molecules, to activation by phosphorylation of metabolic pathways, to changes in transcription and translation of specific genes, to changes in the proteome caused by modulation of the rates of synthesis and degradation.

We have focused recently on the acute response to resistance training in rat and mouse hindlimb muscle. We activate the ankle dorsiflexors maximally while providing resistance from the plantarflexors to achieve a loaded or strength training pattern of repetitions and sets of repetitions.

We will discuss the acute response in terms of the transcriptome and the metabolome. We have established a model of muscle growth in rodents using programmed contractions in which the plantar flexors are used to resist the dorsiflexors of the ankle [1, 2]. We will present data from experiments in the rat that show a marked increase of muscle mass, showing how the acute transcriptomic response 1 hour after an exercise session changes as a muscle adapts to daily exercise over 30 days. We will also show that a similar degree of hypertrophy is achieved after 30 days with exercise every three days, and that the transcriptomic response in this case shows less change towards an 'endurance' expression profile. We note that a pattern of daily training that produces substantial hypertrophy in the rat fails to do so in the mouse. Although other groups have now found methods to generate activity related hypertrophy in some lower limb muscles of the mouse, the cellular signalling around exercise and ageing is different in the two species. We have measured by nmr spectroscopy the metabolic shift after a single bout of unaccustomed resistance training in mouse and rat. The spectra separate by principal components analysis, but identification of the components that make the difference is not well established in muscle for nmr spectra, and identification by mass spectrometry is not yet sufficiently accessible for routine analysis.

Transcutaneous activation of muscles via peripheral nerves in humans

In human, the use of 'activity' to improve health and wellbeing is well-established but there are still many questions surrounding the ideal prescription and how best to achieve a certain level of activity. In persons with neuromuscular deficits, artificial stimulation known as functional electrical stimulation (FES) or neuromuscular electrical stimulation (NMES) may be helpful. There has been recent interest in the use of kilohertz frequency stimulation for activation of brain and peripheral nerve. We have investigated the mechanism and practical application of interferential stimulation gauging activation of the ulnar nerve at the wrist by measuring the force output of adductor pollicis. It is difficult to achieve activation of a nerve below the skin without activation of the skin itself, but we shall show how the type and degree of nerve activation, and the associated skin sensation depends on the frequency and the waveform of the applied currents, and the positioning of the stimulating electrodes relative to the nerve.

As can be seen in figure 1, two identical currents via two independent pairs of axial electrodes may not activate the nerve, but when the frequency of one is increased (offset) by only 0.2%, then significant activation may be achieved. There is ongoing debate over the neural membrane dynamics in this situation but there is also a dearth of experimental data that we are trying to address.

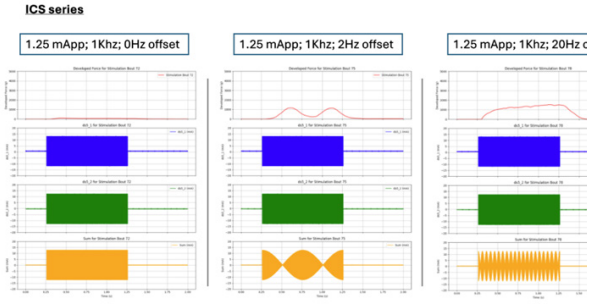

Fig 1. Rows from top to bottom show force, stimulus ch 1, stimulus ch 2, sum of ch1 and ch2

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Key words: muscle adaptation, neuromuscular stimulation, transcriptomic analysis of the exercise response.

References

1. Viggars MR, Sutherland H, Lanmüller H, Schmoll M, Bijak M, Jarvis JC. Adaptation of the transcriptional response to resistance exercise over 4 weeks of daily training. FASEB J. 2023 Jan;37(1):e22686. doi: 10.1096/fj.202201418R. PMID: 36468768.
2. Viggars MR, Sutherland H, Cardozo CP, Jarvis JC. Conserved and species-specific transcriptional responses to daily programmed resistance exercise in rat and mouse. FASEB J. 2023 Dec;37(12):e23299. doi: 10.1096/fj.202301611R. PMID: 37994729.

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2025Pdm3 March 25 - Abstract 002

Electrical stimulation technology, a versatile and effective tool for support of restoring and maintaining neuromuscular integrity

Winfried Mayr

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Functional Electrical Stimulation (FES) has a long tradition along with the first availability of electrical sources and continuous innovation in technological developments. Right from the beginning it stands alone as modality for influencing bioelectrical fields in nerve and muscle fibers, which offers numerous options for vastly different rehabilitation tasks. FES can elicit traveling action potentials in afferent neurons, efferent neurons and muscle fibers, and it can neuromodulate excitability of the same structures to elevate or lower activation thresholds (Figure 2). Based on these simple principles it offers a wide spectrum of possibilities, beginning with pain and spasticity modification, tissue maintenance, support of recovery and relearning of motor control, support or substitution of impaired sensory and motor functions and more, per se or in combination with other therapeutic means. In practice we see FES only applied regularly in very few of the many existing rehabilitation institutions and consequently also rarely in the so important home-based continuation, where it can prevent long-term complications after neural injury, in particular spinal cord injury, or degenerative diseases and maintain sustained quality of life on a substantially elevated level. Reasons are in information deficits causing over- as well as underestimation, and skepticism at the same time. Lack of capacity and time constraints of rehabilitation professionals as well as new regulations for medical instrumentation, that do not consider the needs of small-market products for minorities enough, are currently essential factors, restrictive and shortsighted policies of health care providers, despite little relevance for their budgets, can make access further difficult to impossible. On the other hand, worldwide research keeps being lively and delivers serious clinical evidence, better understanding of mechanisms, technological innovations and exciting novel application fields

2025Pdm3 March 25 - 29, 2029

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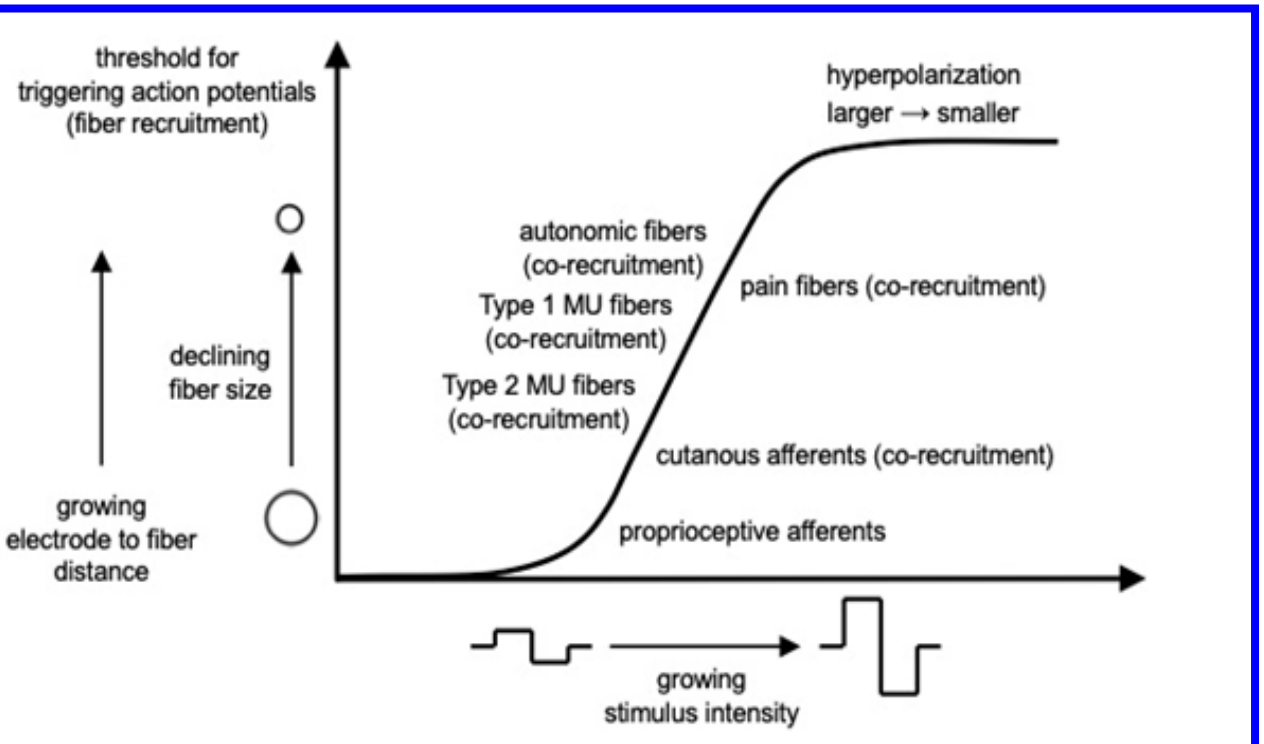

Fig 2. Role of electrical stimulation parameters and electrode setup in neuron recruitment

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2025Pdm3 March 25 - Abstract 003

Ultra Sound evidence of deceleration of denervated facial muscles atrophy through functional electrical stimulation

Johannes Krauss (1,2), Gabriel Meincke (1,2), Maren Geitner (1,2,3), Dirk Arnold (1,2,3), Jonas Ballmaier (1,2,3), Anna Kuttenreich (1,2,3), Timm Büchner (4), Joachim Denzler (4), Orlando Guntinas-Lichius (1,2,3), Gerd Fabian Volk (1,2,3)

(1) Department of Otorhinolaryngology, Jena University Hospital, Jena, Germany; (2) Facial-Nerve-Center, Jena University Hospital, Jena, Germany; (3) Center for Rare Diseases, Jena University Hospital, Jena, Germany; (4) Computer Vision Group, Friedrich Schiller University Jena, Germany
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More and more evidence of the therapeutic potentialities of surface electrostimulation (ES) for the treatment of facial paralysis has been published so far (1,2). Reducing variance to work with small patient numbers, especially studies containing objective imaging methods for paralysis quantification are of special value. Facial muscles as principal target of ES can be directly quantified via ultrasound, a swiftly feasible imaging method (3). We will study with a systematic evaluations of this approach within patients with complete unilateral facial paralysis. Using an established ultrasound protocol for facial muscles, we used it to predict therapeutic effects on patients with facial paralysis. ES-parameters were adjusted during the first visit and confirmed/adapted every four weeks thereafter. At each visit patients additionally underwent needle-electromyography to verify if the complete denervation would still be present as well as ultrasound imaging of the facial muscles. Stimulation was carried out at home for 20 minutes twice a day (morning and evening with an in-between break of at least 6 hours) on the paralytic side of the patients' cheek, focusing mainly on the zygomaticus muscle. For home training, a two-phase stimulation in a triangular waveform with a phase duration of 5 seconds and a pulse pause of 1 second was performed. Patients terminated FES when EMG and clinical findings clearly indicated facial reinnervation. Ten patients (median 61 years, 25th to 75th percentile 38.3 – 71 years; 4 female, 6 male, median time of denervation 130 d) underwent FES for a mean of 95 days (min. 35, max. 301). Facial paralysis etiologies were vestibular schwannoma (n = 3), parotid cancer (n = 3), benign parotid tumor (n = 1), chronic otitis media (n = 1), zoster oticus (Ramsey-Hunt syndrome; n =1) and traumatic temporal bone fracture (n = 1)). They performed surface ES for a maximum of one year. The assessment of ultrasound imaging indicate that paralytic electro-stimulated zygomaticus muscle increases during the first month of ES, while control muscles outside the focus of ES further decreases in cross-sectional area compared. Photo assessment, but also patient related outcome measures (PROMs) support this positive effect during ES.
In conclusion, Intense Electrostimulation can stop the denervation atrophy of facial muscles. Hence, the increase of ultrasound quantified muscle cross-sectional areas, but also photo and PROMs in facial paralysis, provides a clear indication of ES. It is recommended that the procedure be subjected to further investigations based on this pilot study with a larger patient collective and adapted study design. Looking ahead, ES offers a promising prospect of being established as an additional therapeutic pillar in the conservative treatment of facial nerve paresis and paralysis. Furthermore, the method of US quantification of the effect of FES on the denervated muscles by measuring the muscle CSA parameter is well suited and applicable in this context.

Key words: Electrostimulation, facial paralysis, reinnervation, surface electrodes, zygomaticus muscle

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2025Pdm3 March 25 - Abstract 004

Electrostimulation in facial nerve palsy is safe and helpful

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The seventh cranial nerve is known as the facial nerve and is a purely motor nerve. Facial paralysis occurs when the facial nerve becomes damaged, causing weakness,

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drooping, and loss of facial movements. Facial nerve damage can occur for several reasons, including infection and trauma. Electrical stimulation is widely recommended for peripheral nerve palsy because it can help maintain muscle cell structures during the denervation period. However, many articles have advised against this procedure in facial nerve palsy.[1-3] According to these authors, electrostimulation is not effective for nerve recovery and can also cause muscle motor disorders such as synkinesis or dystonic contraction. We report on the clinical case of a 45-year-old patient suffering from Ramsay Hunt syndrome. We used a 0.2 ms pulse at 5 m for 20 minutes once a day for each mimic muscle on the left side of the face for 6 months until complete recovery. After twenty years' experience in electrostimulation in facial nerve paralysis, we believe that the facial nerve is no different from other motor nerves, and that chronic movement disorders result from muscle weakness and incomplete reinnervation.

Key words: Facial nerve palsy; electrical stimulation; Ramsay Hunt Syndrome.

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2025Pdm3 March 25 - Abstract 005

Interplay between Muscle and Bone following Electrical Stimulation Exercises in Persons with SCI

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Spinal cord injury (SCI) negatively impacts muscle quality and bone health. Neuromuscular electrical stimulation-resistance training (NMES-RT) has been shown to enhance muscle quality. It is unclear whether adding NMES-RT to functional electrical stimulation (FES)-lower extremity cycling or FES-rowing may further augment muscle quality and subsequently enhance bone mineral density (BMD) and trabecular microarchitecture. We, hereby, present findings from two clinical trials that are conducted in our lab. Both randomized clinical trials implemented different durations of 6 and 9 months. The first trial enrolled 32 participants that were evenly randomized into 12 weeks of NMES-RT followed by 12 weeks of FES-lower extremity cycling (NMES-RT+FES; n=16) or 12 weeks of passive movement training (PMT) followed by 12 weeks of FES- lower extremity cycling (PMT+FES; n=16). The second trial enrolled six participants that were randomized into either 9 month of vitamin D+ electrical stimulation exercise (vit D+ES-Excs) or vit D+ passive movement training (PMT) groups. The vit D+ES-Excs underwent daily supplementation of vit D with 4.5 months of neuromuscular electrical stimulation-resistance training (NMES-RT) followed by 4.5 months of functional electrical stimulation (FES)-rowing, twice weekly, using a home-based training approach. Isokinetic dynamometer was used to measure knee extensor isometric and isokinetic toques. Magnetic resonance imaging measured whole thigh and knee extensor (KE) muscle CSAs and trabecular microarchitectures of the distal femur and proximal tibia. Dual energy x-ray absorptiometry measured total and regional BMD. Finally, bone biomarkers were captured at different points of the study. Measurements were obtained at baseline, mid intervention (P1) and at the end of the study (P2). In the first trial, NMES-RT elicited a trend towards greater isometric torque at 80 Hz (P = 0.057) and isokinetic torque [60 deg/sec; P = 0.009 and 180 deg/sec; P= 0.003] compared to PMT. Muscle CSA was greater in left whole thigh [F (2,20) =9.1; P =0.007] and KE [F (2,20) =15.5; P =0.001] by 11.0 and 8.0 cm2 respectively at P1 in the NMES-RT+FES compared to PMT+FES. Additionally, NMES-RT+FES maintained BMD at the distal femur. In the second trial, the vit D+ES-Excs showed increases in leg (5.3%) compared to the total body lean mass. The percentage changes indicated that two persons in the vit D+ES-Excs showed decreases in trabecular spacing (28%) and increases in trabecular network (33 -49%). This was accompanied by attenuation of BMD loss at the pelvis (3.6-7.7%), femoral necks (4.5-8.4%) and knees (10.5- 18.7%). and decreases in biomarkers of bone resorption (7 -23.5%). In conclusion, enhancing muscle quality via increasing peak isometric or isokinetic torques as well as muscle hypertrophy may result in positive bone adaptations following electrical stimulation exercise in persons with SCI. Despite differences in durations, the two trials suggest positive bone adaptations as demonstrated by changes in BMD and trabecular microarchitectures after SCI.

Keywords: Electrical stimulation Exercise; Home-Based Training; Trabecular bone; BMD; Muscle and bone interplay; Spinal cord injury.

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2025Pdm3 March 25 - Abstract 006

Tissue Composition Changes in Long-Term Denervated Muscles - Beneficial Effects of Long-Pulse Electrical Stimulation

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Spinal cord injury (SCI) leading to compromised lower motor neuron function can result in atrophy and degenerative changes within the respective muscle. This particular type of lesion assumes notable severity when the gluteal muscles and/or the hamstrings are affected, given their role in providing protective cushioning against skin injury. Advancements in the development of parameters for the optimal application of long pulse stimulation for denervated muscles over the past 30 years have aimed to restore muscle structure and trophic aspects in people with chronic SCI. The objective of the study was to examine the impact on tissue composition and its temporal progression during the initial six months following long pulse stimulation initiation, when electrical stimulation treatment is initiated more than 2 years after denervation of gluteal muscles in a chronic state that exhibits degeneration changes. The study protocol extended over a period of six months, including three measurement periods (Figure 3). 20 people with SCI were included in the study. Inclusion criteria encompassed chronic SCI, aged 18–70, injury levels T10–L5 (AIS A-D), and gluteal muscle denervation, confirmed by non-reaction to neuromuscular ES using specific parameters (50 Hz, 300 µs, 100 mA). Exclusion criteria were arteriosclerosis, pressure injuries, skin irritation, infection, or recent surgery.
A standardized MRI (Figure 4) (3T-MRI Archeva, Philips, Horgen, Switzerland) was performed at the beginning of the

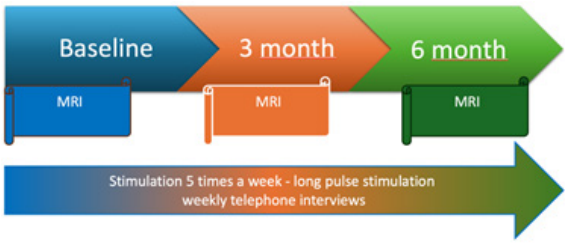

Fig 3. Study workflow

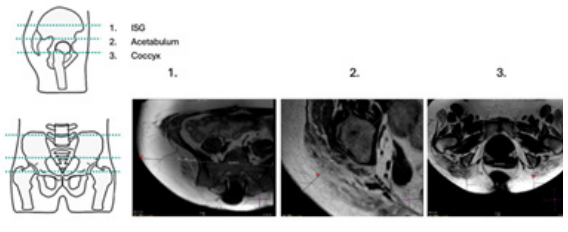

Fig 4. Landmarks of 3 Tesla MRI

study and after three and six months to ascertain alterations in the tissue composition of the pelvic region in the area of the gluteal muscles (gluteus maximus and medius). For home-based administered stimulation training, participants la y in a prone position while electrical stimulation (ES) was applied using Stimulette den2x (Schuhfried GmbH, Vienna, Austria). Sponge pockets with 10 × 13 cm electrodes were placed on the buttocks to generate a horizontal electrical

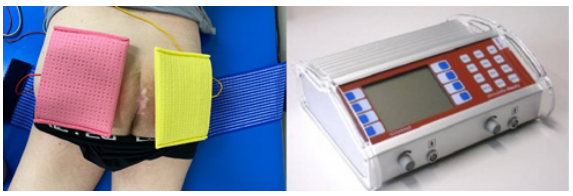

Fig 5. Left side positioning of the electrodes; right side simulation device Stimulette 2 den (Schuhfried GmbH, Vienna, Austria)

field covering the gluteal area (Figure 5). ES was performed five times a week for six months, with each session lasting 45 minutes, including preparation. The session included a 3-minute warm-up and a 30-minute training phase. The warm-up phase involved 11-second bursts at 0.86 Hz, using biphasic ramp-shaped pulses (150 ms duration, 1 s inter-pulse pause), followed by 11-second breaks. The training phase used biphasic rectangular pulses at 20 Hz, with 40 ms pulse durations (20ms per phase) and 10 ms inter-pulse p auses in 2-second bursts with 2-second breaks. Participants used intensities of 90 mA for warm-up and 120 mA for training throughout the study. Data from 5 out of 20 participants are presented. Each voxel within the analyzed regions represents a combination of tissues, including connective tissue, fat, and muscle. The dominant tissue type within a voxel determines its grey value, with grey values in the range of 100–400 primarily reflecting muscle tissue.
The analysis focused on muscle density, tissue composition, and their changes over a six-month period following electrical stimulation (ES). Tissue composition analysis demonstrated alterations in the proportions of muscle, infiltrated fat, and fat over time, providing a detailed depiction of tissue progression in response to the intervention. An increase in the number of voxels with grey values within the muscle range (100–400) indicates an increase in muscle tissue volume or a reduction in fat

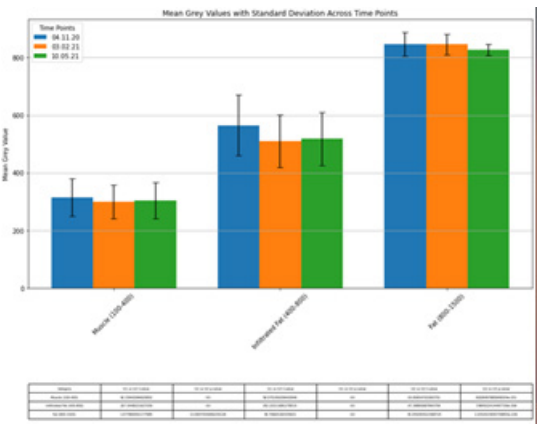

Fig 6. Mean grey values across the time points baseline, 3 and 6 month

infiltration, reflecting improvements in muscle composition. Figure 6 presents changes in mean grey values calculated from a selected area within the muscle, ensuring that the analysis reflects changes in the targeted region of interest while minimizing the influence of adjacent non-muscle tissues. An increase in the number of voxels with grey values within the muscle range (100–400) is indicative of denser and healthier muscle tissue. Conversely, a decrease

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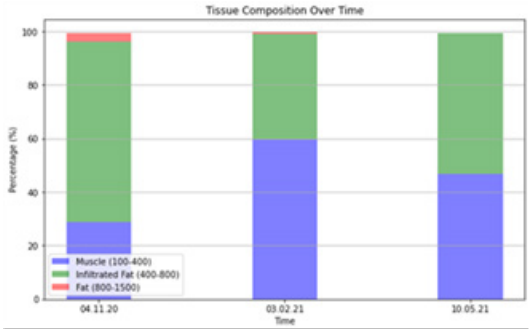

Fig 7. Illustrates the percentage composition of muscle, infiltrated fat, and fat for each measured time point..

in mean grey values within the fat range (800–1500) highlights reduced fat infiltration in the muscle.

Figure 7 illustrates the percentage composition of muscle, infiltrated fat, and fat across all measured time points. The graph demonstrates a favorable progression, characterized by an increase in muscle composition (100–400), indicative of tissue regeneration, and a reduction in infiltrated fat (400–800), reflecting enhanced muscle quality with less fat contamination in the muscle. Additionally, a decrease in fat content (800–1500) further underscores the positive impact of electrical stimulation on tissue composition.

Key words: chronic spinal cord injury; muscle denervation; long pulse stimulation; MRI.

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2025Pdm3 March 25 - Abstract 007

Effectiveness of FES x DDM after twenty years of permanent denervation and degeneration of human muscle: ultrasound evidence of thigh muscle contraction by surface electrical stimulation after ten years of interruption of FES x DDM

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Mr. A.C. (born 18.01.1965) is a patient of the European RISE project of the 5th EU Framework Program. In the period between August 2004 and June 2006, he underwent diagnostic evaluations and performed daily transcutaneous electrical stimulation together with a group of patients with complete and permanent lesions of peripheral motor neurons. He has a fracture of the thoracic vertebral bodies 11 and 12, and a fracture at the L 1 level since 10.28.2003 resulting in a complete lesion of the spinal cord (ASIA grade A). He used a prototype of the special electrical stimulator, which was eventually made commercially available by the Schuhfried company after the positive results of the RISE study under the name Schuhfried Den2x which is the successor to the RISE prototypes. As far as we know from the available scientific literature, it is currently the only RISE STIMULATOR available (Dr. Schuhfried Medizintechnik GmbH, Van Swieten-Gasse 10, 1090 Vienna) that provides sufficiently high current pulses for the treatment of the muscles of patients with complete and permanent lesions of the lower motor neurons such as those of Mr. AC. Mr. AC has been using home stimulation of the thighs and other leg muscles for 12 years, but has stopped therapy with FES x DDM in the last 10 years.

On November 30, 2023 he went to the Rehabilitation Unit of the Padua Polyclinic asking to restart the FES x DDM Protocol with a new device, because his old RISE Prototype was no longer usable after years of abandonment. Checking his quadriceps muscles with ultrasound and dynamic ultrasound, to the surprise of all the specialists present at the Rehabilitation Unit of the University Hospital of Padua, the long-term (20 year) denervated muscles responded to surface FES x DDM with repetitive contractions. Let me stress again that A.C. performed Home FES x DDM for 12 years after enrollment in the RISE Project, but discontinued it in 2015, ten years ago. Though it is the only case we know, it is astonishing that his denervated skeletal muscles respond to the surface-high-current-electrical stimulation more than twenty years after permanent complete denervation. In our opinion the only rational explanation is that FES x DDM was very effective during the first 12 years of denervation. Thus, he can be considered a patient with 10 years of complete rest of his leg muscles, not more than 20 years. During these long years Mr. C.A. suffered of decubitus ulcers in his low back, calves and feet. Unfortunately, despite this strong evidence of the effectiveness of FES x DDM, Mr. A.C. either pays 6.000 euros (Six Thousand Euros) to purchase the device from the Schuhfried Company or continues to wait until his doctors in Piacenza, Italy will be willing and able to convince the Italian Social Security System to cover at least half the costs for home use of the Schuhfried Den2x stimulator. The A&C M-C Foundation offered to rent the stimulator for a symbolic sum for one year, but as far as we know, Mr. A.C. continues to be against this opportunity. Luckily, Mr. A.C. recently changed his mind and accepted the symbolic rental of the device in use at the Rehabilitation Unit of the Department of Neuroscience of the University of Padua, Italy, where he went to be re-evaluated. His muscles responded with minimal series of contractions visible even to the naked eye to FES for DDM stimulation, but FES for DDM only). So now he stays at home to stimulate his muscles that have been

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denervated for twenty years. We are certain that this will help him avoid the very dangerous risks of bed sores over his buttocks, calves and heels. We ask if anyone in the audience finds a permanent solution for this patient. He has the right to be cared for in the best possible way, but too few in Italy believe in this right of A.C. Who will join us for a common petition to the Italian Social Security System?

Key Words: Long-term permanent denervation of skeletal muscles; decubitus ulcers; FES x DDM; Schuhfried Den2x stimulator.

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2025Pdm3 March 25 - Abstract 008

Welcome and Introduction to the Med-El Workshop on Electrical Stimulation Solutions

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MED-EL, Medical Electronics, a world leader in implantable hearing solutions, was founded with the mission of overcoming hearing loss as a communication barrier. Founded by two pioneering scientists in the industry, Ingeborg and Erwin Hochmair, who developed the world's first microelectronic multichannel cochlear implant (CI) in 1977. Since then, MED-EL has grown to have over 2,700 employees and offers the widest range of implantable and non-implantable hearing solutions worldwide, enabling people in 140 countries to hear thanks to a MED-EL device. With our passion for medical technology and our sophisticated way of neurostimulation, our Neurorehabilitation department has over 28 years of experience, focusing primarily on electrical stimulation for neurological conditions, from complex mobility disorders to denervation and spinal cord injuries. Our latest innovation, the STIWELL® PROFES electrical stimulation device, (Figure 8) combines a modern design with intuitive navigation and ease of use. Muscle groups can be activated

Fig 8. "MED-EL STIWELL ® PROFES Electrical Stimulation for Neurorehabilitation".

simultaneously or sequentially, allowing for the retention of complex movement patterns. STIWELL® PROFES addresses a wide range of pathologies of the first motor neuron such as stroke, multiple sclerosis, and facial paralysis; and second motor neuron, including spinal cord injury and denervation. It offers individualized solutions through specific programs and parameter customization. MED-EL is your Electrical Stimulation expert. Our mission is to change people's lives positively and in a sustained manner through electrical stimulation. To achieve our goal, we are counting on great researchers and key opinion leaders in the field in academic and clinical institutions from all over the world. We are privileged to have with us today an esteemed panel of speakers, renowned researchers and clinicians who are at the forefront of their respective fields. Their expertise and insights will undoubtedly enrich our understanding of different aspects of Electrical Stimulation in Neurorehabilitation. I hope you, as well as I, enjoy it.

Key words: Denervation; Electrical Stimulation; FES; Stroke; Facial Paralysis.

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2025Pdm3 March 25 - Abstract 009

Strategies to optimize the integration of therapeutic exercise and peripheral electrical nerve stimulation: a clinical perspective

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In the neurorehabilitation field there is a huge gap between research findings and clinical practice, so that patients rarely receive treatments based on the best available evidence.[1] This is evident for peripheral electrical nerve stimulation, a therapy that may offer unique opportunities such as improvement of muscle trophism,[2] improvement of motor function,[3] and normalization of muscle tone;[4] however, electrotherapy is rarely proposed to patients with severe neuromotor disorders. Furthermore, even in well-structured clinical trials, electrotherapy is often investigated with sub-optimal paradigms, for instance with passive cyclic stimulation eliciting muscle contraction without requiring active participation by the patient, with the consequence of concluding that electrotherapy is ineffective, or even worse that there is very limited potential for recovery in severely impaired patients. Therefore, a perspective grounded on research evidence and clinical experience is beneficial to offer optimal treatments for severely impaired patients, and to design effective interventional research trials. The first step may be represented by a review of the literature published in 2022 on Frontiers Neurology.[1] The core concept is that motor learning principles are the backbone of effective neurorehabilitation treatments, with assistive technologies being particularly useful in those areas where the hands of the therapist are not sufficient. In this perspective, electrotherapy is a precious resource because of its unique ability to provoke a joint movement through a patient's muscle contraction, and for its neuromodulatory effects at the level of the central nervous system.

That said, here is a list of specific strategies to implement electrotherapy with therapeutic exercise:

1. 120' of low-frequency sensory stimulation (10 Hertz, 500 μs, intensity below motor threshold) before motor training to improve motor function by priming brain neuroplasticity (activation of primary sensorimotor cortex).
2. 30' of high frequency sensory stimulation (100 Hertz, 200 μs, intensity below motor threshold) to normalize muscle tone by priming spinal cord neuroplasticity (presynaptic inhibition of hyperactive stretch reflexes).
3. Triggered functional electrical stimulation (typically 30-50 Hertz, 300-500 μs, intensity above motor threshold) to improve motor function by pairing movement execution and patient's intention to move in active-assisted training fashion. The trigger may be a brain computer interface signal, a EMG signal, or simply a button pressed by the patient or by the therapist (Figure 9).
4. Specific parameters and electrodes for denervated muscles (triangular shape, very long biphasic pulse of 120-150 ms at high intensity), to maintain and restore muscle trophism.
5. Integration of electrical stimulation and other assistive devices and technologies, such as splinting, antigravity support systems, and robotics.
6. Non-invasive transcutaneous spinal cord stimulation to improve motor function and normalize muscle tone (currently being under investigation, not available for clinical use).[5]

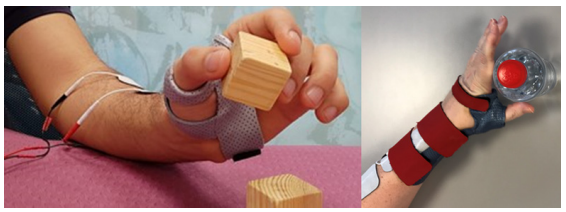

Fig 9. Examples of integration for electrotherapy, functional hand splinting, and therapeutic exercise to perform active-assisted intensive task-oriented training in severely affected patients.

To conclude, there are several opportunities in the neurorehabilitation field for clinicians, researchers, and neurotech developers, that may be achieved by embracing an evidence-based clinical perspective, with the goal of merging existing knowledge with practical patients' needs.

Key words: electrical stimulation; neurorehabilitation; motor learning; clinical perspective.

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2025Pdm3 March 25 - Abstract 010

The phenomenon of lesions of the upper and lower motoneuron in in-and extrinsic muscles of the upper limb in persons with tetraplegia

Development of a stimulation protocol to enhance functionality

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Functional Electrical Stimulation (FES) plays a crucial role in rehabilitation, particularly for individuals with spinal cord injury (SCI). Its application is based on a deep understanding of muscle physiology, stimulation protocols, and integration into functional activities.

Muscle Physiology in SCI

Muscle response to spinal cord injury varies depending on whether the upper or lower motoneuron (UMN/LMN) is affected. Upper motoneuron lesions (UMNL) lead to preferential atrophy of type II muscle fibers, with fiber type grouping due to collateral sprouting. Lower motoneuron lesions (LMNL) cause grouped atrophy, as the loss of motor units disrupts normal muscle structure.

In complete SCI, type II fiber atrophy begins within the first month, followed by type I fiber atrophy later. In incomplete SCI, muscle cross-sectional area can shrink by 33%, while intramuscular fat increases by 126% within six weeks of injury. Over time, SCI patients accumulate three times more intramuscular fat and four times more subfascial fat compared to able-bodied individuals. Reduced oxidative enzymatic capacity further contributes to muscle degeneration.

Stimulation Protocols and Applications

FES is applied differently depending on whether the UMN or LMN is affected (Figure 10). The goal of stimulation may be to substitute function, prevent atrophy, strengthen muscles, or support motor learning. Stimulation parameters are tailored accordingly:

Partially denervated muscles require specialized protocols. In UMNL, stimulation can be applied to muscles innervated by supra-lesional segments, while in LMNL, stimulation targets muscles with damaged anterior horn cells to prevent further degeneration.

Motor Point Mapping and Quality of Contraction

Motor point testing helps identify the optimal stimulation site for each muscle, ensuring efficient activation with the lowest intensity. Muscles are classified based on their contraction response to 300 µs, 35 Hz stimulation:

Stimulation parameters	
Pulse duration	250-400 μsec
Frequency	35 Hz
Amplitude	Sub motor-threshold as well as above
Training duration and number of sessions per week	Daily once 30 minutes Better twice to thrice a day*

Fig 10. Stimulation protocol for upper motoneuron lesions for arm cranking

- ≥3 MRC: Innervated
- <3 MRC: Partially denervated
- 0 MRC: Fully denervated

For partially denervated muscles, stimulation can alternate between nerve stimulation and direct muscle stimulation, either in 30-minute sessions or on alternating days. If partial voluntary innervation remains, traditional active rehabilitation can be combined with direct stimulation.

Integrating FES into Functional Activities

FES can be used both for temporary applications (neuromodulation, motor learning, contracture treatment) (Figure 11) and long-term strategies (supporting function, preventing muscle degeneration). In individuals with chronic SCI, targeted electrical stimulation can improve functional movement, allowing for manipulation of small objects, improved grip strength, and enhanced independence.

Training parameters	Acute /subacute lesion AIS A/B	Chronic lesion AIS A/B	Acute/ subacute lesion AIS C/D	Chronic lesion AIS C/D
Pulse duration	300-400 μsec	300-400 μsec	400 μsec	400 μsec
Frequency	50 Hz	20 Hz	35-50 Hz	20 Hz
Amplitude	Upper extremities 20-80 mA	Upper extremities 20-80 mA	Depending sensibility and tolerance to stimulation current	Depending sensibility and tolerance to stimulation current
Resistance	70% of maximal force 50 rpm	20 % of maximal force 10-20 rpm	70% of maximal force Adaptive training	20 % of maximal force Adaptive training
Training	30 minutes 3 times a week	30 minutes 3 times a week	30 minutes 3 times a week	30 minutes 3 times a week

Fig 11. Stimulation protocol for motor learning.

For example, a 17-year chronic LMN lesion patient underwent 12 weeks of daily stimulation, enabling him to handle objects like credit cards and coins. Stimulation was applied with long pulses (ms instead of µs) to elicit a muscle contraction.

In another case, forearm pronation was improved through motor point mapping, allowing selective electrode placement for optimized function. Training five times per week using 35 Hz, 300 µs, 25 mA helped the patient regain

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controlled movement.

Managing Fatigue and Optimizing Stimulation

One challenge with FES is muscle fatigue, which results from metabolic changes affecting excitation-contraction coupling. Solutions include:

- Multi-pad and array electrodes to distribute stimulation
- Interleaved stimulation to create asynchronous motor unit activation
- Varying stimulation frequencies during a single session

These techniques allow for more natural muscle activation, mimicking voluntary contractions and improving endurance.

Final Thoughts

FES has transformed rehabilitation by enabling individuals with SCI to regain functional movement, prevent muscle atrophy, and improve quality of life. However, successful implementation requires time, experience, anatomical understanding, and technical expertise. Ongoing research, financial support, and motivated clinicians are essential to advancing its applications in treatment, rehabilitation, and education

Key words: spinal cord injury; upper motoneuron lesion; lower motoneuron lesion, electrical stimulation protocol; motor point testing.

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2025Pdm3 March 25 - Abstract 011

Selective surface stimulation therapy for facial nerve paralysis

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High therapy frequencies with up to several training units per day are crucial for the success of many rehabilitation programs. At the same time, such high therapy frequencies cannot be provided by human therapists due to the financial and personnel costs. Surface electrostimulation home training, possibly with computer support or tele medical elements, could be a solution here.[1] Study results for pure audio-visual controlled tele medical training, surface electrical stimulation home-training but also EMG-triggered electro-stimulation of the facial muscles to support facial movements will be presented and compared: Surface electrostimulation can prevent atrophy of denervated facial muscles.[2,3] By placing surface electrodes or needle electrodes in the right way, selective muscle stimulation and on that way specific facial movements can be evoked. By recording high quality, intramuscular EMG signals or multichannel ear EMGs, an automatic distinction between different facial movements is possible.[4] Combining all these components, a closed-loop EMG-triggered electrical stimulation system could be capable of supporting the most important facial movements such as eye blink, eye closure and smile.[5] Therefore, such systems could serve as a valuable tool for rehabilitation, acting as a training system to support facial movement recovery. Additionally, the prospect of adapting this technology for implantable, but also for non-invasive devices presents an intriguing avenue for future research. Patient pathways, application scenarios, and ideas for future medical devices will be developed in an interactive exchange with the participants. Smart implants, but also small adhesive surface stimulation devises to treat facial paralysis with electrical stimulation could be an emerging application and a point of debate of our workshop.

Key words: facial palsy, telemedicine, permanent muscle denervation; electrical stimulation, facial pacing**.**

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2025Pdm3 March 25 – Abstract 012

Disentangling the Effects of Time Restricted Eating, Calorie Restriction, and Exercise on Metabolic Health

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Over the past decade, intermittent fasting (IF) has gained widespread attention as a promising strategy for improving health and metabolic outcomes. Of the various types of IF patterns, time-restricted eating (TRE), which typically involves periods of prolonged daily fasting with shortened eating windows, has become a popular form. Many experts have proposed that the benefits of TRE are solely due to the unintentional reduction in calorie intake that often occurs when individuals adopt a TRE pattern.[1] Thus, the expected effects of TRE on the biology of aging would be expected to be identical to calorie restriction (CR). However, emerging evidence calls this traditional view into question, highlighting the benefits of prolonged daily fasting periods, independent of calorie deficits, for promoting health and longevity. For example, findings from randomized controlled trials (RCTs) demonstrate that prolonged daily fasting, or TRE, improves markers of autophagy, inflammation and insulin sensitivity, independent of CR or significant weight loss.[2-4] One proposed mechanism through which these beneficial effects occur is through improved circadian alignment. Other studies have shown that exercise regimens can also improve insulin sensitivity, with or without calorie restriction.[5] The focus of this presentation is on the nuanced relationship between fasting, specifically TRE, exercise, and CR (Figure 12). We will review evidence that challenges the conventional belief that a calorie deficit is the primary driver of health and longevity. Rather, we propose that complete nutrient deprivation during extended fasting and exercise periods induces cellular and biochemical changes distinct from those induced by CR, thereby enhancing insulin sensitivity and modulating nutrient-sensing pathways associated with healthy aging.

Key words: Time-restricted eating, calorie restriction, circadian rhythms, autophagy, insulin sensitivity

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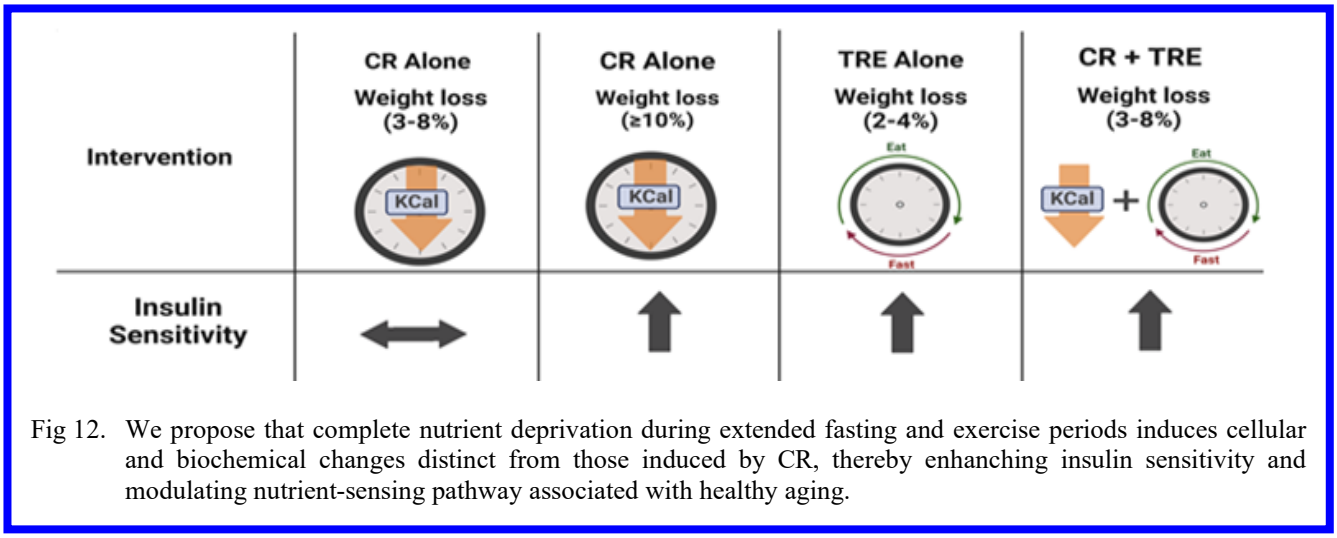

Fig 12. We propose that complete nutrient deprivation during extended fasting and exercise periods induces cellular and biochemical changes distinct from those induced by CR, thereby enhancing insulin sensitivity and modulating nutrient-sensing pathway associated with healthy aging.

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2025Pdm3 March 25 - Abstract 013

Fasting, exercise and skeletal muscle

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Fasting and exercise are key regulators of skeletal muscle metabolism, influencing substrate utilization, mitochondrial function, and protein turnover. Time-restricted eating (TRE), a form of intermittent fasting that limits food intake to specific time windows, has been explored as a strategy to enhance metabolic health while potentially optimizing exercise-induced adaptations.[1] While fasting enhances fat oxidation and insulin sensitivity, its effects on muscle protein synthesis (MPS) remain a critical area of investigation. Resistance training is a primary stimulus for MPS, activating the mechanistic target of rapamycin (mTOR) pathway, which is essential for muscle hypertrophy. However, fasting may modulate this process by reducing circulating amino acid availability, potentially attenuating post-exercise MPS if protein intake is delayed.[2] Prolonged fasting further activates catabolic pathways, leading to muscle protein breakdown (MPB) to provide gluconeogenic substrates. Nevertheless, TRE, when combined with adequate protein intake, may preserve muscle mass while improving metabolic flexibility.[3] Additionally, fasting-induced ketogenesis may mitigate some catabolic effects by providing alternative energy substrates and modulating key molecular pathways involved in muscle metabolism, such as sirtuins and AMP-activated protein kinase (AMPK).[4] The effects of fasting on endurance training are more favorable. Exercising in a fasted state enhances mitochondrial biogenesis, fatty acid oxidation, and peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α) expression, which are beneficial for endurance performance and metabolic adaptation.[1] However, protein remodeling in response to endurance exercise may be suboptimal if amino acid availability is insufficient post-exercise. TRE's effects on skeletal muscle are also influenced by meal timing relative to the circadian clock. Early TRE, where nutrient intake is concentrated in the morning and early afternoon, has been associated with improved insulin sensitivity and muscle oxidative function compared to late TRE, which may impair glucose metabolism.[5] This suggests that aligning nutrient intake with endogenous circadian rhythms may optimize muscle health outcomes. The molecular mechanisms underlying fasting-induced adaptations share commonalities with ketogenic diets (KD), as both increase reliance on fatty acid oxidation and ketone body metabolism. These shifts influence pathways related to muscle preservation, inflammation reduction, and mitochondrial efficiency.[4] However, unlike KD, fasting necessitates precise nutrient timing to prevent prolonged catabolic states. Overall, the interaction between fasting, exercise, and skeletal muscle adaptation is complex and highly context-dependent. While TRE can enhance metabolic health, muscle preservation depends on adequate protein intake and strategic nutrient timing, especially for resistance-trained individuals. Future research should refine fasting-exercise protocols to optimize both metabolic and musculoskeletal benefits

Key Words: time-restricted-eating, muscle protein synthesis, ketones, mTOR, AMPK.

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2025Pdm3 March 25 - Abstract 014

Full-Body In-Bed Gym advancements for elderly subjects

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Rehabilitation for elderly individuals presents a significant challenge, particularly for those with multiple comorbidities. The Full-Body In-Bed Gym is an innovative approach that enables comprehensive rehabilitation exercises directly in bed (Fig. 13, upper and lower panels), aiming to preserve and enhance mobility, muscle tone, cardiorespiratory function, and quality of life.[1,2] The aim of this study was to examine recent developments in the Full-Body In-Bed Gym, with a focus on its effectiveness in preventing muscle mass loss and reducing complications associated with prolonged, reduced mobility/immobility.

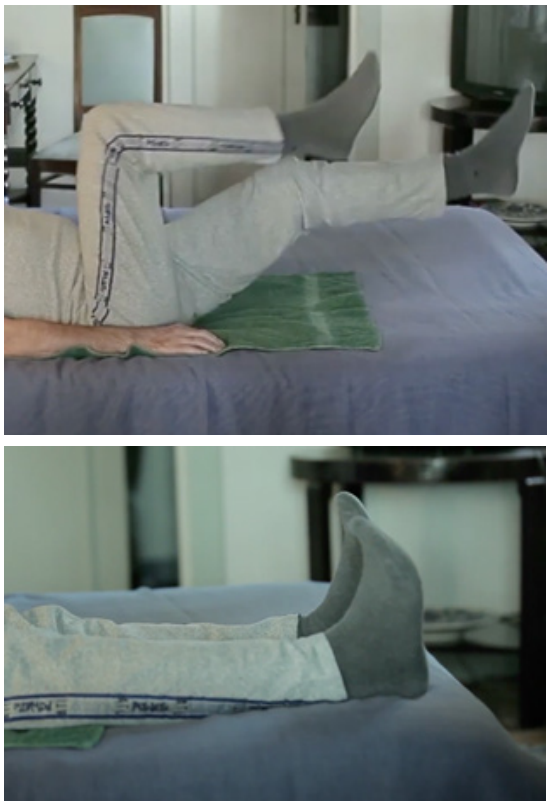

Fig 13.Two examples of the 20 exercises that can be performed in bed by seriously ill patients or simply by very elderly people.
For a full video link to:
https://www.youtube.com/watch?v=pcHKmxCLYFs

This study included an analysis of clinical trials developed over time involving the Full-Body In-Bed Gym. Patients who engaged in regular Full-Body In-Bed Gym exercises experienced significant reductions in muscle loss and improvements in functional capacity. This approach was found to be safe, well-tolerated, and had higher compliance compared to traditional exercises, facilitated by the option for in-bed execution and customization to meet each patient's specific needs.[1,3,4] The Full-Body In-Bed Gym represents an important innovation in rehabilitation of elderly patients, offering substantial benefits in preventing muscle atrophy and improving quality of life. Future developments aim to incorporate digital technologies for remote monitoring and real-time exercise adaptation.

Key words: rehabilitation; elderly; muscle; sarcopenia countermeasures.

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2025Pdm3 March 25 - Abstract 015

Restoring upper extremity motor function in tetraplegia by muscle and nerve transfers

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Regaining hand and upper extremity control is a highly prioritized goal in individuals living with tetraplegia after cervical spinal cord injury.[1] Reconstructive upper extremity surgery can improve hand function in tetraplegia.[2] However, these surgeries are technically challenging because of complicated preoperative diagnostics as well as the real-time intraoperative decisions to be made. During surgery, the following factors need to be addressed: extent of release of donor muscle-tendon complex (Figure 14)[3], routing of donor muscles, tissue preparation and optimization, tensioning of muscle-tendon units, balancing joints, and suturing tendon-to-tendon attachments. Recent advancements of nerve transfer surgeries have added

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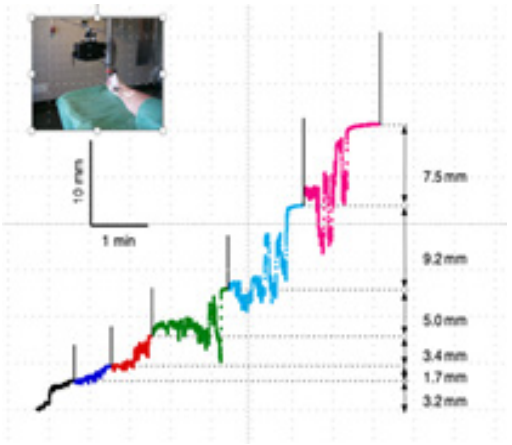

Fig 14. The length-time records measured during progressive release of brachioradialis muscle from the radius and surrounding tissues are shown. Each color represents a 3 cm release with the overall release length obtained for each segment is shown to the right of the panel. Vertical lines separating colors represent the excursion magnitude after each release.

functionality to the patients,[4] but also complexity in the planning of the reconstructions. This overview presents some of the fundamental studies of muscle-tendon-joint mechanics allowing for implementation of single-stage surgical reconstruction of hand function and early postoperative activity-based training in patients with cervical spinal cord injuries.[5] Future studies should address combined nerve and tendon transfer reconstructions in parallel with patient perceived outcome assessments.

Key words: Tetraplegia; surgery; tendon transfers; nerve transfers; donor muscle excursion; tendon-to-tendon attachment integrity.

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2025Pdm3 March 25 - Abstract 016

Differential lower motoneuron damage patterns of potential donor and recipient nerves for upper extremity nerve transfers in tetraplegia

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Regaining hand function is a high priority for individuals with cervical spinal cord injury (cSCI). Conventional therapies rely on residual cortico-spinal tract function and adaptive plasticity. Neuromodulative treatments like paired associative stimulation (PAS) or transcutaneous spinal cord stimulation (tSCS) aim to activate damaged networks and stimulate neuronal plasticity. Optimizing outcomes for incomplete lesions involves utilizing residual functions and careful timing for surgical interventions like neurotization. Adaptive plasticity and recovery depend on injury extent and are often limited. Tendon transfer (TT) has been used to restore upper extremity functions in cSCI. Nerve transfers (NT) can reanimate multiple functions with a single procedure but often yields unpredictable outcomes. Factors such as reinnervation distance, motor axon misrouting, and LMN lesions impact surgical results. For example, NT of supinator branches to the posterior interosseous nerve for finger/thumb extension have excellent outcomes but results for brachialis-to-anterior interosseous nerve transfers for finger/thumb extension are mixed. This study aimed to analyze LMN integrity using motor point (MP) testing for muscles involved in grasp and release (EDC, EPL, 5DP, FPL) and donor brachialis (BRA) muscles (figure 15). It

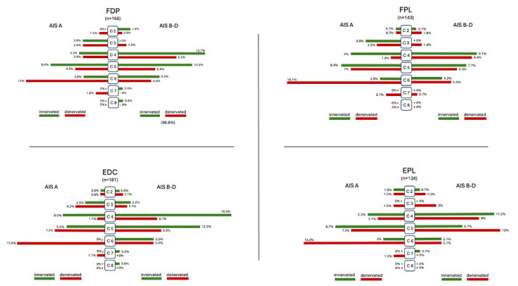

Fig 15 Percentage distribution of all FDP, FPL, EDC, EPL tested by MP mapping.
The classification was conducted according to the British Medical Research Council Scale (MRC) for testing manual muscle strength. “Innervated” indicates that the either the full range of motion could be achieved under standardised testing with electrical stimulation, which corresponds to an MRC value of 3 or a value of MRC 1-2 showing some movement or a visible contraction by MP. The muscle is classified as “denervated”, MRC 0, if no muscle contraction is visible.

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sought to identify key lesion characteristics determining NT outcomes. The retrospective cross-sectional study assessed LMN integrity via MP testing of 15 upper limb muscles in 227 cSCI patients (C1–C8, AIS A–D) from 2017 to 2023. Complete datasets included demographic details, lesion level (ISNCSCI), and muscle testing data recorded 3–4 months post-injury. Muscles with an MRC score of 0 or 1 were included. Recipients were grouped as AIS A (complete) or AIS B-D (incomplete) and categorized by innervation status. BRA was analyzed for denervation.

Muscles	AIS	Innervation Status	p-value
FDP/EDC	A	Denervated	p=0.0019(**)
FDP/EDC	B-D	Denervated	p<0.0001(****)
FDP/EDC	A	Innervated	p<0.000(****)
FDP/EDC	B-D	Innervated	p=0.5038 (ns)
FPL/EPL	A	Denervated	p= 0.6895 (ns)
FPL/EPL	B-D	Denervated	p= 0.5641 (ns)
FPL/EPL	A	Innervated	p<0.0001(****)
FPL/EPL	B-D	Innervated	p=0.9164(ns)

Table 1: Fisher's Exact Test illustrating the association between the matched muscle pairs FDP/EDC and FPL/EPL tested by MP mapping as denervated or innervated for the AIS classification A and B-D. Significance level (□) was set to p<0.05.

Motor Point (MP) Integrity Testing. MP testing detected LMN damage using surface electrical stimulation. MPs were localized on the forearm or upper arm, and responses classified as "innervated," "partially denervated," or "denervated" based on MRC scores. Testing involved patients in a seated position, defined stimulation parameters, and electrode placement based on anatomical references. Stimulation intensity levels correlated with muscle size and function, with partial and complete LMN damage grouped for analysis. Descriptive statistics illustrated LMN integrity relative to lesion level. Fisher's exact test evaluated associations between matched muscle groups, with significance set at p<0.05 (Table 1). Demographics were reported as mean ± standard deviation.

Results: a) Distribution of LMN integrity in FDP/EDC and FPL/EPL. Data from 189 patients (mean age 52.8 ± 19.2 years, C1–C8 AIS A–D) included 166 FDP, 181 EDC, 143 FPL, and 134 EPL muscles. Distribution of innervation and denervation categories by lesion level is shown in Figures 14. In total, 152 FDP and 195 EDC muscles were analyzed for AIS A and B-D groups. Similarly, 142 FPL and 135 EPL muscles were included (Figure 16). Fisher's exact test identified statistically significant differences in three of four comparisons for FDP and EDC muscles. For FPL and EPL, one of four comparisons was significant (Table 1). b) Distribution of LMN integrity in BRA Data from 112 patients (mean age 59 ± 7 years, C1–C8 AIS A–D) showed 19% of BRA muscles were denervated or partially denervated distributed across lesions C2 to C6 (Figure 16).

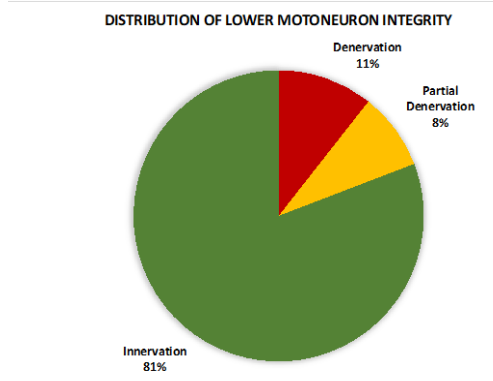

Fig 16. Brachialis muscles (BRA) were denervated or partially denervated and distributed across lesions from C2 to C6.

In conclusion, the study highlights the importance of assessing lower motoneuron (LMN) integrity for determining outcomes of nerve transfer (NT) procedures in individuals with cervical spinal cord injury (cSCI). Motor point (MP) testing revealed variability in the innervation status of key muscles (FDP, EDC, FPL, EPL, and BRA) used for grasp and release restoration. NT outcomes for FDP/EDC muscles in both complete (AIS A) and incomplete (AIS B-D) injuries demonstrated statistically significant associations in most comparisons, whereas FPL/EPL outcomes were less consistent. The brachialis (BRA) muscle, a critical donor for NT, showed that nearly 19% of cases were partially or completely denervated, primarily associated with higher-level cervical lesions (C2-C6). The results suggest that preoperative assessment of LMN integrity is vital to identify suitable donor and recipient muscles for NT. Variability in functional outcomes emphasizes the need for individualized surgical planning. Further research should focus on refining MP testing methods, exploring mechanisms of NT variability, and optimizing timing and techniques to improve functional recovery in individuals with cSCI.

Key words: motor point testing; cervical spinal cord injury; neurotization; lower motor neuron integrity.

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2025Pdm3 March 25 - Abstract 017

Direct Measurement of Human Skeletal Muscle Specific Tension *In Vivo*

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The intrinsic force production capability of human muscle can be expressed as its "specific tension," or, the maximum force generated per cross-sectional area of muscle fibers. This value can be used to determine, for example, whether muscle quality changes during exercise, atrophy, disease, or hypertrophy. A value of 22.5 N/cm2 for mammalian muscle has generally become accepted based on detailed studies of small mammals.[1] Determining the specific tension of human muscle is much more challenging since almost all determinations are indirect. In this study we leveraged a unique surgical technique in which a human gracilis muscle is transferred from the thigh to the arm, restoring elbow flexion after brachial plexus injury.[2] During this surgery we directly measured subject specific gracilis muscle force-length relationship in situ and properties ex vivo (Figure 17 A). [3] From these experimental data we established a human muscle fibre-specific tension of 171 kPa. We also determined the average gracilis optimal fiber length is 12.9 cm. which was about half of the previously reported optimal fascicle lengths of 23 cm4. Thus, the long gracilis muscle appears to be composed of relatively short fibres acting in parallel that may not have been appreciated based on traditional anatomical methods that are based on extensive muscle fiber dissections (Figure 17 B). In a related systematic review, we screened 1,506 published papers and identified the 29 studies published between 1983 and 2023 that used appropriate methods, and which reported 95 human specific tension values. We weighed each parameter based on whether it was directly measured, estimated, or calculated based on the literature, with decreasing weighting used, the more indirect the methods. Based on this exhaustive review of the relevant human literature, we suggest that the most accurate value that should be used for human muscle specific tension is 26.8 N/cm^2**.**

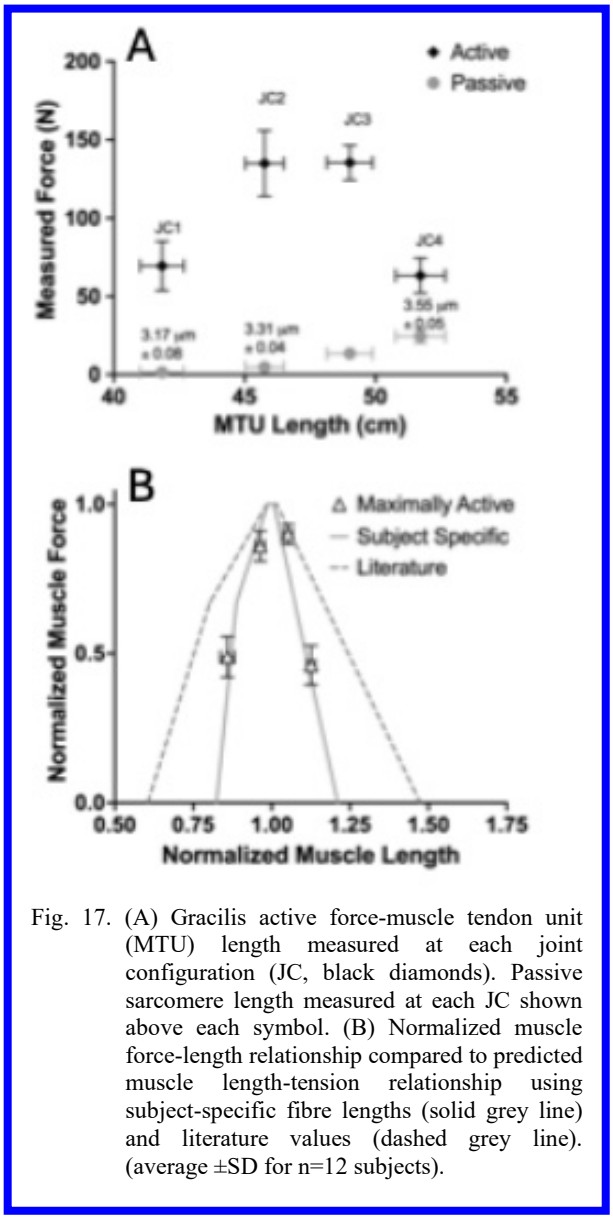

Fig. 17. (A) Gracilis active force-muscle tendon unit (MTU) length measured at each joint configuration (JC, black diamonds). Passive sarcomere length measured at each JC shown above each symbol. (B) Normalized muscle force-length relationship compared to predicted muscle length-tension relationship using subject-specific fibre lengths (solid grey line) and literature values (dashed grey line). (average ±SD for n=12 subjects).

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2025Pdm3 March 25 - Abstract 018

Muscle-muscle cross-talk during unilateral electrical/mechanical stimulation

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The dramatic muscle wasting associated with Critical Illness Myopathy (CIM) is strongly related to the complete mechanical silencing (absence of external and internal strain caused by loss of passive weightbearing and strain caused by the activation of contractile proteins). This complete mechanical silencing is uniquely observed in deeply sedated or pharmacologically paralyzed mechanically ventilated intensive care unit patients (ICU). In experimental and clinical studies, we have studied the restoring effects of unilateral passive mechanical loading or electrical stimulation on contractility muscle fiber size, gene- and protein-expression.[1-6] Restoring effects have been documented in muscle morphology, contractility, regulation of protein synthesis and degradation, apoptotic pathways and mitochondrial properties. However, unexpected findings were observed in significant cross-over effects on glycogen levels and neuromuscular junction morphology in the contralateral pharmacologically paralyzed and immobilized muscles (Figure 18). It was hypothesized that the cross-over effect was mediated by the release of cytokines/chemokines (myokines) systemically having autocrine, paracrine and endocrine functions.[7] A proximity

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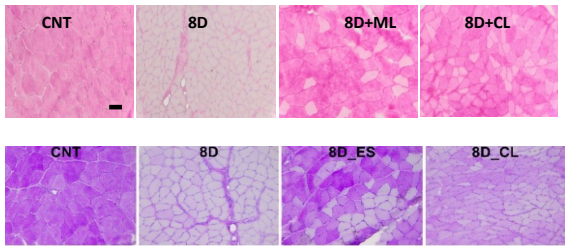

Fig 18. Top: control (CNT), 8 days mechanical ventilation and immobilization (8D), 8 days mechanical ventilation, immobilization and passive mechanical loading (8D+ML), 8 days contra-lateral unloaded limb (8D+CL). Below: control (CNT), 8 days mechanical ventilation and immobilization (8D), 8 days mechanical ventilation, immobilization and days electrical stimulation (8D_ES), 8 days contra-lateral unloaded limb (8D_CL). Scale bar 200µm.

extension assay proteomics approach was taken using a mouse cytokine/chemokine panel to explore the mechanism(s) underlying the muscle-nerve crosstalk and crossover communication. Myokines were searched for demonstrating increased levels in plasma, stimulated and unstimulated soleus and being different from 8 days unstimulated rats. Cytokines Ccl3 and TGFβ1 fulfilled these criteria supporting the hypothesis that myokine production induced by electrical or mechanical stimulation were released systemically and having both paracrine and endocrine functions (Figure 19). Pilot experiments showed complete restoration of myosin when the number of mechanical loadings were increased from 13 to 22 per minute on the loaded, but not on the unloaded side, indicating that mechanosensation may be more important for myosin expression than depolarization calcium triggered events. However, this needs to be explored in a larger group of animals.

Key words: Muscle-muscle cross-talk; unilateral electrical stimulation; mechanical stimulation.

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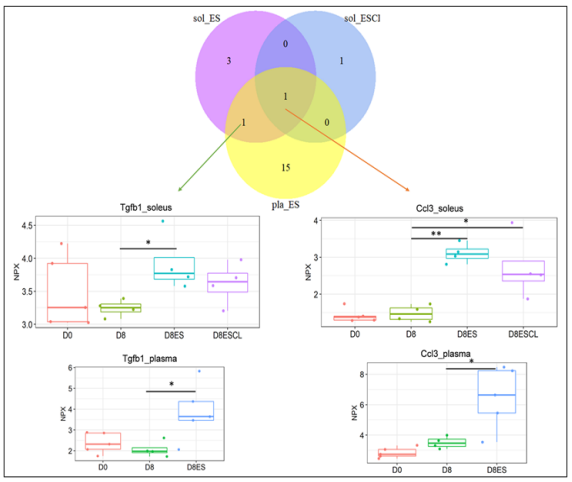

Fig 19. D0: soleus muscle of sham-operated rats (n = 5); D8: soleus muscle of 8-day pharmacological denervated rats (n = 4); D8ES: electrical stimulated soleus muscle of 8-day pharmacological denervated rats with electrical stimulation (n = 5); D8ESCL: unstimulated contralateral soleus muscle of 8-day pharmacological denervated rats with electrical stimulation (n = 5).

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2025Pdm3 March 25 - Abstract 019

Mechanisms of action of hyperbaric oxygen therapy

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Hyperbaric oxygen therapy (HBOT) is a non-invasive method of O2 delivery that induces systemic hyperoxia. Hyperbaric chamber consists of a pressure vessel and a compressed breathing gas supply, which can regulate internal pressure. The chamber delivers 100% O2 to patients according to predetermined protocols and is monitored by trained personnel. HBOT causes hyperoxia that amplifies the tissue-cellular diffusion gradient of oxygen, which as a result raises plasma dissolved oxygen to a level that exceeds the physiological needs of many tissues at rest. The practical clinical use of high-pressure oxygen was framed from commonly accepted physiological principles and the laws of Boyle, Dalton, and Henry. The latter leads to compression

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of all gas-filled spaces in the body and is helpful in treating diseases in which gas bubbles are present in the body, such as intravascular embolism and intravascular or intratissue bubbles in decompression sickness. An elevated O2 partial pressure in certain tissues leads to increased production of reactive O2 species (ROS) and reactive nitrogen species (RNS) due to hyperoxia. Some studies suggested a correlation between ROS levels and higher HBOT exposure time. HBOT also accelerates wound healing by promoting epithelialization and oxygen-dependent collagen matrix formations needed for angiogenesis. Furthermore, HBOT prevents leukocyte adhesion that con tributes to the release of free radicals and proteases, thus protecting cells from pathologic vasoconstriction and cellular damage during reperfusion. HBOT also enhances neutrophil oxygen-dependent microbial killing, reduces edema and inhibits lipid peroxidation in hypoxic tissues. New insights have indicated HBOT potential mechanisms are related to its ability to preserve mitochondrial activities. In addition to that, Inflammation and immune mechanisms may play an important role in the development of neuropathic pain and hyperalgesia as well. Currently, there are 15 indications for HBOT approved by the Undersea and Hyperbaric Medicine Society, categorized into three groups: emergency medicine, wound healing acceleration, and antimicrobial effects. The present narrative review aims to elucidate the mechanisms of action underlying HBOT, particularly oxy-inflammation in various pathologies within these categories.

Key Words: Mechanisms of action; oxy-inflammation; hyperbaric oxygen therapy.

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2025Pdm3 March 25 - Abstract 020

Transient hyperoxia after exercise-until-exhaustion to mitigate aging muscle decay: a new mechanism for training-addiction over time?

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Patients' adherence to rehabilitation prescriptions is an important issue that physiatrists address without often being successful.[1] It is not my case. As many readers know, I have been addicted to every morning exercises in bed since 2017.[2,3] I had to gradually increase in number and intensity my routine to reach my final morning goal: a series of push-ups on the floor until exhaustion.[4] At January 2024, I have achieved what is now my "new 2024 standard" by adding new exercises in bed, specifically some stretching exercises while holding muscle contractions for ten breaths. This new 2024 standard consists of 23 gymnastic exercises: 13 in bed, i.e. 10 repetitions of the hands; Ankles; Arms up; Forced elastic ankles; Ventilation with Arm-Up; MiniBridges; Pedal with both legs raised; Alternative extended leg; Maximum deep ventilation; Alternating stretch of 1 leg; Two-legged caution; Raise your shoulder with your arms outstretched on the bed; Body flexion. Six standard sitting exercises. Three-Stand&Sit, i. e., stand up, stand on tiptoe, sit down with 3 seconds of squats. Push Up on the floor until exhaustion (now in February 2025 between 40 and 50). Final Stand Up. This incremental routine was introduced after I started half-day fasting to lose kilograms of body weight and inches of waistline and testing my blood oxygenation during night's rest and after the Bed-Gym-at-exhaustion using a pulse oximeter applied to the left medial finger. To my surprise, not being an expert physiologist,[2,3] I found that at sea level from 90-92% oxygenation during the night, the pulse oximeter jumped up to almost 100% immediately after push up training on the floor to exhaustion.[4] Whether this is an artifact related to increased cardiac frequency, I do not know, but I think it is not, because the changing values of cardiac frequency and derived percentage of oxygenation do not have the same trends. My blood oxygen saturation slowly decreases over the next 15 minutes and then remains at the 94-96% level, if I start my normal daily activity in Padua. On the other hand, 15 minutes of complete rest brings the value to those of a night's rest. I also recorded the variations in pulse oximeter values in the Dolomites at 1500 meters above sea level. The only variation is a slight drop in values of 1-2% during the night, but after physical activity at exhaustion the values are those very high recorded at sea level. I wonder if the brief increase in oxygen saturation after Bed-Gym to exhaustion is part of the mechanisms improving skeletal and ventilatory muscles, but also brain, contributing to the mood-boosting effect of daily morning exercise at exhaustion. Whatever the mechanism, perhaps a transient acidophilia, the effect on mood is the same as that induced by the good glass of Prosecco which we will have after a brief discussion on this proposal. In any case, what is certain is that oxygen therapy is a well-known aid in many pathologies.[5]

Key words: Addiction to physical exercise; perseverance/compliance exercise at exhaustion; pulse oximeter values at exhaustion; cardiac frequency.

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2025Pdm3 March 26 - Abstract 021

New insights leading to improved designs of micro-dystrophins for use in AAV vectors

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2025Pdm3 March 25 - 29, 2029

Adeno-associated viruses (AAVs) containing versions of truncated dystrophin (micro-dystrophins) are being delivered to patients with Duchenne muscular dystrophy (DMD) in clinical trials. DMD is a progressive, childhood onset muscle wasting disease caused by mutations in the DMD gene that result in the loss of dystrophin protein in all muscle types.[1] These clinical gene therapies aim to overexpress a truncated version of dystrophin in striated muscle capable of achieving partial correction of the disease. To avoid the immune response that is due to the inclusion of N-terminal segments of dystrophin being present in the micro-dystrophins, we have examined a strategy that uses the N-terminal region of utrophin combined with C-terminal components of dystrophin (Figure 20). We have evaluated a series of such constructs that include different C-terminal components using a severe mouse model of DMD, the D2.mdx mouse.[2-4] We administered doses of AAV comparable to those used in clinical trials. We have observed improvement in both the skeletal muscle and cardiac muscle disease progression. We will report on our continued progress in designing a safe construct that should not provoke an immune response in patients and benefit the heart as well as skeletal muscle.

Key Words: Duchenne muscular dystrophy, AAV, gene therapy, cardiomyopathy

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2025Pdm3 March 26 - Abstract 022

Proteomic profiling of the dystrophin complexome in skeletal muscle,

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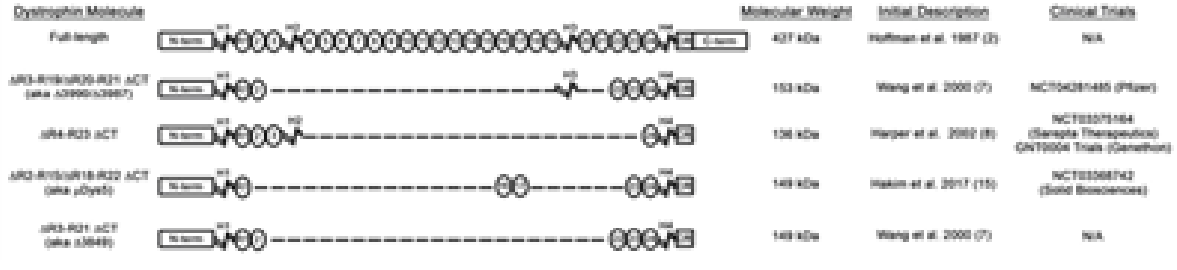

Fig 20. Structure of dystrophin and micro-dystrophin constructs. A schematic diagram of full-length dystrophin, the micro-dystrophin versions currently utilized in clinical trials, and a modified micro-dystrophin construct we used in past studies (ΔR3-R21 ΔCT) that is detrimental to the heart when expressed at high levels (5).

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The membrane cytoskeletal protein dystrophin of 427 kDa (Dp427-M isoform) and its associated glycoproteins, consisting of dystroglycans, sarcoglycans, sarcospan, dystrobrevins and syntrophins, form a supramolecular complex at the sarcolemma of muscle tissues (Figure 21).[1]

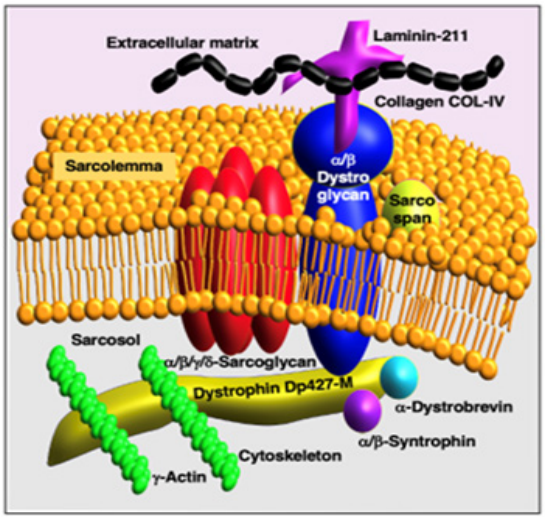

Fig 21. Diagrammatic presentation of the sarcolemmal dystrophin-glycoprotein complex from muscle. Reproduced with permission

The dystrophin node was shown to be involved in a variety of key cellular functions, including the integration of cytoskeletal organization, maintaining lateral force transmission at costameres, promoting myofiber stability during repeated excitation-contraction-relaxation cycles and enabling cellular signaling cascades in skeletal muscle.[2] Importantly, primary abnormalities in the DMD gene result in the almost complete absence of dystrophin and a drastic reduction in dystrophin-associated glycoproteins in X-linked Duchenne muscular dystrophy, the most frequently inherited neuromuscular disorder of early childhood. The collapse of the sarcolemmal dystrophin network causes fragility of the surface membrane system and an increased frequency of plasmalemmal micro-rupturing. The resulting influx of calcium ions was shown to trigger elevated levels of proteolysis which renders dystrophin-deficient myofibres more susceptible to cellular degeneration.[3] Myonecrosis is associated with chronic inflammation, fat substitution, reactive myofibrosis and satellite cell dysfunction.[4] In order to better understand the composition and biological properties of the dystrophin complex in both normal skeletal muscles and X-linked muscular dystrophy, it is crucial to isolate the supramolecular dystrophin assembly for detailed biochemical analyses (Figure 21). The cytolinker and its tightly associated core complex can be conveniently isolated by a combination of ion exchange chromatography, lectin agglutination and density gradient ultracentrifugation. Elaborate studies of the dystrophin complexome were carried out by subcellular fractionation approaches, immuno-precipitation, chemical crosslinking analysis, blot overlays and mass spectrometry. Key techniques used in muscle proteomics were recently reviewed and have been applied to studying dystrophin and its associated proteins.[5] The wider dystrophin complexome appears to contain besides the core elements of the sarcolemmal glycoprotein assembly also key components of the extracellular matrix, such as laminin, fibronectin, biglycan and various collagens, and intracellular components of the cytoskeletal network, such as actin and tubulin.

Key words: dystrophin; dystrophin-glycoprotein complex; mass spectrometry; muscular dystrophy; proteomics.

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2025Pdm3 March 26 - Abstract 023

Lipotoxicity and lipophagy in NLSDM: mechanisms and treatments

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Neutral lipid storage disease with myopathy (NLSDM, MIM #610717) is a rare autosomal recessive lipid storage myopathy characterized by the accumulation of triacylglycerols (TAGs) within cytoplasmic lipid droplets (LDs) across multiple tissues, including skeletal muscles, heart, liver, and peripheral blood.[1-2] Neutral lipid metabolism defect in NLSDM patients is due to the impaired or diminished activity of adipose triglyceride lipase (ATGL). ATGL plays a key role in lipolysis, catalyzing the release of the first fatty acid (FA) from TAGs stored within the LDs.[3] Moreover, this lipase is involved in lipophagy, a form of selective autophagy targeting LDs.[4-5] Indeed, ATGL is able to interact with LC3 throw its LC3-interacting region (LIR) motifs.

Currently, the molecular pathways driving NLSDM pathogenesis are not fully understood. It can be hypothesized that the accumulation of neutral lipids triggers a condition of lipotoxicity in patient cells. In particular, while storing lipids as inert TAGs in LDs is generally safe, the accumulation of lipid intermediates, like non-esterified FAs, and signaling lipids, such as ceramide and diacylglycerol, is linked to lipotoxic effects. Different lines of control and NLSDM fibroblasts were cultured with 100, 200, and 400 µM of oleic acid (OA) for 24 and 48 hours, and cell viability was verified via a trypan blue assay, enabling the tracking of live and dead cells at the two time-points. Treatment with 200 and 400 µM OA resulted in an inhibition of cell growth across all NLSDM lines except one, while in control fibroblasts slight proliferation decrease was detected exclusively after a 400 µM OA supplementation. Since the number of dead cells remained low across all conditions, adding OA likely inhibited fibroblast division without affecting their survival. The absence of caspase 3 or PARP1 cleavage indicated the lack of apoptotic events. Moreover, cellular extracts of control and NLSDM fibroblasts cultured in Earle's MEM with 10% FBS were used to analyze the expression of some proteins involved in lipophagy. As expected, preliminary results revealed an increased amount of Perilipin 2, a coating LD protein, in all NLSDM fibroblasts in comparison with control lines. Interestingly, higher levels of HSC70 were also observed in NLSDM cells. HSC70 is recognized for its role as regulator of chaperone-mediated autophagy/ lipophagy. When OA was added in a serum-free medium, control fibroblasts, where chaperone-mediated autophagy (CMA) was active, showed a decrease in both HSC70 and Perilipin 2 levels. This reduction was not seen in NLSDM fibroblasts. In addition, a control and an NLSDM cell line were cultured with 500 µM of Metformin for 24 hours. Preliminary protein analysis suggests that this treatment may reduce p62 expression in NLSDM fibroblasts. A decrease in levels of p62 is known to indicate an increase in autophagic flux. Our findings seem to indicate that NLSDM fibroblasts show a lower ability to metabolize higher concentrations of FAs compared to control cells. This defect probably correlates with partial or complete impairment of lipolysis as well as decreased lipophagy.

Key words: NLSDM; ATGL; lipolysis; lipophagy; lipotoxicity.

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2025Pdm3 March 26 - Abstract 024

Pharmacological Treatment through HiPSC-based Drug Repurposing for ultrarare congenital myopathies

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Congenital myopathies (CM) are a group of heterogeneous genetic diseases characterized by distinctive alterations on muscle biopsies, usually associated with neonatal or early-onset hypotonia and muscle weakness. Different groups of congenital myopathies exists and at least 40 genes have been associated to these conditions, some of them being ultrarare. Pathophysiological mechanisms underlying muscle dysfunction in ultrarare CM are largely unknown, making it difficult to suggest therapeutic approaches to reduce the disease burden. Despite the emergence of gene therapies for some CM types, challenges like hepatic toxicity and tolerability concerns highlight the complexity of CM gene therapies discovery (Figure 22). To address the unmet

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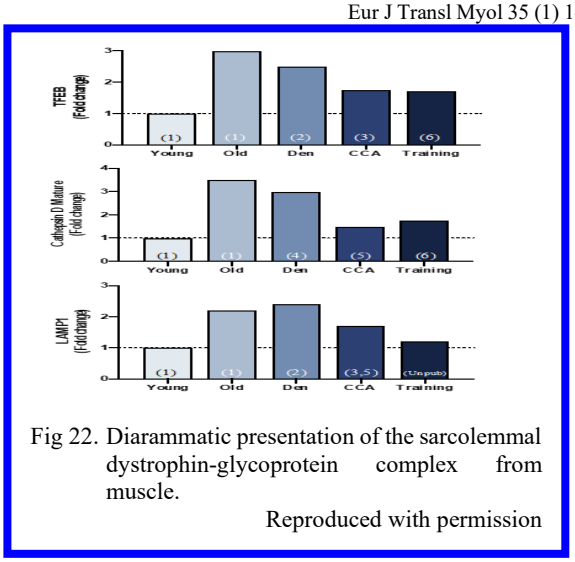

Fig 22. Diarammatic presentation of the sarcolemmal dystrophin-glycoprotein complex from muscle.

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medical need, our project focused on four ultrarare and life-debilitating CM types: CACNA1S-CM, PYROXD1-CM, ACTN2-CM, and FHL1-RB-CM. CACNA1S encodes the pore-forming subunit of DHPR (dihydropyridine receptor) channel in skeletal muscle. DHPR is a voltage-gated L-type Ca2+ channel located on the T-tubule. PYROXD1 is a class I pyridinenucleotide-disulfide oxidoreductase (PNDR), monomeric NAD(P)H-oxidizing flavoenzyme, found in the nucleus and sarcoplasm of skeletal muscle. ACTN2 is a structural skeletal muscle protein localized at the Z-line in both skeletal and cardiac muscle. It regulates the ion channels and is essential for the integrity of the contractile apparatus through a multitude of interactions. FHL1 is a structural skeletal muscle protein and localizes to the I-band and M-line of the sarcomere, the sarcolemma and the nucleus. Importantly, FHL1 mediates protein–protein interactions, scaffolding signaling proteins in the cytoplasm and transcription factors in the nucleus. All the above-mentioned proteins, when defective lead to ultrarare form of CM. As induced pluripotent stem cells (iPSCs) can provide a near-unlimited source of cells while conserving the genetic background of the donor, firstly we generated patient-specific iPSCs in order to establish relevant in vitro models of each CM type. The lines displayed typical iPSC morphology, uniform expression of pluripotency markers, trilineage differentiation potential and normal karyotypes. CACNA1S-CM iPSCs cells obtained from 4 different patients harboring both autosomal dominant and autosomal recessive CACN1AS variants. We obtained mature myotubes and showed that our system model successfully recapitulated the decrease in CACNA1S protein found in the muscles of CACNA1S-CM patients. Dominant and recessive CACNA1S variants did not affect the formation of striated myotubes nor affect their maturation level. Furthermore, Dominant and recessive CACNA1S variants impaired the ECC machinery showing decrease in RYR1 protein, subunits of the DHPR complex (DHPRβ and DHPRγ), CASQ1 and ATP2A1. Eventually they showed decreased Ca2+ release capacity from the sarcoplasmic reticulum upon Ach stimulation. Phenotype analysis of PYROXD1-CM, ACTN2-CM, and FHL1-RB-CM iPSCs cells is ongoing. In conclusion, we are convinced that the characterization of these models will enable the identification of therapeutic targets and assayable readouts. High-throughput screening of repurposable drug libraries will be conducted to identify compounds that correct disease-specific readouts. The most promising compounds will then be validated in available animal models, including zebrafishes and mice. Through the application of induced pluripotent stem cell (iPSC)-derived skeletal muscle cell models and animal models, this project seeks to shed light on underlying pathogenic mechanisms, identify therapeutic targets, and accelerate clinical translation.

Key words: Congenital myopathies; hIPSc, drug; repurposing.

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2025Pdm3 March 26 - Abstract 025

Remodeling of neuromuscular junction in dystrophic sarcomeric muscles

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Neuromuscular junction undergoes several morphological and molecular changes to functionally adapt to the degenerative process characteristic of muscular dystrophies, from, one side generally due to an adaptation to the commonly occurring myofiber necrosis and fibroadipose tissue substitution, and from the other side specifically linked to the unique pathogenic mechanism underlying each one of the different forms of muscular dystrophies depending upon their causative mutated gene. Interstitial fibrosis and fatty acid substitution of degenerated muscle is able to induce post-synaptic acetylcoline receptor subunit 4 proliferation in survival myofibers, this in the attempt to guarantee increased efficiency of post-synaptic sarcolemmal excitability and counteract reduced efficiency of neuromuscular junction small arteries blood supply due to interstitial fibrosis. Also presynaptic acetylcholine reuptake seems to be enhanced, due to some hyperexpression of the protein internalizing carrier. In front of these neuromuscular junctional changes, remodelized diseased myofibers are

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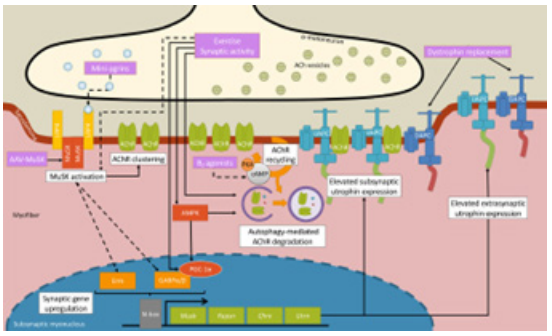

Fig 23. From Ng SY, Ljubicic V, 2020.[5]

susceptible to increased fatigue during contraction owing to their underlying causative genetic defect. Functional Electrical Stimulation (FES) was utilized in our laboratories in 1990 and thereafter in order to reduce low frequency fatigue in dystrophic skeletal muscle, this latter thought to be a detrimental factor in everyday life activities of patients affected by dystrophic disorders. Such an effect of electrical motor nerve stimulation would be associated, at muscle tissue level, to enhanced iNOS mediated mechanisms of controlling small arteries dilatation and flux and capillary permeability at neuromuscular junction with optimal consequences on oxygen delivery to nearby cellular elements of motor plaques, a mechanism that can be considered of value also in view of the emerging disease modifying therapies in muscular dystrophies.

Key words: neuromuscular junction; muscular dystrophies; electrical stimulation; muscle fatigue.

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2025Pdm3 March 26 - Abstract 026

Development of a 3D muscle tissue model of Pompe disease

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Glycogen storage disease type II (GSDII), or Pompe disease (PD), is an inherited lysosomal disorder due to biallelic mutations on the GAA gene, leading to absent or decreased activity of the acid alpha glucosidase enzyme, which is necessary for glycogen breakdown, then leading to its buildup in various organs.[1] The phenotypic spectrum of this disorder ranges from a severe, multisystem involvement manifesting in the perinatal or infantile age (Infantile Onset Pompe Disease, IOPD) to a later, mostly myopathic form with a limb-girdle distribution of weakness (Late Onset Pompe Disease, LOPD); severity of disease greatly depends on the residual enzymatic activity.[2] LOPD exhibits a great phenotypic variability, which has not been yet fully understood. Moreover, the possibility to recapitulate the disease pathogenesis in a complex in-vitro model could enhance biomarkers research and therapeutic development. With this aim, we developed a 3D in-vitro model of the muscular involvement in LOPD. Starting from immortalized myoblasts lines (one from a LOPD patient and one from a matched control) we characterized myoblasts and myotubes LOPD-specific features (GAA transcript levels, enzymatic activity, glycogen content). The same essays were then repeated on 3D models. Moreover, as a parallel project, we generated two new IOPD human induced pluripotent stem cells (hiPSCs) lines which will be utilized for a multisystem involvement modeling.

Key words: Pompe disease; in vitro modeling; 3D modeling; hiPSCs.

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2025Pdm3 March 26 - Abstract 027

Multifactorial Systemic Factors Affecting SMA bone health in patients and a mouse model of the disease

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Spinal muscular atrophy (SMA) is a rare developmental disorder affecting multiple tissues. Among the non-central nervous system tissues implicated in SMA is the skeletal system, including bone and cartilage. Low bone mineral density, increased fractures of the long bones and vertebra, hip pain, and scoliosis have been reported across the spectrum of SMA patients. While lack of ambulation likely contributes significantly to bone pathology, SMA patients have markedly lower bone density compared to other non-ambulatory patients with muscle pathologies such as Duchenne's muscular dystrophy, suggesting that there is a cell-intrinsic contribution of SMN to bone function. Mouse models of SMA have also confirmed the presence of bone and cartilage phenotypes. Recent advancements in therapeutic strategies, approved by both the FDA and the EMA, have represented a leap forward in the management of SMA. Despite these undeniable successes, treatment gaps remain. Post-treatment, patients frequently face continued challenges with skeletal health, underscoring the urgent need for more comprehensive therapeutic strategies that ca target these problems.
To date, no molecular map exists of the changes that occur in SMA patient bone and cartilage, impeding the ability of finding targeted therapies. To address this clinical need, we profiled the transcriptome of the vertebral bone and cartilage in a cohort of 11 Type II SMA patients who were undergoing surgery for scoliosis correction and compared them to 7 idiopathic scoliosis and 2 DMD controls. Additionally, we characterized the skeletal health of a mouse model of type I SMA. We find that multisystemic factors including liver and muscle health affect the underlying SMA bone pathology. Specifically, we find alterations in the balance between osteoclasts and osteoblasts, changes in PPAR signaling, mitochondrial oxidative phosphorylation and fatty acid beta-oxidation, and alterations in the muscle-derived factor Irisin that play a role in overall SMA bone pathology

Key words: Spinal muscular atrophy; bone; combination treatments.

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2025Pdm3 March 26 - Abstract 028

Reversion of RNA toxicity and muscle dysfunction in Myotonic Dystrophy

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Abstract: WITHDRAW

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2025Pdm3 March 26 - Abstract 029

Effects of age and sex in human muscle secretome,

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During aging there is a decline in physiological health, leading to reduced functionality of tissues1. Relating to skeletal muscle, it leads to reduced strength and mass, accompanied by a reduced regenerative capacity. Muscle is a secretory organ capable of regulating its own function and/or influencing the activity of other tissues via myokines2. In this context, how muscle secretion is modified during aging and how this affects muscle regeneration and homeostasis is still not known. Combining bioinformatic analysis and in vitro experiments we have analyzed how age affects the skeletal muscle secretome. For that, we have analyzed by proteomic approaches the medium of differentiated human muscle cells isolated from muscles of young (15 to 25 years old) and old (60 to 86 years old) subjects. The analyzed cells from old donors presented did not present any difference to the young cell lines regarding cell proliferation and fusion index. However, myotubes from old donors presented impaired mitochondrial function and increased in the protein aggregation, two hallmarks of aging3. Regarding the muscle secretion, we have identified 127 proteins differentially secreted between the young and old samples. In parallel, it is known that male and female respond differently to muscle aging and present different DNA methylation and gene expression profiles4. Using In silico transcriptome analyses from male and female using the Genotype-Tissue Expression study of young adults (12 females and 30 males) and older adults (6 females and 12 males) we observed that besides age, sex acts as a major source of variation in the muscle transcriptome. We also identified by using Principal component analysis in our data, that the sex has an impact in the secreted proteins, but not the in the proteome profile of the same cells. Altogether, these results suggest that aging and sex difference have major effects in the muscle secretome and we aim to identify specific targets to reduce the effects of muscle aging in the elderly, by testing in vitro the proteins of interest identified in the muscle secretome

Key words: Aging; Secretome; Proteomics; Sex-effect.

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2025Pdm3 March 26 - Abstract 030

Transcriptomic characterization of Type II SMA muscle to understand the variability in phenotypes and treatment response,

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Spinal muscular atrophy (SMA) is a recessive, developmental disorder caused by the genetic loss or mutation of the gene SMN1 (Survival of Motor Neuron 1). SMA is characterized by neuromuscular symptoms and muscle weakness. Several years ago, SMA treatment underwent a radical transformation, with the approval of three different SMN-dependent disease modifying therapies. This includes two SMN2 splicing therapies – Risdiplam and Nusinersen. One main challenge for Type II SMA patients treated with these drugs is ongoing muscle fatigue, limited mobility, and other skeletal problems. To date, few molecular studies have been conducted on SMA-patient derived tissues after treatment, limiting our understanding of what targets remain after the principal spinal cord targeted therapies are applied. Therefore, we collected paravertebral muscle from a cohort of 28 SMA Type II patients spinal surgery for scoliosis, some treated and other not treated with the state-of-the-art therapies, and 11 controls. We used RNA-sequencing to characterize their transcriptional profiles and correlate these with muscle histology and generate subgroups of transcriptional profiles to describe the evolution of the disease. Using single-nucleic RNA-sequencing, we were further able to understand changes in muscle cell type composition and the crosstalk between these cellular populations. Epigenetic characterization of these samples using 5hmC-sequencing further highlighted changes in enhancer use that may determine muscle changes. Despite the cohort size and heterogeneity, we observed a consistent loss of oxidative phosphorylation machinery of the mitochondria, a decrease in mitochondrial DNA copy number, and a correlation between signals of cellular stress, denervation and increased fibrosis. This work provides new putative targets for combination therapies for Type II SMA.

Key words: Spinal muscular atrophy; Transcriptomics; mitochondria.

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2025Pdm3 March 26 - Abstract 031

Cell specific loss of MBNL: implication for Myotonic Dystrophy skeletal muscle homeostasis

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Abstract: WITHDRAW

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2025Pdm3 March 26 - Abstract 032

Role of the lysosome in maintaining muscle health across the lifespan

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Regulation of skeletal muscle health involves the coordinated activity of cellular organelles. Mitochondria produce energy for muscle contraction, and they can be increased in muscle by exercise training. In contrast, mitochondria can be reduced within the cell by extended periods of muscle disuse. This decline in mitochondria occurs when mitochondria display dysfunction, and it is mediated by the process of mitophagy in which they are delivered to lysosomes for degradation. The terminal step of mitophagy involves the fusion of autophagosomes containing defective mitochondria with the lysosome for degradation and recycling. Lysosomes have an acidic interior and many hydrolytic enzymes that operate at a low pH which facilitates the degradation of dysfunctional cargo. Our previous work has shown that chronic exercise via training or chronic contractile activity (CCA) leads to improved mitochondrial function and content and can induce coincident increases in lysosomal proteins as well (Fig. 1; 1,5,6,7, unpublished data). This suggests that situations of reduced lysosomal function could potentially be rescued by exercise. However, lysosomal proteins are also increased in muscle with age (Fig. 1, Old; 1,7), and with disuse imposed by denervation (Fig. 1, Den; 2,4). However, we do not know whether this increase represents more lysosomes that are functional or dysfunctional. Determination of this functional distinction requires the isolation of purified lysosomal fractions, and it is critical to establishing the therapeutic value of exercise in maintaining mitophagy flux and muscle health as we age. This presentation will focus on how exercise can be used as a stimulus for both mitochondrial targeting via mitophagy as well as lysosomal biogenesis, and how it can serve as a useful behavioral therapeutic modality to reverse impairments in the mitophagy pathway that arise with age and muscle disuse

Key words: Mitochondria; mitochondrial dysfunction; muscle adaptations, lysosomal biogenesis, aging

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2025Pdm3 March 26 - Abstract 033

The role of AMPK in the neuromuscular system

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Skeletal muscle, its innervating α-motoneurons (αMNs), and their connection, the neuromuscular junctions (NMJs), are all essential for respiration and mobility. AMP-activated protein kinase (AMPK) is an important mediator of muscle biology and may also affect NMJ and αMN phenotype determination, maintenance, and plasticity.[1,2] We recently found fragmented endplates, decreased acetylcholine receptor turnover, and axon blebbing in muscles of AMPK skeletal muscle-specific knockout (mKO) mice, indicating that there are AMPK-specific functions at the NMJ, both pre- and post-synaptically.[3] Furthermore, our novel AMPK inducible mKO mice present with muscle deficits and have altered αMN morphology, demonstrating that skeletal muscle-specific AMPK has retrograde impact on αMNs. Additional preliminary data demonstrate that novel AMPK agonists augment muscle force and improve cardiac morphology and function in Duchenne muscular dystrophy (DMD) mice. Moreover, small molecule-induced AMPK activation in DMD and spinal muscular atrophy (SMA) patient cells highlight the mutation agnostic effects of stimulating the kinase. Complementary results from our lab demonstrate: i) neurotrophic effects of AMPK at the NMJ that may be leveraged for the maintenance and remodelling of the synapse (3); ii) exercise-induced AMPK stimulation augments muscle function without exacerbating the dystrophic pathology in DMD mice (4); iii) a single dose of exercise- or drug-induced AMPK activation in SMA mice or patient cells enhance mitochondrial health,[5,6] and iv) exercise training stimulates AMPK and improves mitochondrial and muscle health in myotonic dystrophy type 1 mice,[7,8] and patients.[9] In this presentation, I review the role of AMPK as a regulator of neuromuscular biology in health and disease. This information may be useful for engineering AMPK-targeted pharmacological- or lifestyle-based strategies to treat disorders of the neuromuscular system

Key words: Skeletal muscle, NMJ, αMN, exercise, neuromuscular disorders.

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2025Pdm3 March 26 - Abstract 034

The importance of Ca^{2+} signalling in skeletal muscle adaptations to exercise

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Calcium ions (Ca^{2+}) play a pivotal role in skeletal muscle adaptations to exercise due to their involvement in the excitation-contraction process and their function as a signalling molecule. Unsurprisingly, altered Ca^{2+} handling has been identified as a key metabolic factor in skeletal muscle fatigue [1]. In our

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laboratory, we adopt a translational approach—spanning from cellular models to exercising humans—to explore the interplay between neuromuscular and metabolic adaptations to exercise. For example, we reported in humans that the main intracellular Ca^{2+} release channel in skeletal muscle, the type 1 ryanodine receptor (RyR1), undergoes alterations following a single session of sprint interval training (SIT) [2]. In a subsequent study, muscle biopsies collected from recreationally-trained participants after a single session of SIT or moderate-intensity continuous training (MICT) revealed dissociation of calstabin1 from RyR1, a hallmark of leaky RyR1, specifically in response to SIT. Using pharmacological interventions in cellular models mimicking SIT and MICT, we established that Ca^{2+} leaking through RyR1 was taken up by mitochondria, enhancing mitochondrial content and function. This was evidenced by increased levels of mitochondrial oxidative phosphorylation proteins and improved NADH-linked mitochondrial respiratory capacity [3]. We have now collected preliminary data investigating whether combining exercise with a mitochondrial Ca^{2+} uniporter (MCU) activator can enhance exercise performance. Additionally, I will highlight findings from a recent study in which we demonstrated that under conditions of functional hypoxia, mitochondrial Ca^{2+} uptake decreases in response to sarcoplasmic reticulum Ca^{2+} release for muscle contraction. In both cellular and human models, this reduction in mitochondrial Ca^{2+} uptake blunted adaptive responses and remodelling following muscle contractions [4]. Leveraging the translational approach developed in these projects, this presentation will emphasize the critical role of Ca^{2+} signalling in skeletal muscle adaptations to physical exercise.

Key Words: calcium; muscle contraction; mitochondria; fatigue.

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2025Pdm3 March 26 - Abstract 035

Molecular mechanisms of muscle adaptations: role of PGC-1a

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Skeletal muscle exhibits an enormous plasticity triggered by external perturbations and internal stimuli. Most notably, changes in the amount of physical activity lead to a remodeling of signaling pathways, bio-chemical processes, cellular metabolism and contractile properties, collectively affecting muscle function (1). This not only affects performance but has also a very broad impact on health and well-being, morbidity and mortality. Surprisingly, despite the clear clinical significance, the molecular mechanisms that underlie skeletal muscle plasticity in (patho)physiological contexts remain poorly understood. For example, it is unclear how the short-term perturbations evoked by an individual exercise bout ultimately lead to long-term chronic adaptations, how the molecular patterns of an untrained and a trained muscle at rest differ (2), and even how specification, e.g. in endurance compared to resistance training is brought about (3). In my presentation, I will summarize the current knowledge and present recent data providing more insights onto the fundamental process of muscle adaptation to contractile activity. A particular focus with the role of the peroxisome proliferator-activated receptor gamma coactivator 1alpha (PGC-1alpha) in this process. PGC-1alpha is activated by an acute endurance exercise bout, and will control a complex gene program aimed at metabolic and contractile remodeling to provide adequate support for sustained muscle contractions. As other key regulators, including calcium signaling, the AMP-dependent protein kinase (AMPK) or mammalian target of rapamycin (mTOR), PGC-1alpha is only transiently engaged. I thus will present the current data on how such regulators, in particular PGC-1alpha, could nevertheless be crucial for long-term training adaptation of muscle.

Key words: PGC-1alpha; exercise; skeletal muscle plasticity; transcriptional regulation

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2025Pdm3 March 26 - Abstract 036

Mitochondria-derived vesicles in physical frailty and sarcopenia

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Biological aging is the failure of resilience mechanisms opposing to cell damage in favor to processes that lead to damage accrual manifesting as an increase in negative outcomes and poor health. Reduced mitochondrial quality and altered mitochondrial signaling contribute to the age-related cell and organismal decline. Mitochondrial failure and inflammation characterize older people with physical frailty and sarcopenia (PF&S) in a complex relationship requiring multi-marker and complex analysis to be dissected (1). Circulating extracellular vesicles (EVs) have recently been characterized and recognized as potential tools for capturing age-related secretory characteristics. Mitochondria also generate vesicles, referred to as mitochondria-derived vesicles, as a rescue strategy from organelle disposal in the setting mild mitochondrial injury and/or lysosomal function impairment for the incorporation of mitochondrial proteins and DNA (2). At the extracellular level, mitochondrial constituents as well as MDVs themselves hold pro-inflammatory roles and trigger innate immunity. A thorough analysis of these vesicles unveiled specific patterns of mediators associated with PF&S (3) that may also shed light on the chronic low-grade inflammatory process accompanying the aging process that may lead to the identification of novel mitochondrial routes operating in aging and related disorders.

Key words: aging; exosomes; mitochondrial quality control; mitochondrial-lysosomal axis; mitophagy.

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2025Pdm3 March 26 - Abstract 037

Testosterone depletion and intracellular calcium in skeletal muscle

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Abstract WITHDRAW

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2025Pdm3 March 26 - Abstract 038

Effects of exercise and chemotherapy in cancer cachexia

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Central objectives for successful cancer treatment include increased survival and an improved quality of life. Skeletal muscle loss and metabolic dysfunction are barriers to the cancer patient achieving these positive outcomes. For years, we have studied the mechanistic basis of cancer-induced muscle waste in preclinical models. Historically, mechanistic investigations into cancer-induced skeletal muscle wasting have focused on cachexia prevention and have not accounted for chemotherapy effects, which could alter the outcomes of these investigations. While progress has been made in identifying molecular drivers of cancer cachexia, our mechanistic understanding of chemotherapy's consequences on skeletal muscle metabolism and function was primarily focused on acute toxicities for years. Thus,

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understanding the long-term consequences of chemotherapy on skeletal muscle metabolic and functional properties is insufficient. We have examined the adverse effects that persist after the completion of chemotherapy with 5-fluorouracil (5-FU) in combination with other therapies, including leucovorin, methotrexate, oxaliplatin, and irinotecan**.** While established regimens Folfox (5-FU, leucovorin, oxaliplatin) and Folfiri (5-FU, leucovorin, irinotecan) have been widely investigated for acute muscle toxicity, little is known about their lasting effects on the regulation of skeletal muscle fatigue and mitochondria quality control. We also have explored how sex and exercise interact with chemotherapy. Although exercise is widely prescribed post-cancer treatment, the mechanistic cellular underpinnings of exercise and chemotherapy's interaction are poorly understood, which has limited exercise as a therapy. Additionally, many cancer patients can become hypogonadal from weight loss, systemic inflammation, and aging. How these conditions impact skeletal muscle and interact with chemotherapy to regulate skeletal muscle function will be discussed.

Key words: 5-fluorouracil; colon cancer; mitochondria; AMPK; osteocalcin.

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2025Pdm3 March 26 - Abstract 039

Oxytocin treatment reduces cancer cachexia in a pre-clinical model

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Oxytocin (OT), a neurohypophyseal peptide that declines with age, has been shown to counteract sarcopenia in aged mice.[1,2] We and others have shown that its receptor is expressed in skeletal muscle and that OT promotes myogenic differentiation. However, OT's capacity to counteract cancer cachexia has not been studied.[3] While examining OT plasma levels in cancer patients, we noticed a significant dicrease of OT associated to the occurrence of cachexia, a mascle wasting syndrome associated to late stage cancer and a poor prognosis. Similarly, OT mRNA level and that of its receptor, OTR, dicrease in elderly,

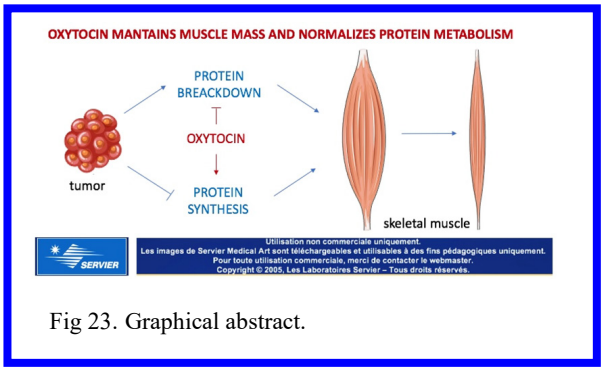

Fig 23. Graphical abstract.

sarcopenic patients. This promped us to use OT to counteract the effect of tumor-derived factors on muscle cells and tissues Figure 23). As a proof of principle, OT's effects were initially assessed in vitro using L6C5 myoblasts,[4] treated with colon cancer C26-conditioned medium (C26-CM).[5] Since OT counteracted the C26-CM, we evaluated its efficacy against cachexia in an in vivo C26/Blab/C cancer. Finally, transgenic MetRSL274G C57BL/6 mice were used to assess OT effects on de-novo proteins synthesis. In vitro, OT reversed the inhibition of myogenic differentiation by C26-CM, increasing the fusion index, the number of nuclei per myotube and the myotube diameter. In mice submcutaneooulsy injected with the C26

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tumor, OT treatment restored skeletal muscle mass, increased fiber cross-sectional area and improved the body weight. Muscle mass is largely linked to protein metabolism, thus we measured the proteasome-mediated protein degradation by using the expression of ubiquitin ligases (MuRF1 and Atrogin1) as markers of this pathway. WhIle the C26 tumor increased the RNA expression of the ubiquitin ligases, OT totally rescued their basal level of expression. As for protein synthesis, measured through the use of bio-orthogonal non-canonical amino acid tagging (BONCAT), we observed that OT rescued the synthesis of key proteins involved in muscle homeostasis, regeneration, and inter-organ communication, which were disrupted by the C26 tumor. OT has an established clinical safety and widely used in obstetric care. Our findings that OT rescues protein homeostasis and muscle mass in a preclinical model suggest that it could quickly be translated into effective therapies for preventing or treating cachexia in cancer patients.

Key words: cancer cachexia; oxytocin; protein metabolism; BONCAT.

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2025Pdm3 March 26 - Abstract 40

RAGE activity at myofiber level sustains cancer cachexia

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Cancer cachexia (CC) is a debilitating syndrome characterized by progressive muscle wasting and responsible for about half of cancer patients' deaths (1). The receptor RAGE (receptor for advanced glycation end-products) is re-expressed in myofibers of tumor-bearing mice undergoing cachexia and overstimulated by high amounts of cachexigenic RAGE ligands thus amplifying catabolic pathways (2). Tumor-bearing RAGE-null (Ager−/−) mice showed reduced hallmarks of CC, delayed muscle atrophy, and increased survival (3). To understand the specific contribution of muscular RAGE to CC, we generated a conditional tamoxifen-inducible mouse model in which the RAGE gene is selectively deleted in skeletal muscles (AgermKO mice). Following subcutaneous injection of Lewis lung carcinoma (LLC) cells, AgermKO and Ager−/− mice showed almost complete maintenance of muscle mass and performance at 25 dpi, the opposite being observed in control, Agerflox mice. Moreover, the absence of RAGE only in muscles of tumor-bearing mice (LLC/AgermKO mice) slowed down body weight loss and increased survival, although to a lesser extent than in the complete absence of RAGE (Ager−/− mice). Restrained degradation of fast myosin heavy chain (MyHC)-II, typically degraded in cancer conditions, and increased expression of slow isoform MyHC-I, which confers resistance to cancer-induced muscle atrophy, characterized muscles of LLC-AgermKO mice. Moreover, contrary to LLC/Agerflox mice, LLC/AgermKO muscles showed an increased activation state of the anabolic kinase, Akt, inhibition of the Akt downstream target, GSK-3β, and unchanged levels of PGC-1α compared to their internal controls, suggesting that the maintenance of physiological activation of the Akt-GSK-3β-PGC-1α pathway might contribute to restrain muscle wasting in these animals in cancer conditions. The proteomic analysis revealed distinct signatures in tumor-bearing Agerflox, AgermKO, and Ager–/– mice, and suggested additional factors linked to the absence of RAGE at muscle levels which might concur to restrain muscle wasting in cancer conditions by promoting a fast-to-slow myofiber transition. Indeed, we found higher amounts of the SUMO-conjugating enzyme UBC9, which is highly expressed in slow-twitch muscles and is involved in the determination of myofiber type specificity, and reduced amounts of MYOZ1 (myozenin-1/calsarcin-2), which is expressed exclusively by fast-twitch muscles where it

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inhibits the calcineurin/NFAT pathway responsible for fast-to-slow myofiber transition. Altogether, our results suggest that RAGE engagement at the myofiber level contributes to muscle wasting in cancer conditions, even though the total absence of RAGE translates into the highest protection against CC. Thus, approaches pointing to inhibiting RAGE might represent promising tools to counteract the cachectic syndrome and prolong survival in cancer patients.

Key words: cancer cachexia; RAGE; animal models.

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2025Pdm3 March 26 - Abstract 041

Silencing Tumor-Muscle Crosstalk

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Cachexia has been defined as an intricate wasting syndrome that appears concomitant to underlying illness, frequently adding up to pre-existent poor muscle function and sarcopenia. Marked and fast weight loss, reflecting skeletal muscle and adipose tissue wasting are hallmarks of the syndrome (1). Systemic inflammation is a common finding in cancer and even more prominent in cachexia. We (2) described tumours of cachectic colorectal cancer patients to present a decreased macrophage phenotype M1 to M2 ratio within the tumour microenvironment, accompanied by the description augmented CCL3, CCL4, and IL-1β expression by the total tumour, as compared with those obtained from weight-stable colorectal cancer patients. These differences were paralleled by impairment of autophagic processes in the tumour of cachectic patients (3). We thus postulated that attenuation of the inflammatory output of the tumour would induce improvement of cachexia-related symptoms and recovery of metabolism, directly suppressing muscle wasting. As to be effective in downregulating systemic inflammation we chose a strategy with systemic impact: chronic endurance exercise (Figure 24). Treatment-naïve cachectic and weight-stable patients (n= 50) engaged in 6 weeks of assisted submaximal treadmill exercise and the content of circulating inflammatory cytokines was robustly decreased in the patients, while a small appendicular muscle mass gain was detected. Tumours from trained patients also showed a reduction of mass, as assessed by computerized tomography and micro-anatomic analysis. Immune system function was increased (dendritic cells in the tumour microenvironment) and cachectic patients showed improved tumour vascularization after exercise. We shall discuss the results of the trial, with special emphasis on the anti-inflammatory effect of endurance exercise in cachexia with impact in the skeletal muscle.

Key Words: Cancer cachexia; endurance exercise; inflammatory crosstalk; wasting.

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2025Pdm3 March 26 - Abstract 042

Impact of sarcopenic myosteatosis on patients with esophagogastric cancer

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Alterations in muscle mass, including sarcopenia and myosteatosis, have been shown to negatively impact surgical outcomes in cancer patients. In particular, these changes in body composition can contribute to increased

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morbidity, prolonged hospital stays, and impaired recovery following major oncologic surgery. However, the correlation between body composition, biochemical markers, and surgical outcomes in esophagogastric cancers remains incompletely understood. Further investigation into these relationships may provide valuable insights for improving preoperative risk stratification and patient management. A prospective clinical trial was conducted between May 2019 and November 2024, enrolling patients with esophagogastric cancer undergoing curative-intent

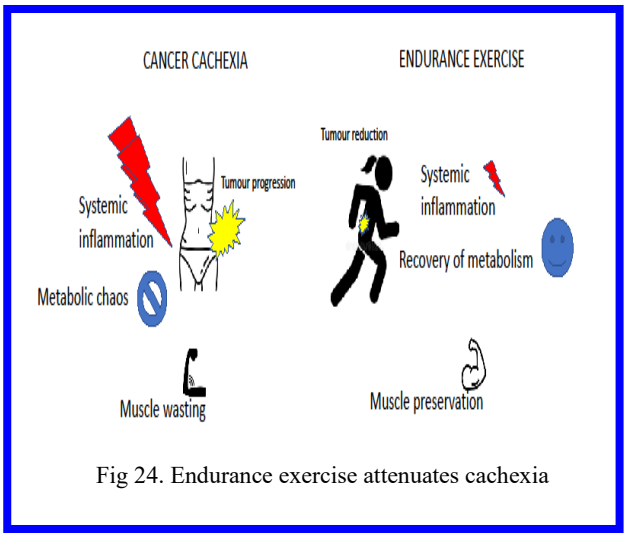

Fig 24. Endurance exercise attenuates cachexia

resection. At presentation, patients were assessed for anthropometric measures, medical history, and biochemical markers. Body composition was analyzed using contrast-enhanced CT scans, focusing on the lumbar skeletal muscle index (SMI) and mean muscle attenuation, based on cutoffs established by Martin et al. The presence of sarcopenia and/or myosteatosis was evaluated in relation to malnutrition and systemic inflammation. Statistical analyses included univariate and multivariate models to determine the impact of these factors on surgical outcomes. A total of 200 patients with esophagogastric cancer undergoing surgery were enrolled, with a preliminary analysis conducted on 42 patients. Postoperative morbidity did not differ significantly between sarcopenic and non-sarcopenic patients ($p=0.749$). However, myosteatosis was associated with a higher severity of postoperative complications ($p=0.015$) and prolonged hospitalization ($p=0.027$), with the latter confirmed in multivariate analysis ($p=0.036$). Independent risk factors for myosteatosis included malnutrition, as indicated by low albumin levels ($p<0.001$), an increased Charlson comorbidity index ($p=0.031$), and a previous history of cancer ($p=0.034$). In Conclusion,
muscle quality, rather than muscle quantity, appears to play a more critical role in influencing surgical outcomes in patients undergoing upper gastrointestinal cancer surgery. Preoperative assessment of nutritional status, combined with body composition analysis, could serve as an effective strategy for risk stratification and guiding nutritional interventions to optimize patient outcomes.

Key Words: Sarcopenia; Low Muscle Mass; Myosteatosis; Esophagogastric cancer; Postoperative complications; Albumin; Surgical Outcome.

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2025Pdm3 March 26 - Abstract 043

Involvement of Satellite cells in the pathogenesis of Neuromuscular disorders

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Muscle health depends on resident stem cells, the satellite cells, key players in postnatal muscle growth, maintenance, and repair. However, in many muscular dystrophies and congenital myopathies, muscle repair is progressively impaired, arguing for diminished satellite cell function. A critical question is whether a pathogenic mutation in a gene responsible for a neuromuscular disorder (myopathogene) directly disrupts satellite cell function, hindering the regenerative process. To identify whether a myopathogene disrupts satellite cell function, we developed a multimodal pathway integrating differential expression analysis of murine satellite cell activation, regulation by PAX7 (a master transcriptional regulator of satellite cells) and review of satellite cell numbers/function in related neuromuscular disease/animal models. This led us to define Satellite cell-opathies: a class of neuromuscular disorders where the dysfunction of satellite cells plays a key role in the pathogenesis (Ganassi et al., 2022; Ganassi and Zammit, 2022). Conditions where the pathogenic mutation solely impacts satellite cell function, we defined as Primary Satellite cell-opathies, typically presenting as congenital onset with hypotonia, involvement of respiratory, trunk, and facial muscles. In contrast, pathogenic mutations impairing both satellite cells and muscle fibres cause Secondary Satellite cell-opathies, with a more variable onset and pattern of affected muscles. To further expand the potential

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of our discovery approach, we generated a transcriptomic dataset from human muscle cells expressing PAX7. Our refined pathway identified novel myopathogenes causing potential Satellite cell-opathies, expanding the current portfolio and knowledge on neuromuscular disorders. It also provides a discovery tool to advance assessment of genotype-phenotype correlation for several orphan diseases with similar clinical features. Understanding the role of satellite cell dysfunction in neuromuscular diseases will enhance diagnosis, prognosis, and treatment, particularly in regenerative therapies.

Key Words: Satellite cell-opathies; neuromuscular disorders; regeneration; skeletal muscle, PAX7.

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2025Pdm3 March 27 - Abstract 044

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Morphological and Functional Instability of the NMJ with Chronic Inactivity in Humans,

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Abstract: WITHDRAW

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2025Pdm3 March 27 - Abstract 045

Reduction of daily steps alters whole body and muscle oxidative metabolisms without affecting mitochondrial dynamics and function

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Although there is evidence that mitochondrial dysfunction co-occurs with insulin resistance in skeletal muscle and may play a causative role in its development, the issue remains controversial1. Physical inactivity is associated with both mitochondrial dysfunction and insulin resistance in skeletal muscle. Step reduction (SR), a model of mild inactivity, simulates a reduction in daily physical activity and provides a useful model to study such relationships. A total of 30 participants (mean age 23±3 years) underwent a 14-day SR protocol, resulting in an 82% decrease in their average daily steps. Maximal oxygen consumption (VO2max), measured during incremental cycling exercise before and after SR, and muscle oxidative capacity (muscle VO2 off-kinetics) determined by NIRS were reduced post-SR ($p=0.022$) indicating a decline in whole-body and muscle aerobic function. Blood glucose concentration was unchanged, insulin concentration was higher ($p=0.006$) and HOME index was higher ($p=0.015$) following SR, indicating insulin resistance. Vastus lateralis biopsies were collected. Analyses of muscle fibre cross sectional area revealed no significant change following SR. However, there was a shift in muscle fibre type composition, with an increased percentage of type 2A-2X fibres ($p<0.05$), which is consistent with the SR stimulus. Western blot analyses of protein levels associated with mitochondrial content (TOM 20, Citrate synthase), dynamics (MNF1, MNF2, OPA1, DRP1, FIS1), and biogenesis (PGC1α) indicated no significant changes ($p > 0.05$), suggesting that mitochondrial integrity was maintained. The results of High-Resolution Respirometry determinations (e.g. LEAK CI, LEAK CI+CII, OXPHOS, ETS CI+CII, ETS CII) were consistent with such findings, demonstrating no changes in maximal ADP-stimulated mitochondrial respiration ($p > 0.05$). Insulin resistance in vivo prompted the analysis of the basal phosphorylation levels of key insulin signaling molecules (IRS-1, Akt, AS160) and of the GLUT4 protein level. They were unchanged suggesting that the observed decrease in insulin sensitivity occurs without affecting basal insulin signaling in skeletal muscle. Present findings indicate that, following mild inactivity, mitochondria are preserved and are not a major determinant of alterations in oxidative metabolism. Other determinants are presumably involved. The lower insulin-sensitivity appeared no to depend on either mitochondrial dysfunction or insulin signalling in basal conditions. Preliminary analyses of microvascular-endothelial function, potentially involved in the latter phenomena, do not show adaptations following SR.

Key Words: step reduction; oxidative metabolism; mitochondria; insulin sensitivity.

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2025Pdm3 March 27 - Abstract 046

Oxidative metabolism and mitochondrial function: adaptations to disuse in humans

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Skeletal muscle oxidative metabolism and mitochondrial function represent "the last step" in the long pathway for O2, from ambient air to oxidative phosphorylation. This metabolism is often neglected in studies dealing with the effects of disuse on skeletal muscle, which mainly take into consideration muscle mass and muscle force. This is unfortunate, considering that all activities lasting longer than 1-2 minutes substantially rely on oxidative metabolism for ATP turnover.[1-5] The classical functional variable evaluating the maximal performance of oxidative metabolism is the maximal O2 uptake (V̇O2max). Apart from its direct effects on exercise tolerance, a decreased "cardiorespiratory fitness" determined by inactivity/disuse, as identified by the observation of a decreased V̇O2max, is intrinsically associated with profound negative consequences on the general health status of the subjects, comprehending a decreased insulin sensitivity, a "pro-inflammatory" condition, impaired endothelial function, mitochondrial dysfunction, altered function of the neuromuscular junction, altered redox status and increased oxidative stress, etc. A V̇O2max decrease during inactivity/disuse has been described for example in studies in which human subjects are voluntarily put to bed for periods ranging from a few hours to a few months ("bed rest" studies). These studies are of scientific and practical interest also for space agencies, since bed rest simulates on Earth several effects of a reduced gravity ("microgravity") on body functions. According to Ade et al. (2017)[1] impairments of convective (cardiovascular) O2 delivery and peripheral O2 diffusion contribute to the V̇O2max decrease observed during bed rest or actual spaceflights. Pulmonary respiratory function, characterized by ample functional reserves (in healthy subjects and in normoxic conditions) related to respiratory volumes, flows, alveolar-capillary diffusion, flat portion of the O2-hemoglobin dissociation curve, etc., does not appear to be relevant in limiting V̇O2max during inactivity and disuse. Microvascular endothelial impairments have been identified even after short bed rest periods (Zuccarelli et al. 2021). The role of muscular/mitochondrial factors in limiting oxidative metabolism in inactivity/disuse is characterized by controversial findings. Recent studies point to a relative "resilience" of mitochondrial function to short periods of inactivity/disuse. Zuccarelli et al. (2021)[4] did not observe impairments of mitochondrial respiration, evaluated both ex vivo and in vivo, following 10 days of bed rest in young subjects. Longer periods of bed rest would be needed to determine functional impairments of maximal mitochondrial respiration. Zuccarelli et al. (submitted) observed "positive" effects of a short bed rest on other variables evaluating mitochondrial respiration, in terms of an enhanced mitochondrial sensitivity to submaximal [ADP]. According to Zuccarelli et al. (2021)[4] and Baldassarre et al. (2022)[3] following relatively short bed rest periods the main impairments to oxidative metabolism would reside "upstream" of mitochondria, at the level of cardiovascular/microvascular/endothelial functions. A short period of inactivity/disuse could have another interesting effect on skeletal muscle and whole-body oxidative metabolism in resting conditions. During 21 days of bed rest in young subjects (Y), and 10 days of bed rest in elderly subjects (E), we recently observed (Baldassarre et al. 2025)[5] a substantial decrease in resting muscle V̇O2 (-39% in Y, -30% in E), estimated by the linear increase in deoxygenated [hemoglobin] and [myoglobin], determined by near-infrared spectroscopy on the vastus lateralis muscle during a transient limb ischemia, obtained by the rapid inflation of a pneumatic cuff at the root of the thigh. The resting muscle V̇O2 decrease, already described in a previous study by our group in young subjects following a 10-day bed rest (Zuccarelli et al. 2021), was accompanied by a decreased whole-body resting energy expenditure (REE), determined by indirect calorimetry. The REE decrease occurred to a similar extent both in Y (-17% over 21 days) and in E (-12% over 10 days). Even by being far less pronounced compared to the typical reduction of REE (>90%) observed in obligate hibernating animals, the observed inactivity-related decrease in resting muscle V̇O2 and REE, possibly aimed at preventing ATP accumulation or excessive ROS production, could mitigate numerous biological and logistic challenges of prolonged spaceflights by lowering rates of crewmember consumable use (food, water, O2) and CO2 production. On the other hand, the inactivity-related decrease in REE would have negative consequences on the health status of subjects, by altering body mass homeostasis and increasing the risk of metabolic diseases.

Key words: inactivity, microgravity, skeletal muscle, oxidative metabolism, metabolic diseases.

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2025Pdm3 March 27 - Abstract 047

Human Motor Unit Remodelling with Chronic Inactivity

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Abstract: WITHDRAW

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2025Pdm3 March 27 - Abstract 048

Circulating Factors Associated with Extremes of Physical Function in Octogenarians

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Physical function declines with aging, yet there is considerable heterogeneity, with some individuals declining very slowly while others experience accelerated functional decline. To gain insight into mechanisms associated with extremes of physical function with aging, we performed proteomics, targeted metabolomics, and targeted kynurenine-focused metabolomic analyses on serum specimens from three groups of octogenarians: high functioning master athletes (HF, n=16), healthy normal functioning non-athletes (NF, n=12) and lower functioning non-athletes (LF, n=11). Higher performance status was associated with a circulating biomarker profile suggesting: lower levels of pro-inflammatory markers, as well as unperturbed tryptophan metabolism, with normal function of the kynurenic pathway; higher circulating levels of lysophosphatidylcholines that have been previously associated with better mitochondrial oxidative capacity; lower activity of the integrated stress response; lower levels of circulating senescence associated secretory phenotype (SASP) protein members; and lower levels of proteins that reflect neurodegeneration/denervation.[1-3] These serum biomarkers in HF parallel our observations in skeletal muscle where we saw higher abundance of KAT3 and KAT4 which metabolize kyurenine into the cytoprotective kynurenic acid, better retention of oxidatively competent muscle fibers and higher abundance of nuclear and mtDNA-encoded mitochondrial proteins in skeletal muscle of HF (Ubaida-Mohien et al., 2022).[3] Notably, many of the changes in serum biomarkers we have previously seen to increase with aging (Tanaka et al., 2018)[2] were attenuated in HF participants, suggesting a more favorable aging trajectory in HF individuals. Given the exceptionally high function evident in the HF group (8 were world record holders in their discipline at the time of testing), physical activity alone is unlikely to explain their abilities and an intrinsically slower aging biology trajectory is a tempting explanation. Extending the observations of previous studies focused on biomarkers of aging that predict poor function, our findings show that many of the same biomarkers associated with poor function also change with aging, suggesting poor function may result from exacerbated aging biology. Collectively, our results imply that common mechanisms related to aging biology explain heterogeneity in physical function with aging, consistent with the geroscience hypothesis of aging (Justice et al., 2016).[1] Accordingly, our findings support the premise that identifying therapeutic strategies that target fundamental aging biological processes, whilst easier said than done, is a logical strategy to increase the fraction of the lifespan with high function. Because of the cross-sectional nature of this study, our results should be interpreted with caution, and bi-directional causality, where physical activity behavior is both a cause and outcome of differences in the biomarker changes, remains a possible interpretation.

Key Words: Aging, biomarkers, physical function, frailty, masters athlete

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2025Pdm3 March 27 - Abstract 049

A transcriptomic and spatial proteomic atlas of human aging and sarcopenia

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Background: Aging is associated with a progressive decrease in muscle mass and strength. Sarcopenia is the clinical manifestation of the extreme age-related muscle atrophy and weakness and affects approximately 50 million people worldwide. Severe consequences of sarcopenia include increased frailty and reduction in ability to perform basic life functions, leading to higher risk of falls, increased healthcare costs, institutionalization, and mortality risk. Diagnosing and treating sarcopenia is challenging because of the complex pathophysiology of sarcopenia, which is a multifactorial syndrome. Current research lacks comprehensive studies investigating the mechanisms involved in sarcopenia development and progression in humans, which hinder the ability to identify biomarkers for its diagnosis and effective drugs to slow down its progression. We hypothesize that sarcopenia is associated with neuromuscular junction (NMJ) and mitochondrial impairment, an increase in inflammation and fibrosis, as well as alterations in muscle tissue architecture and cell-to-cell communication. Relative to inflammation, our lab has shown that prostaglandin E2 (PGE2), a metabolite part of the body's natural healing mechanism, is important for muscle stem cells activation upon injury1. We also showed that PGE2 degrading enzyme 15-PGDH is elevated and plays a role in murine muscle atrophy, and its inhibition enhances muscle mass, strength, and exercise performance in old mice by improving mitochondrial function and promoting NMJ reinnervation through the elevation of PGE22,3. The present study aims to (1) comprehensively characterize the features of sarcopenia in human skeletal muscles by employing unbiased single nuclei RNA sequencing (snRNASeq) and multiplex-imaging spatial proteomics (CODEX) and (2) identify 15-PGDH as a potential biomarker for early detection of sarcopenia in human patients and explore therapeutic strategies for counteracting muscle atrophy and weakness in sarcopenic patients. Methods. 67 patients were recruited, including 15 young (18-35 years old) and 52 aged (>70 years old). Aged individuals were further categorized as non-sarcopenic and sarcopenic basing on DEXA and functional tests, in accordance with the most updated clinical guidelines. Vastus Lateralis muscle biopsies were collected and processed using snRNASeq and CODEX spatial proteomics technologies, with the aim to generate a transcriptomic and spatial proteomic atlas of human aging and sarcopenia, encompassing changes in muscle cell type composition and spatial interaction and changes in gene and protein expression. Western blot analyses were used to confirm changes in mitochondrial protein concentration and 15-PGDH. After stratifying old patients basing on DEXA and functional tests, the following categories were generated: young (Y), non-sarcopenic (NS, age range 70-74 years old), non-sarcopenic aged matched (NSAM, age 74+ years old) and sarcopenic (S, age 74+ years old). Analyses of snRNAseq and CODEX showed changes in the cell populations within the muscle of young and old patients. We observed an increase in macrophages as well as inflammatory and pro-fibrotic cell populations which infilitrate the aged and, in particular, the sarcopenic muscle. We defined novel gene signatures for these inflammatory and pro-fibrotic cells that are specific to sarcopenia. The prevalence of NCAM+ fibers, an indirect sign of denervation, and the number of denervated nuclei, were both increased in S patients compared to other groups. The snRNAseq also revealed alterations in mitochondria-related genes, a reduction in the mitochondria complexes, dynamics and mitophagy, suggesting important impairment of these organelles. These changes were confirmed by western blot. Spatial proteomics revealed changes in cell-cell interaction within the aged muscle tissues compared to young. 15-PGDH transcript and protein expression measured by western blot were increased selectively in S versus all the other categories, and correlated with measures of muscle function and mass, suggesting 15-PGDH may be a suitable biomarker to identify sarcopenic muscles. In conclusion, 15-PGDH may represent a suitable biomarker to identify sarcopenic muscles. Our hypotheses of an overall change in muscle cell composition and spatial reorganization, alterations in innervation, mitochondria biogenesis and dynamics, increased fibrosis and inflammation support the existing literature and expand animal and human findings to a rigorously classified sarcopenic versus non-sarcopenic and young population. Establishing a comprehensive understanding of the pathophysiology and identifying specific biomarkers of sarcopenia is key for the development of novel therapeutic strategies, which would improve patient quality of life and provide economic benefit by reducing healthcare costs.

Key words: sarcopenia, skeletal muscle, human neuromuscular system, omics, biomarker.

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2025Pdm3 March 27 - Abstract 050

Muscle Gene Expression and Physiological Adaptations to Overloading Following Disuse in Humans

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Abstract: WITHDRAW

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2025Pdm3 March 27 - Abstract 051

Adaptation of the Muscle Extracellular Matrix to Contracture due to Cerebral Palsy

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Spasticity, secondary to upper motor neuron (UMN) lesion, can result in muscle contractures. We have studied the mechanics and biology of muscle from children with wrist flexion contractures secondary to cerebral palsy (CP). One of the most dramatic and unexpected structural changes observed in these children is the dramatically increased sarcomere length relative to patients without upper motor neuron lesions.[1]. This has been observed both in upper and lower extremities.[2,3] This result suggests dramatic alterations in the regulation of muscle growth in these children. Biomechanical studies of isolated single muscle cells reveal a slightly increased passive modulus,[4] but a very large change in the amount and quality of extracellular matrix.[5] The dramatic alterations in mechanical properties are associated with significant changes in the extracellular matrix (ECM). In three of the four muscles studied, the modulus (normalized stiffness) of fiber bundles of CP patients' muscles were greater than muscles from typically developing children (TD; Fig. 25A). Paradoxically, the increase in stiffness was accompanied by an increase in titin isoform size (Fig. 25B) which was negatively correlated with stiffness (Fig. 25C). A separate experiment in mouse EDL muscles also demonstrated a significant mechanical effect of the ECM over the simple increase in force measured with increased number of fibers (Fig. 25D). A mechanistic explanation for how an UMN lesion results in these dramatic muscle changes is not currently available. Expression profiling reveals that a number of active

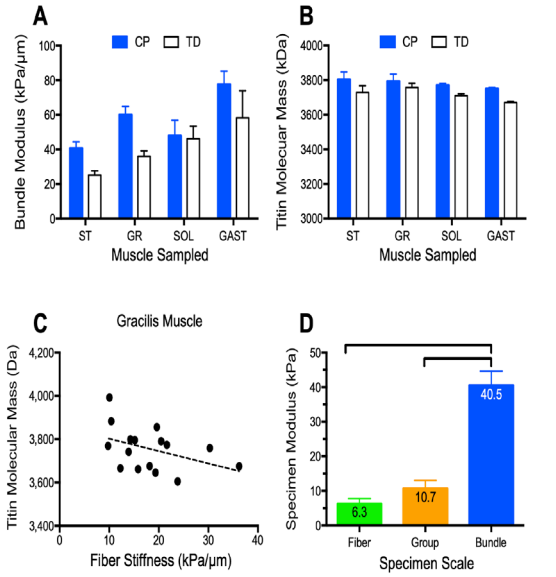

Fig 25. Passive biomechanical properties of muscle specimens are altered in contractures because of cerebral palsy (CP) compared with typically developing (TD) muscle. **(A)** bundle modulus measured *in vitro* from intraoperative muscle biopsies **(B)** titin molecular mass measured using specialized electrophoresis (note expanded vertical scale). **(C)** in the gracilis muscle, linear regression reveals a weak correlation between muscle fiber stiffness and titin molecular mass (r^2=0.3) that is not significant (P>0.2). This was typical for all muscles tested, suggesting that, titin mass is not a major determinant of fiber stiffness in humans. **(D)** modulus of three different specimen types from the mouse EDL muscle clearly demonstrates that the skeletal muscle extracellular matrix, present in fiber bundles only, bears most of the tensile load**.** (Data represent mean±SE, n=6 –10/group.)

"conflicting" biological pathways in spastic muscle. There is activation of growth and growth inhibition pathways. Additionally, CP muscle adapts by altering processes related to extracellular matrix production, fiber type determination, fiber hypertrophy and myogenesis. We also obtained evidence that calcium handling is altered secondary to cerebral palsy and may be a significant component of this disease. These transcriptional adaptations were not characteristic of muscle adaptations observed in Duchenne muscular dystrophy or limb immobilization. We hypothesize that CP muscles have difficulty growing and lengthening with increased bone length as is observed in most mammalian muscles.[8,9] Importantly, we have also measured a loss in the number of satellite cells that are located throughout CP muscle.[10,11] The remaining satellite cells have epigenetic changes that may influence our ability to rehabilitate these muscles using traditonal therapeutic methods.[12] The specific pathways disrupted in these cells in culture imply premature senescence of muscle satellite cells due to DNA hypermethylation, as is common for some pediatric cancers.[13] One anti-cancer drug, 5-azacytizine can demethylate CP muscle satellite cells in culture and restore

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their normal division time and ability to fuse into large myotubes. These results support the notion that, while spasticity is multifactorial and neural in origin, significant structural and biological alterations in muscle occur. An understanding of the changes that occur in the muscle and extracellular matrix may facilitate development of new conservative or surgical therapies for this devastating problem.

Key words: Spasticity, cerebral palsy, contracture, stiffness, extracellular matrix.

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Loss of Calpain 3 perturbs junctional sarcoplasmic reticulum protein stability at rest and following exercise

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Healthy skeletal muscle can undergo structural remodeling following exercise to ensure that intracellular calcium stores and force generation capacity are maintained. This includes T-tubule elongation and Sarcoplasmic Reticulum (SR) formation of flat, parallel stacks to form Calcium Entry Units (CEUs) that enable Store Operated Calcium Entry

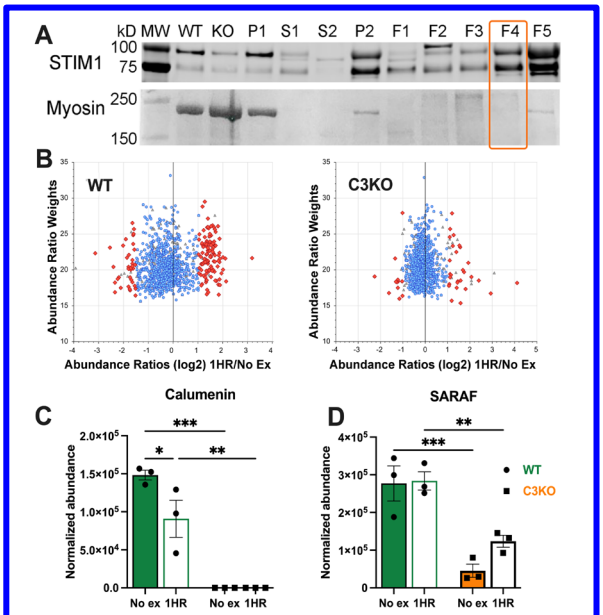

Fig 26. Sucrose gradient SR protein enrichment. Pooled muscles from N=3 mice were utilized for discontinuous sucrose gradients to enrich for SR proteins. **A**. Immunoblotting for STIM1 shows Fraction (F) 4 has highest levels without myosin contamination (by Coomassie staining) compared to pellets (P), supernatants (S) or whole lysates (WT, KO). **B.** Bland-Altman plot of Abundance for LC/MS/MS of F4 from WT and C3KO samples. Red points indicate significant differences between +/- exercise. Calumenin (**C**) has exercise and strain dependence. SARAF (**D**) is lower in C3KO. *, p<.05, **, p<.01, ***, p<.001, 2-way ANOVA & Tukey post-hoc test. N=3 samples per condition, muscles from N=3 mice per sample.

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(SOCE) and underly functional benefits. Muscles from Calpain-3 knockout (C3KO) mice exhibit heightened CEUs at rest, which decrease in abundance after treadmill running.[1] It is unknown which proteins regulate remodeling in healthy skeletal muscle and if and/or how they are affected with loss of CAPN3. Here, we used discontinuous density sucrose gradients to enrich for the junctional sarcoplasmic reticulum (Figure 26) and utilized liquid chromatography, mass-spectrometry (LC/MS) aimed to identify proteins involved in the remodeling in WT and C3KO mice.[2] LC/MS revealed numerous junctional SR proteins that differ after exercise or loss of CAPN3. Among these hits were proteins involved in either Ca2+ regulation and/or SR/ER stabilization, including store-operated Ca2+ entry regulatory associated factor (SARAF), calumenin, TMCO1, and lunapark.[3-5] Their protein abundance altered with either exercise, loss of CAPN3, or both. This study provides insight into regulators of healthy skeletal muscle's exercise response to exercise and a new understanding of proteins affected by loss of CAPN3.

Key words: Limb Girdle Muscular Dystrophy; Calpain 3, Store-operated calcium entry; proteomics

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Over-Expression of the HERG1A potassium channel in C_2C_{12} myotubes modulates sodium current amplitude, but not SCN4A gene expression

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Skeletal muscle atrophy is characterized by loss of muscle size and strength, resulting from imbalance in protein synthesis and degradation.[1] It is also reported that fast sodium current increases in atrophic muscle, potentially reducing resistance to muscle fatigue.[2] The HERG1A K^+ channel is upregulated in mouse skeletal muscle atrophying in response to denervation, disuse, and cancer cachexia.

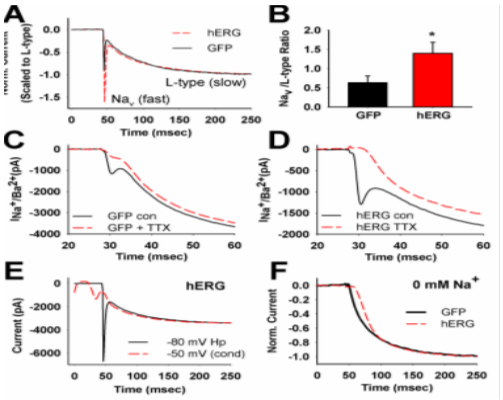

Fig 27. HERG1A Expression increases sodium current in C2C12 myotubes.
A: Example current traces recorded in bath solution containing both 140 mM Na+ and 10 mM Ba2+. Traces were elicited by stepping to 10 mV from -80 mV for 250 msec. Note the fast Nav current and the slow Cav (L-type) Ba2+ current. B) Peak Na+ currents were normalized to peak Ba2+ current in myotubes transduced with GFP or HERG1A. HERG1A expression increased the peak Na+ current a significant ~64% ($p<0.05$) relative to the peak Ba2+ current. C,D) Fast Na+ currents were blocked by 1 µM tetrodotoxin in both GFP (C) and HERG1A (D) transduced myotubes. E) Fast Na+ currents were inhibited by a 20 msec conditioning pulse to -50 mV. Both traces were recorded from the same myotube expressing HERG1A. These data strongly suggest that the source of the HERG1A-enhanced sodium current is the Nav1.4 sodium channel. F) Removing Na+ from the bath solution eliminates the fast Na+ current, demonstrating the current is indeed sodium flux. Traces were recorded as described for panel A except the bath solution contained no Na+.

Over-expression of this channel increases both ubiquitin proteasome proteolysis and calpain activity with a concurrent decline in both mouse muscle fiber cross-sectional area and cultured C_2C_{12} myotube area.[3,4]

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Here, we report that our laboratory has also observed a significant ~64% ($p<0.05$) elevation of fast sodium current amplitude in C_2C_{12} myotubes overexpressing HERG1A (Figure 27). We hypothesized that this enhanced sodium current possibly results from modulation of the skeletal muscle voltage-gated Nav1.4 channel. Here, using electrophysiology, we show that the increased fast Na^+ current was blocked by 1 µM tetrodotoxin and inhibited by a 20 msec conditioning pulse to -50 mV in HERG1A-overexpressing myotubes, which strongly suggests that the source of the HERG1A-enhanced sodium current is the Nav1.4 sodium channel (Figure 27). However, it is not clear how this channel is being modulated. Thus, we performed RT-qPCR to determine if adenovirus induced HERG1A over-expression modulates Nav1.4 gene expression levels. The data reveal that there is no statistically significant difference in expression of the SCN4A gene (encoding the skeletal muscle Nav1.4 channel) in cells overexpressing HERG1A compared to control cells at 48, 96, and 144 hours post transduction. Nor is there any significant difference in expression of the SCN5A gene (which encodes the primarily cardiac Nav1.5 sodium channel but is reported to be upregulated in denervated muscle).[5] This demonstrates that HERG1A over-expression is not affecting expression of the SCN4A or SCN5A genes. In summary, our work shows that HERG1A over-expression increases the amplitude of the Nav1.4 channel current in myotubes, but likely does not do so through modulation of SCN4A (or SCN5A) gene expression. However, it is also feasible that HERG1A modulates Nav1.4 channel protein abundance and/or channel kinetics. For future work, we will investigate the effect of HERG1A over-expression on Nav1.4 protein abundance. We will also study the effect of HERG1A on Nav1.4 channel kinetics. Our work highlights the possible involvement of HERG1A K^+ channels in regulation of sodium channels in myotubes. We intend that further work will aid development of novel therapies designed to combating muscle wasting disorders like denervation atrophy.

Key words: HERG1A (ether-a-gogo related gene); SCN4A and SCN5A sodium channel genes; cultured skeletal muscle cells; muscle atrophy

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2025Pdm3 March 27 - Abstract 054

Nerve activity inhibits mTORC1-dependent protein synthesis in skeletal muscle

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Skeletal muscle can be classified based on their metabolism, distinguishing between glycolytic and more oxidative muscle fibers. It is well known that these different fiber types have different susceptibilities to various muscle wasting stimuli, however, due to lack of experimental models measuring protein synthesis, which are the intracellular signaling pathways regulating this fiber type specific muscle trophism is not known. Here, we have generated a new mouse model, which allows us to label specifically muscle proteins by overexpressing a mutated tRNA synthetase only in muscle fibers. Interestingly, using this mouse model, we observe that loss of muscle activity by

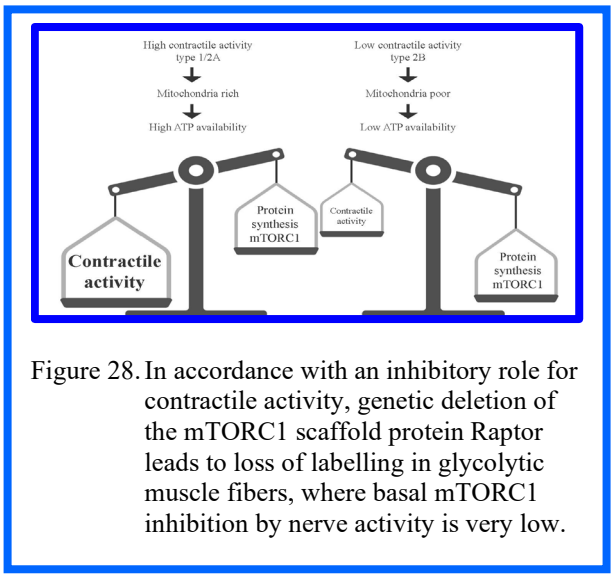

Figure 28. In accordance with an inhibitory role for contractile activity, genetic deletion of the mTORC1 scaffold protein Raptor leads to loss of labelling in glycolytic muscle fibers, where basal mTORC1 inhibition by nerve activity is very low.

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denervation induces a strong increase of protein labelling in oxidative, mitochondria-rich, muscle fibers. Mass spectrometry analysis of labelled proteins and treatment with the mTORC1 inhibitor rapamycin shows this increased protein labelling requires increased activation of mTORC1. In accordance with an inhibitory role for contractile activity, genetic deletion of the mTORC1 scaffold protein Raptor leads to loss of labelling in glycolytic muscle fibers, where basal mTORC1 inhibition by nerve activity is very low (Figure 28). On the contrary, increased activity leads to an acute reduction in protein synthesis, which is accompanied by reduced mTORC1 signaling, glycogen depletion and increased AMPK activation. Overall, our results identify nerve activity as an inhibitory signal upstream of mTORC1-dependent protein synthesis in skeletal muscle, improving the understanding of the fiber type specific response to exercise or in certain pathological situations.

Key Words: Nerve activity, mTORC1-dependent protein synthesis; skeletal muscle.

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2025Pdm3 March 27 - Abstract 055

Reduced ATP turnover during hibernation in relaxed skeletal muscle of brown bear

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Hibernating brown bears experience a significant reduction in metabolic rate, resulting in only moderate muscle wasting (Figure 29). In this study, we investigate whether the ATPase activity of resting skeletal muscle myosin plays a role in this energy conservation. By analyzing single muscle fibers from the same bears during both hibernation and summer, we observe that fibers from hibernating bears exhibit a slight decrease in force production alongside a substantial reduction in ATPase activity. Proteomic analyses of single fibers, along with western blotting and immunohistochemical studies, reveal significant remodeling of the mitochondrial proteome during hibernation. Additionally, bioinformatics and western blotting indicate that phosphorylated myosin light chain—a known enhancer of basal myosin ATPase activity—is reduced in both hibernating and disused muscles. These findings suggest that skeletal muscle minimizes energy expenditure by decreasing myosin ATPase activity, highlighting the potential for modulating this activity in various muscle wasting conditions. In our study, we obtained biopsies from active and hibernating bears to investigate the possible contribution of the myosin super relaxed state to the energy-saving mechanisms during winter. Our results confirmed the reduced number of mitochondria and the limited loss of skeletal muscle contractile force during hibernation, as previously shown. Additionally, we found that skinned muscle fibers from hibernating animals exhibit slower ATP turnover and a more stable myosin super relaxed state. These differences correlate with the reduced abundance and activity of myosin light chain kinase 2 (MYLK2), the kinase associated with myosin SRX stability, in winter samples compared to active animals during summer. In summary, our paper supports the idea that myosin futile energy consumption and the stability of the super relaxed state contribute to the energy-saving mechanisms activated during hibernation in large mammals.

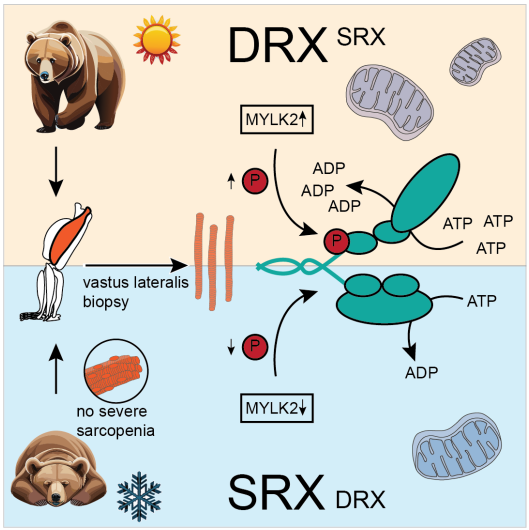

Fig. 29. Bears undergoing hibernation do not eat, drink, or engage in sustained physical exercise for several months; nevertheless, they retain muscle mass by prioritizing adipose tissue as an energy source through metabolic conversion.

Key Words: skeletal muscle; myosin; hibernation; super relaxed state; myosin light chain kinase 2 (MYLK2).

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2025Pdm3 March 27 - Abstract 056

Exercise-driven remodeling of Mitochondria and Sarcotubular System: a muscle strategy to improve function and resistance to fatigue.

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Mitochondria are the powerhouse of the cell (the sites of cellular respiration) and their activity is controlled by Ca^{2+} entry in the mitochondrial matrix. Ca^{2+} ions are provided by Ca^{2+} release units (also known as triads) during excitation-contraction (EC) coupling and supplemented by store operated Ca^{2+} entry (SOCE) during repetitive and prolonged muscle activity (see Figure 30). In 2009 we demonstrated that triads and mitochondria are closely associated at the I band of sarcomeres in adult muscle (Boncompagni et al. 2009).[1] A few year later, we identified junctions between sarcoplasmic reticulum (SR) and transverse tubules (TTs) (together the sarcotubular system) (Boncompagni et al. 2017).[2] These newly identified junctions were named Ca^{2+} entry units (CEUs) as we demonstrated that they are the sites of SOCE (Michelucci et al. 2019).[3] In the past 15 years, we have collected several lines of evidence demonstrating that: i) reduced muscle activity results in loss of proper association between mitochondria and triads and reduced presence of CEUs (Zampieri et al. 2015; Boncompagni et al. 2021)[4,5]; ii) regular exercise improves disposition and association between triads and mitochondria and maintenance of CEUs (Zampieri et al. 2015; Boncompagni et al. 2021) [4,5]; iii) acute exercise triggers remodeling of the sarcotubular system at the I band to promote increase in size/number of CEUs, hence boost SOCE and sustain contractility during repetitive muscle contractions (Boncompagni et al. 2017).[2] Long-term (during training) and short-term (triggered even by a single bout of exercise) plasticity of mitochondria and sarcotubular system are likely strategies of muscle fibers aiming to improve resistance to fatigue during prolonged and repetitive activity.

Key words: mitochondria; sarcotubular system; excitation-contraction coupling; store operated Ca^{2+} entry.

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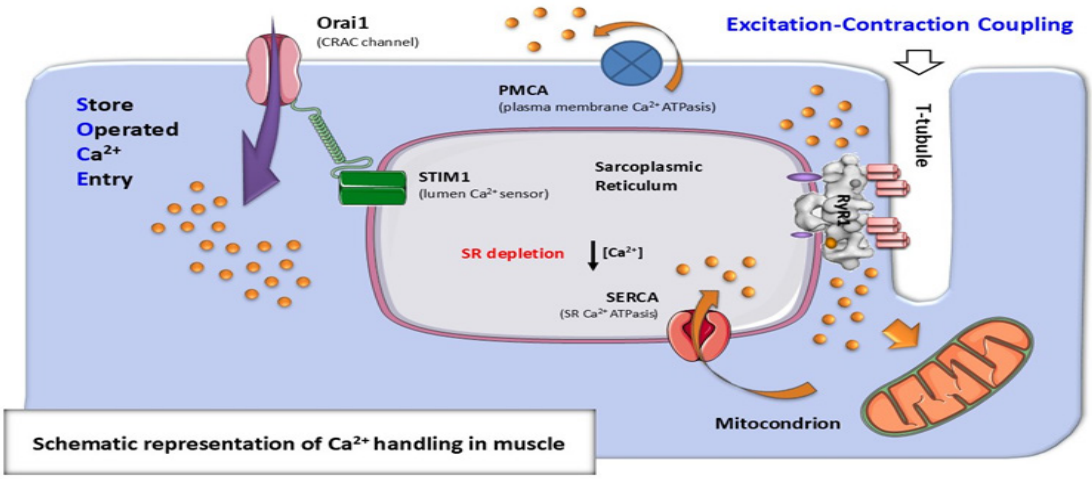

Fig 30. Schematic representation of Ca^{2+} handling in muscle.

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2025Pdm3 March 27 - Abstract 057

Extracellular matrix alteration and force transmission in older humans: A finite element analysis

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Aging is associated with a decline in muscle performance, characterized by a disproportionate loss of muscle force compared to muscle mass.[1] This study aims to numerically investigate the role of the extracellular matrix (ECM) in the lateral transmission of force in humans and to evaluate how age-related ECM modifications contribute to the loss of transmitted force. Finite element models of muscle bundles were developed from data for young and elderly human subjects,[2] considering a small number of muscle fibers connected through an ECM layer. The active behavior of muscle fibers was described using a three-element-based Hill model, while the ECM was represented with an isotropic hyperelastic neo-Hookean constitutive formulation. Numerical analyses were performed to replicate, at the bundle scale, two experimental protocols reported in the literature.[3,4] The results reveal a significant reduction in the total transmitted force in elderly subjects compared to young ones. Specifically, elderly subjects exhibited a 22% loss in transmitted force, compared to only 7.5% in young subjects. These findings align with literature on animal models, which report reductions in the range of 20–34%. The observed decrease in transmitted force can be attributed to the impaired lateral force transmission mechanism in elderly subjects, caused by a reduction in ECM shear stiffness related to its increased thickness. This computational modeling approach highlights how the age-related increase in ECM thickness between fibers negatively impacts the lateral transmission of force at the bundle level. The results suggest that the increased ECM thickness associated with aging is sufficient to explain the observed reduction in total transmitted force, emphasizing the critical role of ECM alterations in muscle weakness during aging.

Key words: extra-cellular matrix, lateral force transmission, aging, finite element models

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How does the acute response to exercise depend on prior activity?

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We used the Spillover electrical stimulation model to activate the common peroneal and tibial nerves in rats to provide programmed resistance training (PRT) with antagonistic interaction of concentric and eccentric contractions in plantar flexion and dorsiflexion.[1,2] A contralateral design was used, with the left leg as the exercised limb and the right leg as the control. Data was collected from a sham group and two 30-day experimental groups: 24h Recovery, in which exercise occurred daily with a 24h recovery period, and 72h Recovery, in which exercise occurred every three days after stimulation with a 72h recovery period. We examined the acute transcriptional response in the tibialis anterior (TA) muscle one-hour post-exercise and its relationship with proteomic adaptations in the same muscles following these 30 days of RT. The mean TA wet muscle mass increased in both experimental groups, while the sham group showed no change between stimulated and control limbs. Acute transcriptional responses and proteomic adaptations differed between groups. The 72h recovery group had 464 unique differentially expressed genes, while 337 genes were shared irrespective of training recovery time, and 275 genes were specific to the 24h Recovery group. Protein analysis identified two distinct clusters: 38 proteins were more responsive to 72h Recovery, while 140 proteins responded more to 24h Recovery. The cluster of 38 proteins contained proteins associated with muscle growth and regeneration, whereas the cluster of 140 proteins contained proteins related to metabolic enzymes and mitochondrial proteins. Figure 31 is a heatmap illustrating differences in protein abundance after PRT with 24h or 72h recovery periods. The abundance profile of 993 proteins was compared between the two recovery groups

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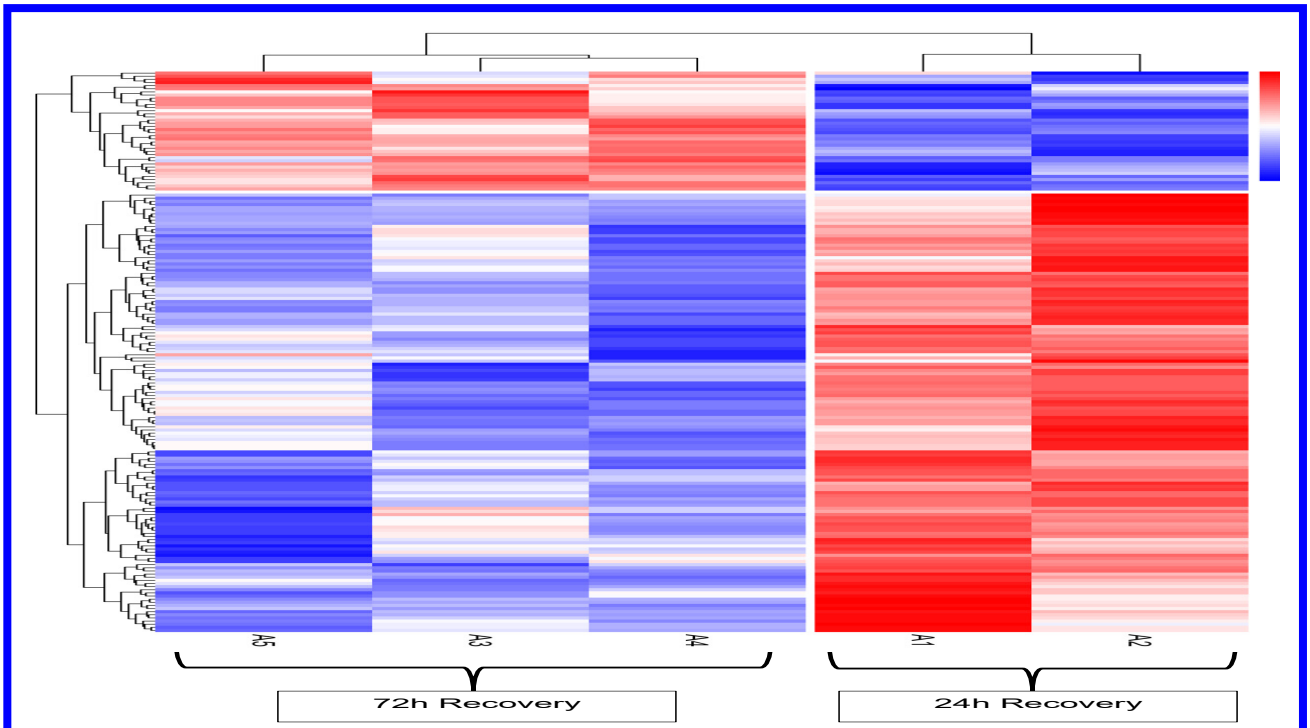

Fig 31. Rat Muscle Proteome Responses to Programmed Resistance Exercise with 24-h or 72-h Recovery Periods.

using a two-way ANOVA. A Log_2 fold-change heatmap highlights 178 proteins that showed significant interaction (recovery × stimulation) effects between recovery time and stimulation ($P < 0.1$). We provide evidence that muscle growth can be accompanied by differential adaptations in muscle phenotype, depending on the manipulation of training volume and frequency (Figure 30). Although similar increases in hypertrophy are observed, differences at the molecular level suggest distinct physiological pathways underlying these adaptations. This aligns with findings that increasing the frequency of resistance training frequency may not significantly impact muscle growth above a certain threshold.[3] Others have suggested that optimal volume and frequency interactions are muscle-dependent.[4] Our data validates PRT as a valuable tool for investigating the response to acute and chronic RT, as it enables precise, mechanistically driven research into how training volume and frequency shape muscle adaptation beyond just hypertrophy. This has broad implications for understanding how resistance training can be optimised at both molecular and physiological levels.

Keywords: Programmed Resistance Training (PRT); Muscle Adaptation; Transcriptional and Proteomic Response; Training Volume and Frequency; Skeletal Muscle Hypertrophy.

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2025Pdm3 March 27 - Abstract 059

Plasma and Salivary Irisin Response to Resistance Training: A Comparative Study

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Irisin is a myokine released in response to physical exercise that enhances energy expenditure, the browning of white adipose tissue, bone homeostasis, muscle hypertrophy, and

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the regulation of glucose and lipid metabolism1. Existing literature clearly indicates that aerobic exercise leads to increased plasma irisin levels2; instead, the effects of resistance exercise remain unclear. Some studies suggest that resistance exercise increases plasma irisin levels, while others report no change or a decrease3-4. Furthermore, irisin is typically analysed in blood samples, which is invasive and poses potential risks. The substitution of saliva samples for blood would represent a less invasive method for irisin detection; however, only a limited number of studies have evaluated irisin levels in saliva5. This preliminary study aimed to investigate the acute release of plasma and saliva irisin in response to resistance exercise. A total of seven healthy, trained men (age: 23.5 ± 2.5 years; training experience: 5 ± 3 years) were recruited. The protocol included three test sessions (10RM, TUT, 1RM) and one experimental training session (TS). TS sets (n.30) were carried out to muscular failure, with a time under tension (TUT) of 5-1-2-1, emphasising the eccentric phase of the movements. Blood and saliva samples were collected at baseline (T0), 15 minutes (T1), 24 hours (T2), and 48 hours (T4) post-exercise. Plasma samples were used to evaluate irisin and CK levels, while salivary samples were only used for irisin detection, assessed using an ELISA Assay Kit (#EK-067-29). Both plasma and salivary irisin levels demonstrated a significant increase in response to TS between T0 vs T1 (plasma 10.44 ± 0.9 to 11,38 ± 1,4 ng/mg, p:0.02*; saliva 0.051 ± 0.006 to 0.053 ± 0.008 ng/ml, 0.021, p:0.02*). CK values revealed significant differences between T0 Vs T1 (130.2 ± 27.9 to 295.4 ± 111.9 U/L, p:<0.001***), T0 vs T2 (406.4 ± 160.8 U/L, p:<0.001***), T0 vs T3 (248.4 ± 93.2 U/L, p:<0.001***); T1 vs T3 p:0.01**; and T2 vs T3 p:0.006**. A significant correlation was found between percentage changes in plasma vs saliva irisin increase between T0 and T1 (plasma 9.6 ± 15.2%, saliva 3.9 ± 4.4%; rho: 0.86, p:0.02*). This preliminary study is the first to explore irisin production following resistance training sessions in both saliva and plasma. The results show a moderate but significant increase for both plasma and saliva irisin. Correlation analysis, although preliminary, suggests that saliva sampling might be a sensitive method for detecting changes in irisin levels in response to resistance training exercises. Further studies with larger sample sizes and additional sampling points are required to comprehensively understand irisin's role in resistance training.

Key words: Irisin; Resistance Training; Muscle Damage; Muscle Hypertrophy.

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2025Pdm3 March 27 - Abstract 060

Adaptive Functional Electrical Stimulation Kinesitherapy added to cycling boosts plasma irisin levels

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Although the impact of endurance training on irisin levels has been widely investigated in the past decade,[1,2,3] no studies have examined the response of this myokine to endurance training with percutaneous Neuromuscular Electrical Stimulation (NMES). The study compared the acute irisin response to cycling with and without a novel technology Adaptive Functional Electrical Stimulation Kinesitherapy (AFESK™) delivered through the VIK8 device (AFESK™ technology, VIK8, VIKTOR S.r.l., Italy) at both the beginning and end of a 6-week training period (14 sessions), aiming to examine the additional load of AFESK and assess potential adaptation effects. Sixteen active male participants (age 39 ± 10 years, $\dot{V}O_{2peak}$ 48.0 ±

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4.8 ml·min·Kg^{-1}) were randomly allocated to two groups and matched for $\dot{V}O_{2peak}$ and age. The cycling (C) group performed 4x5m intervals at 60% peak power output (PPO) (achieved during an incremental test to exhaustion) interspersed with 3m recovery at 40% PPO. The cycling with C + AFESK group did the same training program using the VIK8 device to deliver AFESK on lower limbs muscles. Irisin response was evaluated before and after (15m, 24h, 48h post) the first (S1) and the last training session (S14). Irisin plasma concentration was detected by ELISA assay. Timepoint x Group repeated measures ANOVA and Wilcoxon signed-rank test were used for statistical analyses. Both C and C+AFESK caused significant increases in irisin levels ($p<0.001$) from baseline (S1, C: 7.3±1.7 ng/ml, C+AFESK: 8.2±1.5 ng/ml; S2, C: 7.3±1.5 ng/ml, C+AFESK: 8.6±1.5 ng/ml) peaking at 24h (S1, C: 9.9±1.3 ng/ml, C+AFESK: 11.8±1.6 ng/ml; S2, C: 10.0±1.0 ng/ml, C+AFESK: 13.0±1.6 ng/ml) and returning to baseline after 48h (S1, C: 7.2±1.7 ng/ml, C+AFESK: 8.1±1.5 ng/ml; S2, C: 7.3±1.4 ng/ml, C+AFESK: 8.7±1.5 ng/ml). Before and after the training period, concentration of irisin in the C+AFESK group was significantly more elevated than in the C group 24h post-exercise (S1, $p<0.05$; S2, $p<0.001$). No significant changes in baseline concentration were observed in both groups, however, after 6 weeks of training, the irisin quantity from baseline to 24h (expressed as delta) increased significantly in the C+AFESK (from 3.6±0.4 to 4.4±0.5 ng/ml, $p<0.05$) and remained unchanged in the C group (from 2.6±0.8 to 2.6±0.8 ng/ml). AFESK during cycling led to a greater release of irisin one day after exercise compared to traditional cycling. The training period, with or without AFESK, does not appear to affect baseline irisin levels. The AFESK, by delivering the electrical stimulus in synchrony with the voluntary contraction of the targeted skeletal muscle, may further enhance irisin release relative to normal cycling training, providing valuable insights into the mechanisms underlying irisin secretion.

Key words: irisin, Adaptive Functional Electrical Stimulation Kinesitherapy (AFESK), exercise, cycling, plasma.

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2025Pdm3 March 27 - Abstract 061

The effects of pedaling exercise with superimposed adaptive functional electrical stimulation (AFESK) on the physiological and perceptual responses to exercise and performance in healthy humans: a training study

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Percutaneous Neuromuscular electrical stimulation (NMES) is a well-known methodology used in sports medicine both for strength training and rehabilitative issues (1). Recently, the effects of NMES during pedaling exercise have been investigated, suggesting a higher metabolic and cardiorespiratory response compared to a control condition that might enhance training effects (2). Despite this, training studies failed to show a higher effectiveness of this method compared to normal cycling (3). One of the reasons might be ascribed to the time asynchrony between NMES and voluntary contraction. The aim of this pretest-posttest training study (6 weeks period/ 2-3 sessions per week) was to investigate the effects of a novel technology Adaptive Functional Electrical Stimulation Kinesitherapy (AFESK™) delivered through the VIK8 device (AFESK™ technology, VIK8, VIKTOR S.r.l., Italy) that can trigger the electrical stimulus in synchrony with the voluntary contraction of the stimulated muscle. Sixteen active male participants (age 39 ± 10 years, VO2peak 48.0 ± 4.8 ml·min·Kg-1) were randomly allocated to two groups. The control (C) group performed 4x5m intervals at 60% peak power output [PPO] (achieved during an incremental test to exhaustion) interspersed with 3m recovery at 40% PPO. The experimental (EXP) group did the same training program superimposing AFESK on lower limbs muscles during all the training sessions. Before and after the training period, aerobic and anaerobic lactate thresholds, cardiorespiratory and perceptual responses to incremental step (5 min) exercise, maximal power output for 6 seconds sprint, performance (5 km time trial) were assessed during cycling. Similarly, the neuromuscular function of the knee extensors muscles (NMF) was investigated in isometric conditions.
Change scores between post and pre assessments were determined in each group and for each dependent variable. Change scores between groups were compared using Mann-Whitney U test. Data are presented as mean ± standard

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deviation. Power outputs at aerobic (CON +4 ± 19 W vs EXP +27 ± 22 W, p = 0.031) and anaerobic (CON +1 ± 14 W vs EXP +28 ± 23 W, p=0.021) lactate thresholds statistically increased in EXP. Heart rate and perception of effort remained stable in both groups (all p values > 0.05). Similarly, during the incremental step exercise at the cycle ergometer none of the dependent variables ($\dot{V}O2$, $\dot{V}CO2$, RER, $\dot{V}e$, Bf) changed (all p values > 0.05). During the 6 seconds sprint cycling, mean power output statistically (p = 0.028) increased in EXP (+26 ± 29 W) but not in CON (-3 ± 23 W), while peak power output (CON +3 ± 44 W vs EXP 29 ± 37 W, p = 0.372) was unchanged in both groups. The 5 km total time did not statistically change (CON +1 ± 15 s vs EXP -8 ± 8 s, p = 0.226). The training period did not impact on maximal voluntary contraction (CON -1 ± 45 Nm vs EXP -8 ± 30 Nm, p = 1.000) and activation levels (CON -1 ± 4 % vs EXP +3 ± 6 %, p = 0.161) but reduced evoked twitch at 1 Hz (CON +3 ± 6 Nm vs EXP -2 ± 4 Nm, p = 0.038) and 100 Hz (CON +4 ± 9 Nm vs EXP -7 ± 7 Nm, p = 0.038).
Using AFESK during cycling for a period of 6 weeks seems to increase the power output at the Aerobic (2 mmol/l b[La]) and Anaerobic (4 mmol/l b[La]) thresholds more than normal training; this occurred with unaltered physiological and perceptual responses to exercise (Pre – Post training period) in both groups. Furthermore, mean power output during 6 seconds cycling sprint at the cycle ergometer seems to increase only in EXP. The mechanical response of the quadriceps muscle to a single and a double twitch (100 Hz), measured after the training period, seems to decrease in EXP (likely higher fatigue). Changes in power output at the aerobic and anaerobic thresholds might be partly ascribed to a small higher level of muscle strain caused by the administration of AFESK.

Key words: lactate thresholds; adaptive functional electrical stimulation; cycling, neuromuscular function.

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2025Pdm3 March 27 - Abstract 062

Improved Irisin and Mental Well-being in Breast Cancer Survivors Following 8 Weeks of Aerobic Exercise

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Physical exercise (PE) is essential for breast cancer survivors (BCSs) since it contributes to cancer prevention, enhances psycho-physical health, and improves survival rates [1]. Additionally, during PE, the muscles secrete irisin, a myokine that has positive health benefits, including an anticancer impact by suppressing tumor proliferation [2]. Nevertheless, no research has assessed the relationship between psychological well-being and irisin levels in BCSs undergoing aerobic training. We designed an 8-week intervention, by administering a tailored, moderate-intensity, PE program. After a pilot training, women engaged in training sessions twice weekly for 40 minutes on a cycle ergometer (5 min of warm up, 30 min of cycling, and 5 min of cooling down), receiving assistance from a multidisciplinary team of specialists. Assuming a holistic approach to health and the interdependence of mind and body [3, 4], the aim of this pilot study was to investigate the improvement in the psycho-physical well-being of BCSs, starting with the hypothesis of a positive association between psychological well-being and salivary irisin production of patients during the 17 trainings Participants were recruited through a convenience sampling strategy in collaboration with an Italian non-profit association. Inclusion criteria comprised: having received a diagnosis of breast cancer; having already undergone surgery; being at the end of adjuvant therapies (excluding hormonal therapy); and being suitable for PE. Before being included in the study, all the potential participants underwent a cardiological examination for the release of the medical certificate for PE and filled out a test (IPAQ) for the evaluation of their physical activity behavior. For this pilot study, we recruited 9 women, and 4 of them, with a mean age of 63.25±7.32 years, were included. Irisin levels were analyzed with an Elisa Kit, using the saliva samples [5] that were collected before, 15 min and 24h after the pilot training (baseline observation) and the last training session. In addition, the Italian validation of psychometric tests was administered via CAWI at T0 (baseline), T1 (4-week), T2 (8-week, end of intervention), T3 (1-month follow-up), and T4 (3-month follow-up) to study: symptoms of anxiety, depression, and distress (HADS); body image concerns (BIS); general quality of life (EORTC-QLQ-C30); psychological flexibility (PACT); self-esteem (RSES); and self-efficacy (GSES). Statistical analyses were performed using SPSS, version 29. Procedures were approved by the Ethics Commission of the Department of Psychology (CERPS) of Università Cattolica del Sacro Cuore of Milan. The result of biochemical analyses showed an increase in irisin production 24h after exercise. Longitudinal psychometric analysis, instead, showed a better psychological state of women at the end of the intervention and in the follow-up phase, with a decrease in body image

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concerns, lower depressive and anxious symptoms, and a better quality of life. These preliminary results are encouraging and show for the first time an investigation of irisin in BCSs engaged in a supervised PE program with simultaneous monitoring of psychological health.

Key words: Irisin; Breast Cancer; Psycho-Physical Health; Cycling Training; Multidisciplinary Intervention.

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Increased serum levels of adiponectin upon a single bout of exhaustive exercise in amateur athletes,

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Adiponectin is a serum hormone that plays a significant role in the prevention of metabolic disorders, such as obesity, type 2 diabetes, coronary heart disease, and metabolic syndrome.[1] It is secreted from white adipose tissue into circulation in three different oligomeric forms: trimers (low molecular weight, LMW), hexamers (medium molecular weight, MMW), and high-molecular-weight (HMW) oligomers. The HMW form of adiponectin is the most active in the regulation of body weight and energy balance.[2,3] Since previous studies indicated that exercise leads to higher levels of circulating adiponectin, in this work we investigated serum concentrations of this hormone after a single bout of exhaustive exercise on a cycle ergometer in 25 male amateur athletes. Participants were divided into young adults (YA) and middle-aged adults (MA), and total adiponectin was measured at baseline, upon 15 minutes and 24 h post-exercise, using ELISA. HMW oligomer levels were assessed at baseline and at 24 h post-exercise by western blotting analysis. A significant increase in total adiponectin levels was found both upon 15 minutes and 24h after the exercise protocol, especially in the YA group. Considering all participants HMW oligomers also increased 24 h post-exercise, but when analyzed separately this increase was found only in YA subjects. Correlation analyses revealed that adiponectin concentration is associated with VO2peak and Powerpeak levels in YA subjects, highlighting a positive relationship between its regulation and exercise capacity. Moreover, baseline adiponectin negatively correlated with VO2peak and Powerpeak suggesting adaptation mechanisms of adipose tissue. In conclusion, a single bout of exhaustive exercise evokes a significant, rapid, and lasting increase in adiponectin serum levels in healthy subjects, particularly due to an increase in HMW oligomers.

Key words: physical exercise; adiponectin; HMW oligomers.

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2025Pdm3 March 27 - Abstract 064

Characterization of a knock-in mouse model carrying a human mutation (D44N/+ in Calsequestrin-1) associated to Tubular Aggregate Myopathy.

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Tubular aggregates (TAs) are regular arrays of highly ordered and densely packed straight-tubes of sarcoplasmic reticulum (SR) origin found in muscle biopsies of patients affected by tubular aggregate myopathy (TAM) and in fast twitch muscle of ageing male mice (Engel et al. 1970; Boncompagni et al. 2021).[1,2] TAM is a heritable myopathy primarily characterized by progressive muscle weakness, elevated levels of creatine kinase, and exercise intolerance. About a decade ago, TAM has been linked to mutations in the genes encoding for stromal interaction molecule-1 (STIM1), a Ca^{2+} sensor placed in the lumen of the SR, and the Ca^{2+} release-activated Ca^{2+} channel ORAI1, the pore that allows entry of external Ca^{2+} when activated by STIM1-dimers (Bohm et al. 2013 and 2017).[3,4] STIM 1 and Orai1 mediate store-operated Ca^{2+} entry (SOCE), a mechanism that allows recovery of external Ca^{2+} when intracellular stores are depleted. More recently, the Casq1 gene was also found to be mutated in patients with TAM. CASQ1 is the main Ca^{2+} buffer of the SR and a negative regulator of SOCE (Barone et al. 2017).[5] We generated a knock-in mouse model of TAM harboring the mutation p.(Asp44Asn) in the Casq1 gene (Casq1D44N/+ or D44N mice). D44N mice are viable and exhibit a modest in vivo ed ex vivo weakness. Nevertheless, by 8 months of age male Casq1D44N/+mice exhibit robust presence of TAs in EDL muscle, whereas in females TAs start to form later (at around 13 months of age). Other morphological features of the progressing disease are mitochondrial damage and SR modification similar to those found in vacuolar myopathy. Following our previous experience in ageing mice, we evaluated the therapeutic potential of voluntary running in wheel cages and verified that mild exercise reduces formation of TAs and vacuoles also in D444N mice. D44N mice may represent in the future years a tool for investigation of the pathophysiological mechanisms of TAM in humans.

Key words: tubular aggregate myopathy; sarcoplasmic reticulum; calsequestrin-1; store operated Ca^{2+} entry.

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Advances in hyaluronans and glycosylated proteins: from skeletal muscle disorder research to clinical applications

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This presentation will explore the multifaceted roles of hyaluronans (HA) and glycosylated proteins in musculoskeletal disorders, emphasizing their potential in regenerative medicine. HA are naturally occurring biopolymers crucial for maintaining tissue architecture and regulating essential cellular functions, such as cell proliferation, wound healing, migration, and intracellular signaling. These biopolymers interact with various cell surface receptors, notably cluster determinant 44 (CD44), a membrane-embedded glycoprotein that facilitates adhesion, migration, and intracellular signaling. The interplay between HA and CD44 forms a dynamic interface between the pericellular environment and intracellular cytoskeletal networks, which is highly responsive to oxidative stress factors such as reactive oxygen and nitrogen species (ROS/RNS). These oxidative agents fragment native HA, disrupt CD44 microarchitecture, and activate signaling pathways involved in injury response and disease progression (Cowman M. K., 2023).

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Due to its structural and functional versatility, HA has emerged as a key molecule in biomedical research and regenerative therapies. It has been widely implemented in tissue engineering, particularly in muscle, ligament, and tendon repair. Over the last decade, researchers have developed various HA derivatives with promising clinical applications, further broadening its therapeutic potential. Specifically, HA has been found to directly and indirectly enhance the wound healing process by modulating inflammation, cellular proliferation, and extracellular matrix remodeling. Recent findings demonstrate that HA is integral to muscle regeneration, as it activates muscle stem cells to promote repair following injury. Notably, the regenerative effects of HA appear to be mediated by its synthesis within muscle stem cells, highlighting its endogenous role in tissue repair (Nakka et al., 2022). In our preliminary studies, we investigated the effects of a HA blend (2 to 1000 KDa, 2 mL) on rescuing myoblast C2C12 cells under stress-induced conditions that mimic chronic inflammatory states and muscle damage. We assessed the wound healing potential of this HA formulation in the presence of pro-inflammatory agents (IL-1β, TNF-α, LPS) and oxidative stressors (H2O2), which typically impair cellular proliferation. Initial findings suggest that HA significantly enhances cell proliferation and accelerates wound healing within 24 hours post-injury (Ferrini F. et al., in preparation). Moreover, HA has been extensively investigated for its chondroprotective effects in osteoarthritis (OA). Exogenous HA administration enhances endogenous HA synthesis by chondrocytes, mitigates cartilage degradation, and supports tissue regeneration (Barbieri E. et al. 2019). Additionally, HA regulates the release of pro-inflammatory mediators even the the responses elicited by Extracellular vesicles, which are implicated in OA pathogenesis (Carrabs et al., 2024). The past decade has seen remarkable progress in understanding the interactions between HA, glycosylated proteins, and the extracellular matrix in musculoskeletal disorders. Despite strong evidence linking matrix macromolecules to disease progression, their therapeutic potential remains underexplored. Future research should focus on leveraging these molecular insights to develop innovative treatment strategies for musculoskeletal conditions, ultimately bridging the gap between basic science and clinical applications.

Key Words: Musculoskeletal disorders; Hyaluronans; Regenerative Medicine.

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Intra-articular injections with Carboxymethyl-Chitosan in patients affected by knee osteoarthritis non-responders to hyaluronic acid: a pilot study

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Osteoarthritis (OA) is a debilitating chronic degenerative disease, affecting over 300 million patients worldwide. Pain and functional limitation are two of the main features of OA related to progressive loss of autonomy in Activities of Daily Living (ADL) and worsening of Quality of Life (QoL). No definitive treatment for OA is yet available; strategies for pain control and improvement of joint function and mobility can be implemented in mild cases (e.g. non-steroidal anti-inflammatory drugs, corticosteroids, analgesics such as paracetamol or opioids, viscoinductive/viscosupplementary drugs, administered orally or inside the affected joints). Hyaluronic acid (HA) stands as a viable treatment option for advanced knee OA. In case of treatment failure, arthroscopic or surgical approaches (i.e. knee replacement) are available. Total knee arthroplasty is a surgical option with a good success rate, but with biomechanical implications that often cause progression of OA in the contralateral knee. Nowadays, non-surgical alternatives for HA non-responders with advanced OA are however very limited. Finding a new treatment option would thus be of paramount importance for two reasons. The first is to give patients time to think without rushing about the management of their body, having the opportunity to choose the course of care and surgical setting they prefer. The second is to improve patients' QoL even if only for a short period (e.g., up to 4-6 months), empowering them to carry on their personal passions, hobbies, and even work activities. This pilot study aimed to evaluate the efficacy of a single injection of Carboxymethyl-Chitosan, a novel compound with anti-inflammatory and lubricating capacity, for advanced (Kellgren-Lawrence ≥3)

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and symptomatic knee OA in non-responders to HA. Outpatients assessed at the Physical and Rehabilitation Medicine (PRM) Unit of Tor Vergata University Hospital were enrolled for the study until October 2023. Male and female patients were included if older than 50 years, showing advanced and symptomatic gonarthrosis (KL ≥ 3), non-responder to previous intra-articular therapy with HA. Eligible patients underwent an initial intra-articular injection of corticosteroids (Metil-Prednisolone acetate 40 mg/ml); after one week, a single intra-articular infiltration of CM-Chitosan (60 mg/3 ml - 2% CM-Chitosan supplemented with 3.5% sorbitol, in a 3 ml prefilled sterile syringe) was carried out. The Visual Analogue Scale (VAS) was applied for pain measurement and the Knee Injury and Osteoarthritis Outcome Score (KOOS) for functional

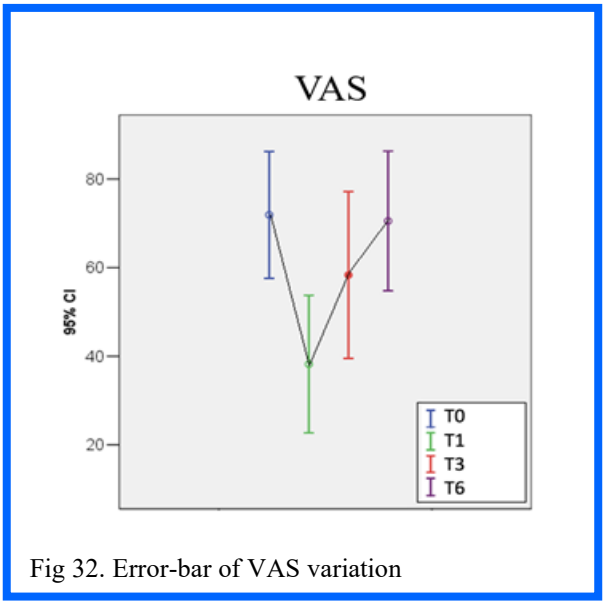

Fig 32. Error-bar of VAS variation

outcomes. Both scales were administered at the time of enrollment (T0), one month (T1), three months (T3), and six months (T6) after treatment. All data were initially entered into an Excel spreadsheet (Microsoft, Redmond, Washington, U.S.A.) and analysis was performed using the statistical package for the social sciences Windows, version 15.0 (SPSS, Chicago, Illinois, U.S.A.). The Kolgomorov-Smirnov test was applied to assess if variables were normally distributed. Comparisons between variables at different times were performed with ANOVA for repeated measures and post-hoc Bonferroni test. A value of $p<0.05$ was considered statistically significant. According to the aforementioned inclusion criteria, five females and five males and were enrolled for the study. Pain and function outcomes showed a significant improvement at T1, with a subsequent gradual resumption of symptoms. VAS was statistically significant at T1 ($p<0.01$) with an ascending trend in the following timepoints and significant worsening at T3 ($p=0.02$) and T6 ($p<0.01$) (Figure 32). All KOOS domains showed significant improvement at T1 compared with T0 and a worsening trend after T1 that was not statistically significant. Symptoms domain was an exception, with a significant worsening at T6 compared with T1 ($p=0.03$). To the best of our knowledge, our study is the first in Italy to evaluate the efficacy of a single intra-articular injection of CM-Chitosan in patients with advanced, symptomatic knee osteoarthritis non-responders HA. After data analysis, CM-C seems to have a substantial efficacy one month after treatment (T1: significant reduction in pain and a significant increase in knee function, independence in ADL, and general QoL) with tendency to worsen in subsequent months. At T3 several scores maintained better raw values than at T0 without reaching statistical significance and at T6 almost all variables returned to raw values that still showed a small improvement (Figure 31). Our study comes with some limitations (i.e. small sample size, short follow-up period, absence of a control group) and will need a subsequent deeper analysis in the future. This retrospective study suggests a good overall efficacy of CM-C for the treatment of patients with advanced knee OA (KL≥3) non-responders to intra-articular HA injection. CM-C could then appear as a treatment option for this population to extend the time to surgery and make the decision more informed. Albeit small improvement in QoL in people who have few or no alternatives for treatment of a disabling condition such as advanced knee OA should not be neglected.

Key Words: knee osteoarthritis; intra-articular injections; Carboxymethyl-Chitosan; hyaluronic acid; quality of life.

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2025Pdm3 March 28 - Abstract 067

Conservative treatment of Achilles tendinopathy with infiltrative hyaluronans: a study on biochemical, functional and viscoelastometric parameters in recreational runners

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Achilles tendinopathy (AT) is more often diagnosed in sport practitioners and physical workers whose activity is associated with significant mechanical loading that exceeds the tendon's capacity. In EU AT affects ca. 10 millions recreational runners and causes 5% of professional athletes to end their careers;[1] other risk factors contributing to AT are medications (steroids, quinolones and oral bisphosphonates), obesity and diabete.[2] Conservative treatment of AT includes local

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therapies, namely corticosteroids, hyaluronic acid (HA) or platelet-rich plasma (PRP) injections. HA injections are safer than local steroids and simpler than PRP. HA is an ideal biological lubricant with known analgesic, anti inflammatory and anti-adhesive effects. HA has been shown effective in the treatment of tendon disorders by decreasing pain, supporting tissue healing, and improving the lubrication of the tendon. The aim of this study was to evaluate the efficacy of a three-local injections regimen of HA in ameliorating clinical, functional, viscoelastometric and biochemical parameters of the tendon in middle aged recreational runners with AT. Eight recreational runners previously diagnosed for monolateral AT were enrolled. AT was confirmed before the first local HA injection (T0) by clinical examination. At T0 patients were assessed for maximal voluntary isometric contraction (MVIC) involving Achilles tendon (both injured and healthy contralateral side), and pain level with a Likert scale; Achilles tendon viscoelastic conditions, i.e. tone and stiffness, were then measured (8 cm from the heel) at relaxed state with MyotonPro (Myoton Ltd, UK). Finally, patients received the first HA injection (a blend of 200 to 1000 KDa HA). All the measurements were repeated at T1 (15 days after the first injections and immediately prior the second), at T2 (15 days after the second injection and prior the third) and at T3 (15 days after the third injection), i.e. over a total of 45 days in which clinical visits were also performed. Furthermore, at T0 and T2, injured tendon exudates were collected by needle aspiration and analyzed for IL-1 and MMP-3 content with an ELISA test. Our results indicate that at T0, tone and stiffness values were significantly different between injured and contralateral tendons. MVIC, coherently with clinical assessment, including pain score, was significantly lower in injured tendons. Interestingly, the above differences gradually disappeared at T1, 2 and T3. In keeping with these results, the volume and the inflammation status (IL-1β and MMP-3 levels) of the tendon exudates significantly decreased. Peritendonous HA injections were effective in the management of AT, as determined with a multi-methodological approach. Accordingly, to elastosonographic observations,[3] we also found that AT alters the viscoelastic parameters of the tendon and that its healing process is paralleled by recovery of these mechanical features. The evaluation of viscoelastic status associated with AT might also represent a simple, non-invasive and unexpensive tool to integrate imaging techniques (ultrasonography, elastosonography) in the diagnostic assessment and clinical grading of tendon conditions.

Key words: Achilles tendinopathy; hyaluronic acid; viscoelastometry.

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2025Pdm3 March 28 - Abstract 068

Blue turmeric: a novel food targeting inflammatory molecular networks in osteoarthritis to better quality of life

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Osteoarthritis is a widespread, age-related condition characterized by the progressive deterioration of the articular cartilage and surrounding joint tissues. Its etiopathogenesis is multifactorial, with aging and chronic inflammation playing pivotal roles alongside other predisposing factors. Disruption of chondrocyte homeostasis predisposes the tissue to degradation rather than repair, leading to matrix deterioration and exacerbation of inflammation. OA induces joint pain and has a powerful impact on decreasing joint mobility and causing a loss of quality of life.[1] Among turmeric types, blue turmeric (Curcuma caesia Roxb.) is a less explored species we previously studied for its anti-inflammatory and protective activities. Here, we investigated the benefits of a Curcuma caesia rhizome extract (CCRE),[2] rich in polyphenols, in C-28/I2 human chondrocytes exposed to IL-1β stimulation for 24 hours.[3] Intriguingly, a 48-hour pre-treatment with CCRE improved the cell viability of IL-1β-stimulated chondrocytes, as evidenced by their increased metabolic activity. Furthermore, the IL-1β-driven release of the pro-inflammatory cytokines IL-6 and IL-8 was significantly reduced by pre-treating C-28/I2 cells with CCRE for 24 and 48 hours. Noteworthy, this study highlights the potential of a polyphenol-rich rhizome extract of Curcuma caesia in mitigating inflammation and impairments in cell viability within the cellular compartment of cartilage tissue, paving the way for the development of nutraceuticals and food supplements aimed at delaying osteoarthritis and other age-related conditions. OA intervention aims to improve the quality of life during the aging process.

Key Words: Osteoarthritis; Nutraceutical compounds; Curcuma caesia.

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2025Pdm3 March 28 - Abstract 069

A Novel Fascial Mapping of Muscle Spindles Distribution: Insights from Murine Model Study

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Muscle spindles (MSs) are pivotal in proprioception and motor control. The precise distribution and localization of MSs have always been one of the research hotspots in MSs study, serving as a foundation for understanding their involvement in various diseases and motor dysfunctions. However, there are disagreements in distribution pattern of MSs at present, the discrepancies in the reported distribution patterns of MSs have hindered the advancement of novel physical therapy techniques based on MS functionality. In the present study, we present an innovative fascia-based distribution pattern for MSs (Figure 33). Using the rat quadriceps femoris muscle, serial sections of the muscle were meticulously prepared following tissue sampling, fixation, and embedding. The MSs were identified and characterized using Sirius Red staining, with their locations, quantities, associated structures, and basic parameters documented under microscopy. Our findings demonstrated that MSs are primarily located within the fascial layers, predominantly within the perimysium. The MSs capsule and perimysium are continuous in structure, and the capsule is connected to the perimysium from multiple directions simultaneously. This study proves from the structure that MSs are not only affected by the change of muscle length but also the change of fascia tension or state may have a more profound impact

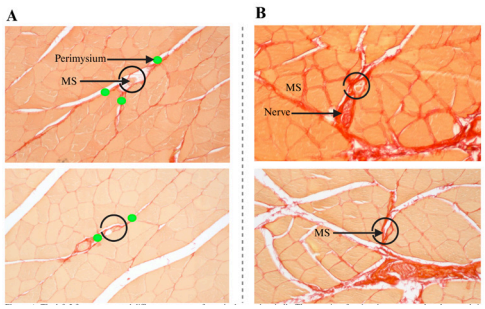

Fig 33. The left two Figures presented different segments of one muscle spindle. The quantity of perimysium connected to the capsule is variable in different segments of the soindle. B: The right two figures were collected from one single spindle. The nervedoes not accur in all segments of the muscle spindle.

on MSs. Furthermore, both nerves and vessels were observed near or within the muscle spindles' capsule, although they were not always present. In some sections, no microscopically distinguishable vessels or nerve fibers were observed around the MSs. This study proposes a novel fascial-based distribution model for MSs, highlighting that MSs are embedded within the fascial matrix and that fascia may serve as a key structural marker for locating MSs. Additionally, the fascia's structural continuity with the MS capsule suggests its role as a mediator in MS function. This research challenges traditional concepts of MS distribution and introduces a more refined and efficient approach to studying MSs through the fascial perspective, representing a significant advancement in the field.

Key Words: Fascial Mapping of Muscle Spindles; Distribution; Murine Model.

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2025Pdm3 March 28- Abstract 070

The impact of MACO stroke on forelimb ECM in mice

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Stroke is a leading cause of disability, with approximately half of stroke survivors losing of arm function due to hypotonia. However, the post stroke extracellular matrix (ECM) remodelling in musculoskeletal tissues remains unclear. This study examines changes in extracellular matrix (ECM), specifically hyaluronan (HA) and collagen, in forelimb muscles following middle cerebral artery occlusion (MCAO) in mice (Figure 34). Eighteen 8-week-old

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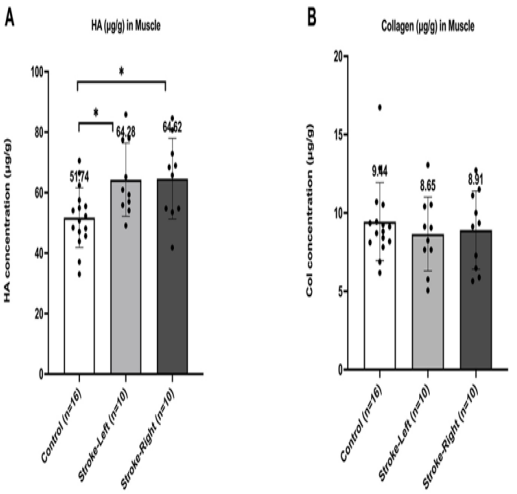

Fig 34. (A): The HA concentration in the forelimb muscle on the left and right side of health mouse in control group, on the left (stroke affective) side and on the right (non-affective) side of stroke mouse in experimental group (* $p<0.05$). (B): The collagen concentration in the forelimb muscle of the health mouse in the control group, on the left (stroke affective) side and on the right (non-affective) side of stroke mouse in experimental group($p>0.05$).

C57BL mice (6 male, 12 female) were randomly assigned to the experimental group (n=10; 4 male, 6 female) or the control group (n=8; 2 male, 6 female). 4 weeks post-stroke, forelimb muscle samples were analysed for HA and collagen distribution and concentrations. HA concentrations were significantly elevated in both the left (affected side: 64.28 ± 12.11 µg/g) and right (64.62 ± 13.33 µg/g) forelimb muscles of stroke mice compared to healthy controls (51.74 ± 9.85 µg/g; p=0.028 and p=0.024, respectively). No significant difference in HA levels was observed between the affected and unaffected sides of stroke mice (p=0.998). Collagen concentrations showed no statistically significant differences among groups, with levels of 9.44 ± 2.49 µg/g in healthy controls, 8.65 ± 2.35 µg/g in the affected side, and 8.91 ± 2.49 µg/g in the unaffected side of stroke mice. In conclusions, the results revealed a systemic increase in HA concentration in the stroke group, while collagen levels remained unchanged. The elevated HA concentrations may impair tissue mechanics and accelerate post-stroke spasticity, highlighting the importance of targeting ECM remodelling in therapeutic strategies.

Key words: stroke; extracellular matrix; hyaluronan; collage.

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2025Pdm3 March 28 - Abstract 071

Meteorological, chronobiological and thermal factors impacting postural control in knee osteoarthritis

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Osteoarthritis (OA) characterized as a degenerative joint disease, is the most common rheumatological disorder and affects millions of people around the world. The joints of the lower limbs are frequently affected. Pain is often accompanied by functional impairment and loss of independence and postural control. There is an ancient popular belief that OA symptoms may be related to changes in the weather. This belief is deeply rooted in many cultures. For example, in the Chinese language, “rheumatism” is translated as “Fēngshī zhèng” (風濕), “Fēng” (風) meaning “wind” and “Shī” (濕) meaning “wet.” In several countries (e.g., Germany and Japan), television weather reports entitled “Health weather” warn patients about pain they might feel due to weather changes. One of our studies aimed to determine if pain and balance control were related to **meteorological modifications** in patients with OA.[1] One hundred and thirteen patients with knee OA (65 ± 9 years old, 78 women) participated in this study. Posturography was performed, recording the sway area covered and sway path traveled by the center of pressure under six standing postural conditions that combine three visual situations: eyes open, eyes closed, vision altered by a sway-referenced visual surround using virtual reality goggles. Two platform conditions were tested: firm and foam supports (Figure 35. Knee pain score was assessed using

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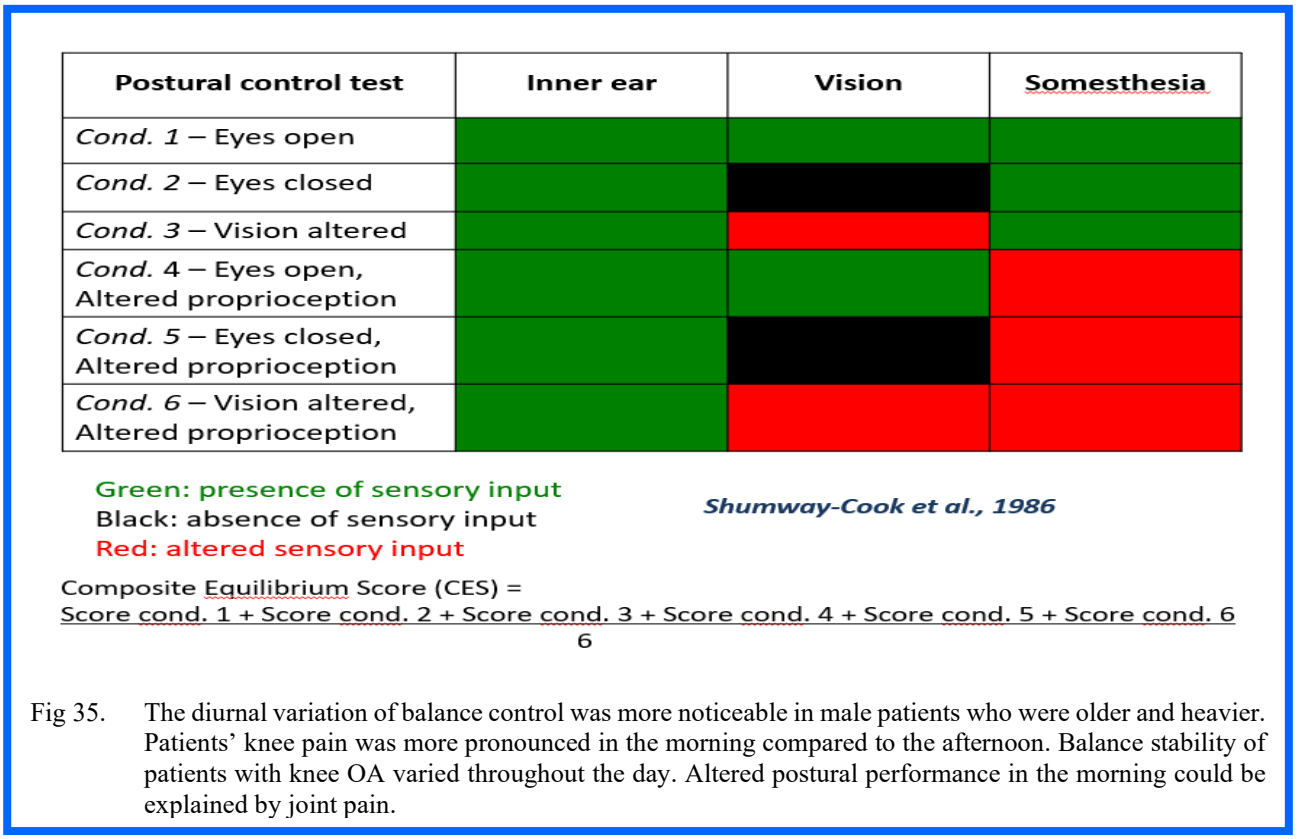

Fig 35. The diurnal variation of balance control was more noticeable in male patients who were older and heavier. Patients' knee pain was more pronounced in the morning compared to the afternoon. Balance stability of patients with knee OA varied throughout the day. Altered postural performance in the morning could be explained by joint pain.

a visual analog scale. Balance control and pain measurements recorded in the morning were correlated with meteorological data. Morning and daily values for temperature, precipitation, sunshine, hourly rainfall, wind speed, humidity, and atmospheric pressure were obtained from the nearest weather station. The relationship between postural control, pain, and weather variations was assessed for each patient on a given day with multiple linear regressions. A decrease in postural stability was observed when atmospheric pressure and maximum humidity decreased in the morning and when atmospheric pressure dropped over the course of a day. Knee pain experienced by patients was more enhanced when it was warmer in the morning and when it became wetter and warmer within a day. In addition, increasing evidence supports balance control impairment in older adult patients with knee OA (2). However, one of our studies showed **diurnal variation of balance control** in these patients (3). This study aimed to investigate the variation of postural stability in older adult patients with symptomatic knee OA during different periods of the day (Figure 34). Two-hundred and forty-one patients with knee OA (65±12 years; 82 males) were enrolled in this study. Static posturography was performed under four standing conditions: eyes open and eyes closed, without and with foam support. To assess diurnal postural variations, testing sessions were defined as follows: 8–10am, 10–12am, 1pm–3pm, 3pm–5pm. The influence of sex, age, height, weight, and body mass index on postural stability was evaluated. Knee pain was also assessed during these four testing sessions. This study showed that better postural stability was observed in patients with knee OA in the afternoon, (especially the early afternoon), compared to the morning. The diurnal variation of balance control was more noticeable in male patients who were older and heavier. Patients' knee pain was more pronounced in the morning compared to the afternoon. Balance stability of patients with knee OA varied throughout the day. Altered postural performance in the morning could be explained by joint pain. Knowledge about the relationship between weather, diurnal variation, pain and postural control can help patients with knee OA and health professionals better manage daily activities.

Hydrokinesitherapy uses the physical and chemical properties of water to help heal patients suffering from certain osteoarticular and neurological diseases. In the aquatic environment, Archimedes' principle (describing the upward buoyant force exerted on a body immersed in a fluid) enables a patient to be supported more effectively. Hydrostatic pressure also helps to counter oedema. Warm thermal water provides an analgesic effect. Movement is facilitated, muscle strengthening is secured and somesthetic work is intensified by the aquatic environment. For the above reasons, the physical properties of water in balneotherapy have also been shown to improve postural control by reinforcing proprioceptive input and increasing muscle strength. Hydrostatic pressure associated with viscosity improves exteroceptive sensory input, allowing for better limb perception. Hydrotherapy treatment can help facilitate recovery mechanisms through healing instead of by compensation,[4,5] where adaptive mechanisms are used to counterbalance the effects of impairments that disrupt balance after an incomplete recovery of the functional activity of the affected structures.

Key words: knee osteoarthritis; chronobiology; thermal factors; balance control.

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2025Pdm3 March 28 - Abstract 072

Eustachian tube dysfunction: possible role of crenotherapy

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Sinonasal disease, including rhinitis and acute or chronic rhinosinusitis, Eustachian tube dysfunction with consequent middle ear problems, represent a significant disease burden and burden on the healthcare system. The economic burden of chronic rhinosinusitis (CRS) alone is estimated to be between $4.3 and $5.8 billion per year in the United States.[1] The total costs (direct and indirect) ranged from USD 232.7 to USD 977 (UK) per episode of otitis media (OM). The economic burden per year is highest in the USA (USD 5 billion).[2] If antibiotic therapy is obviously the main bulwark during the acute phase, other possible therapeutic approaches must be taken into consideration both to reduce inflammation in the acute phase and, above all, to prevent flare-ups. Over the past two decades, significant research has been done to evaluate the role of nasal irrigations in the treatment of sinonasal disease.[3] Crenotherapy, with a therapeutic role that is still debated in the literature, could represent a valid therapeutic option; because scarce adverse effects and contraindications are, it can be safely used in elderly patients with comorbidities. [4] Ottaviano et al. compared the effects of nasal irrigations with sulfurous, salty, bromic, iodic (SSBI) thermal water or isotonic sodium chloride solution (ISCS) in patients with nonallergic chronic rhinosinusitis and demonstrated that crenotherapy effectively improves olfactory function in elderly patients with CRS.[5] Apparently, crenotherapy acts as an anti-inflammatory, mucolytic, and mucus and trophic regulator, thereby boosting the body's immune defenses. According to Cantone et al.,[4] crenotherapy induces vasodilatation and capillary permeability; stimulates the synthesis of IgAs; and reduces serum and tissue levels of IgE, thereby improving mucociliary clearance. The difficult evaluation of crenotherapy efficacy is also due to the fact that this therapy is slow acting (6,7). The efficacy of tubal catheterizations was also reported in post-surgical ears (8). In this review we try to present the state of clinical research in this field.

Key Words: sinonasal diseases; acute or chronic rhinosinusitis; Eustachian tube dysfunction; middle ear problems; tubal catheterizations.

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2025Pdm3 March 28 - Abstract 073

AQTOX Study: a single blind controlled pilot study on aquatic therapy after spasticity treatment with botulinum toxin injection

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Spasticity is the cause of several issues in patients affected by upper motor neuron syndrome. It determines pain, discomfort as far as joint contractures, reducing functional mobility and has been estimated to affect 38% of stroke survivors after 12 months. Spasticity management may include various treatment options including botulinum neurotoxin type A (BoNT-A), used to provoke a chemical denervation of hypertonic muscles. Rehabilitation after BoNT-A injections is crucial to obtain better results on patients affected by spasticity,[1] however there is still lack of evidence regarding which rehabilitation approach is the best.[2] In this pilot study we investigate the effects of aquatic therapy as rehabilitation therapy after BoNT-A injection for spasticity treatment.[3] We randomized 20 patients, all affected by spasticity of heterogeneous etiologies (stroke, multiple sclerosis, cerebral palsy, etc.). 10 were assigned to the control group and 10 to the experimental group. All patients were treated with BonT-A injections and then the control group received standard physiotherapy treatment, while Experimental group received aquatic therapy. We found the experimental treatment to be safe and well tolerated even for patients with a high grade of disability. No significant adverse effects were observed in both groups. Experimental group expressed high scores on self-reporting satisfaction forms regarding treatments received. In terms of efficacy (measured with range of motion of different key joints and Modified Ashwoth scale) there was not inferiority of experimental treatment versus conventional physiotherapy. To date, this is the first study that investigates the effects of aquatic therapy as adjunctive treatment after BoNT-A injections for spasticity management

Key words: spasticity, botulinum toxin, aquatic therapy

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2025Pdm3 March 28 - Abstract 074

Method of pelvic symmetry recovery in musculoskeletal disorders

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In recent years, there have been important changes in approaches to patient rehabilitation, taking into account the understanding of the importance of biomechanical characteristics and structural organization of the musculoskeletal system (MSB). Biomechanical properties and interaction of both superficial and deep fascia with various muscle groups allows for modern methods of physical and rehabilitation medicine. Given the various biomechanical properties of these structures, the study sets the task of recovery the pelvic symmetry, joints and muscles in relation to the spine in different

Fig 36. Method of pelvic symmetry recovery in musculoskeletal disorders

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planes. A clinical study led to the use of a multidisciplinary approach to the treatment of patients with musculoskeletal disorders (Figure 36). The results of the studies showed the effectiveness of the technique in the rehabilitation of scoliosis, myofascial syndromes, sacroiliitis, cervical and facial dystonia, treatment of temporo-mandibular joint (TMJ) dysfunctions. Innovative approaches to rehabilitation can be offered in health resorts due to their advantages and ease of implementation.

Key words: Pelvic asymmetry; musculoskeletal system; fascial system; biomechanical characteristic; scoliosis; TMJ dysfunctions.

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2025Pdm3 March 28 - Abstract 075

Rehabilitation approach to recover post-stroke diaphragm dysfunction

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Diaphragm is the main respiratory muscle, and it also helps to maintain intra-abdominal pressure, balance, and other vital functions. Unilateral diaphragmatic paresis due to stroke can lead to a number of functional impairments that complicate the recovery process. Timely diagnosis and appropriate rehabilitation strategy applications may improve the effectiveness of the entire rehabilitation process. To conduct an objective ultrasound assessment of diaphragm parameters in patients with hemiparesis in the recovery period of a stroke. To identify the potential predictors of diaphragm dysfunction. To develop specific measures to diaphragm function recovery, including the Repetitive Peripheral Magnetic Stimulation (rPMS) and define the potential risk factors to the effectiveness of the rehabilitation process. A clinical trial of 80 patients with hemiparesis in the early and late recovery period of stroke to be presented. The ultrasound examination of the diaphragm, main rehabilitation scales evaluation, respiratory function, upper limb and balance assessment were used to assess the results; rPMS was used as a specific treatment method. Diaphragm dysfunction in patients with hemiparesis was detected in 61,3% of cases. Slightly more often (65%) in patients with ischemic type of stroke than with hemorrhagic (50%). In 100% of cases, diaphragm dysfunction was detected in the presence of severe and moderate levels of upper limb

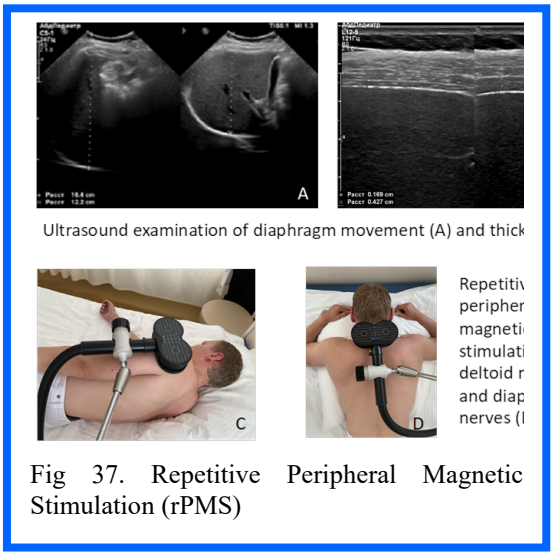

Fig 37. Repetitive Peripheral Magnetic Stimulation (rPMS)

paresis (Figure 37). Significant correlations were revealed between diaphragm dysfunction and indicators of balance, upper limb function, and indicators of external respiration function. RPMS increases the effectiveness of the diaphragm function recovery by 35 %. The results of rehabilitation are significantly negatively affected by pain, low serotonin level, depression, overall patient severity, and high levels of upper limb spasticity. In conclusion, diaphragmatic dysfunction may persist in 61,3% of cases in hemiparetic patients during the first year after the stroke, which correlates with impairments in the function of external respiration, upper limb and balance. RPMS of the phrenic nerves and the diaphragm may preserve and restore the motor and contractile functions of the

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diaphragm, which improve the upper extremity and balance status. RPMS of the phrenic nerves has a number of advantages over electrical stimulation and repetitive transcranial magnetic stimulation (rTMS), since it allows achieving an effective motor response with a lower intensity of exposure, is a painless and non-invasive method, better tolerated by patients. It may increase the efficiency of rehabilitation by 35 %.

Key Words: stroke; diaphragm dysfunction; rehabilitation: repetitive peripheral magnetic stimulation.

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2025Pdm3 March 28 - Abstract 076

Repetitive Peripheral Magnetic Stimulation to recover balance function in hemiparetic patients

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Balance impairment in patients with hemiparesis due to stroke requires multimodal correction. Targeted stimulation of the core muscles can increase the effectiveness of balance recovery and improve the mobility and quality of life of post-stroke patients. Development of a diagnostic and therapeutic approach to comprehensive restoration of balance function using Repetitive Peripheral Magnetic Stimulation (rPMS) of the core muscles in patients with hemiparesis due to stroke. The results of our own prospective randomized clinical study of 90 patients in the recovery period of stroke will be presented. The results of the X-ray examination of the spine, pelvis, ultrasound examination of the abdominal and lumbar muscles, stabilometry, gait video analysis, basic rehabilitation assessment conducted. RPMS was used to stimulate the core muscles on the hemiparetic side and peripheral nerves in lumbar area (Figure 38). As a result of the treatment, reliable

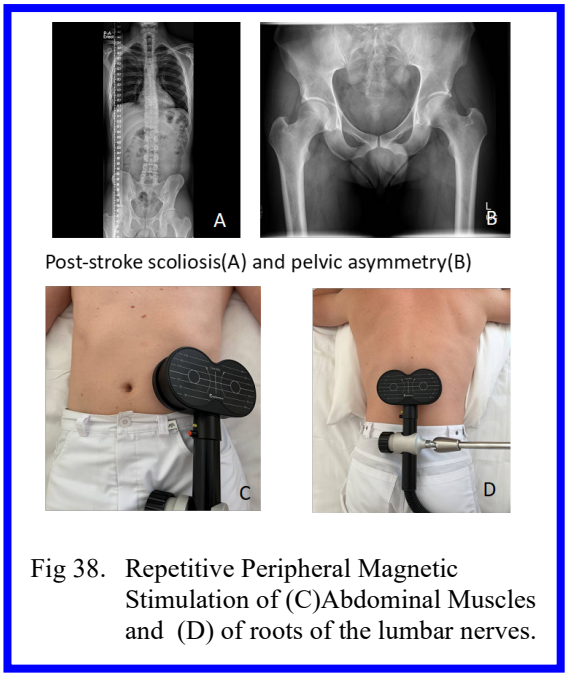

Fig 38. Repetitive Peripheral Magnetic Stimulation of (C)Abdominal Muscles and (D) of roots of the lumbar nerves.

signs of improvement in all the main indicators of balance and gait were obtained. The results of the main group showed an 25% higher efficiency than the control group. Factors influencing balance disfunction and factors complicating the restoration of balance and gait in this category of patients were identified. The efficiency of post-stroke balance recovery may increase due to introduction of the rPMS of peripheral nerves in the lumbar region and core muscles into the rehabilitation program.

Key Words: stroke; balance; repetitive peripheral magnetic stimulation (rPMS)

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2025Pdm3 March 28 - Abstract 077

Taopatch nanotechnology integrated into hearing aids, improves the parameters of the balance in hearing-impaired subjects

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Hearing loss, or hypoacusis, is a prevalent condition, particularly among older adults, characterized by partial or total inability to perceive sound. Beyond its impact on communication and quality of life, hearing loss has been increasingly associated with balance disorders and postural instability, leading to a higher risk of falls.[1,2] The auditory and vestibular systems are interconnected, and alterations in auditory input may affect postural control mechanisms. Taopatch® (Tao Technologies, Italy) is an innovative device utilizing nanotechnology to act as a neuromodulator. It combines quantum dots activated by body heat and sunlight, emitting near-infrared and far- infrared light, which has been shown to improve postural stability.[3] Given the established link between hearing and posture, this study explores the integration of Taopatch® technology into hearing aids. The aim of this study is to assess whether this combined approach can provide postural benefits to patients with hearing loss, potentially mitigating the associated risks of instability and falls. 40 subjects, 19 men and 21 women, with hearing loss (77.28 ± 15.58 years) were recruited through Audioclinik, a company specializing in hearing aids. Each participant was evaluated while wearing both a standard hearing aid and a hearing aid integrated with Taopatch® technology. Postural measurements were conducted using a SensorMedica® stabilometric platform with Motux software installed, and stabilometric parameters were compared between the two conditions (Figure 39). The collected data were analyzed using statistical software to calculate the mean percentage variation of the parameters and assess statistical significance through t-tests Statistical analysis revealed a significant reduction (p-value < 0.05) in key stabilometric parameters when using hearing aids integrated with Taopatch® technology compared to standard hearing aids.[4] Specifically, improvements included a reduction in sway path length, mean velocity, and mean acceleration. In the static analysis, an average percentage increase in the support surface area was observed for both feet, with a 14.9% increase for the right foot

Fig 39. Case study during stabilometric analysis using the SensorMedica

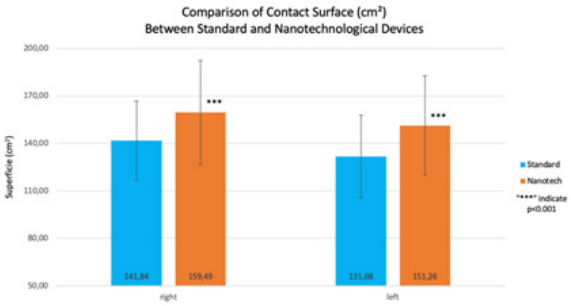

Fig 40 Comparison of Contact Surface (cm²) Between Standard and Nanotechnological Devices.

and a 12.4% increase for the left foot. Integrating Taopatch® technology into hearing aids demonstrates promising effects in improving postural stability among hearing-impaired individuals (Figure40). The observed reductions in sway and improved balance parameters suggest that this novel approach could have meaningful clinical implications, particularly in mitigating fall risks associated with hearing loss. Further studies could explore long-term outcomes and applications in broader patient populations.

Key words: Nanotechnological device, hearing loss, posture

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2025Pdm3 March 28 - Abstract 078

Adolescent idiopathic scoliosis treatment through the PosturalSpine® D'Amanti Method and the Chêneau brace. A case study,

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Scoliosis, a complex three-dimensional deformity of the spine, involves lateral curvature and vertebral rotation, impacting the frontal, coronal, and sagittal planes. Adolescent idiopathic scoliosis (AIS) is the most prevalent form, with treatment strategies varying based on severity. AIS often manifests with physical asymmetries, such as chest deformities and trunk imbalances, and disproportionately affects females (female-to-male ratio of 3:1 to 5:1).[1] Left untreated, scoliosis can lead to worsening curvature, biomechanical dysfunction, and quality-of-life impairments.[2] Management of scoliosis varies based on curvature severity and skeletal maturity, with therapeutic options including observation for mild cases, bracing for moderate curves, and surgical interventions for severe deformities. Physiotherapy scoliosis-specific exercises (PSSE) are frequently integrated into conservative management to enhance postural alignment, strengthen musculature, and mitigate curvature progression.[3] Recent innovations, such as the PosturalSpine® D'Amanti method, integrate advanced biomechanical and proprioceptive exercises performed on a specialized bench to enhance therapeutic outcomes.[4,5] This case report describes the treatment of an 8-year-old girl diagnosed with a 32° thoracolumbar rotoscoliosis of likely hereditary origin. Corrective therapy, initiated at Studio Kinesis in Ragusa, combined the use of the Chêneau brace with a 24-month rehabilitation program utilizing the PosturalSpine® bench, patented by Prof. Carmelo D'Amanti (Figure 41). The

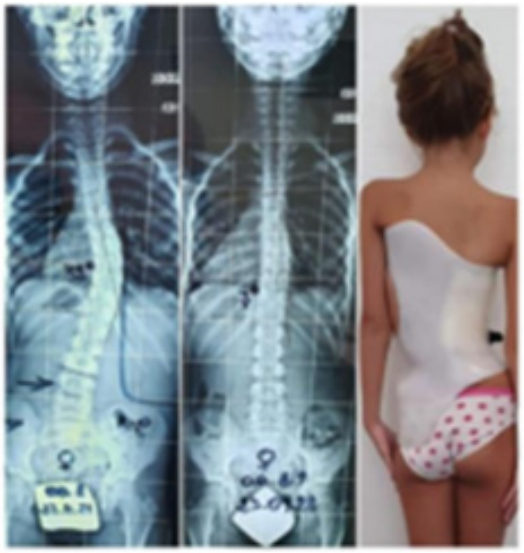

Fig 41. Corrective therapy, initiated at Studio Kinesis in Ragusa, combined the use of the Chêneau brace with a 24-month rehabilitation program utilizing the PosturalSpine® bench, patented by Prof. Carmelo D'Amanti.

program included eight monthly sessions of 30 minutes each, focusing on targeted exercises designed to improve body awareness, breathing mechanics, spinal alignment, and overall posture. The PosturalSpine® bench allowed for precise, patient-specific adjustments using features such as an anti-gravity cushion, customizable straps, and dynamic angular components. Radiographic evaluations were performed at baseline and during follow-up assessments at 7, 12, and 24 months to monitor changes in the thoracolumbar Cobb angle. (Figure 42). The results revealed a significant reduction in the Cobb angle from 32° to 9°, with the most pronounced improvement occurring during the initial 12 months. However, a slight regression from 7° to 9° was observed in the final year, coinciding with a 10 cm growth spurt. This underscores the challenges of managing scoliosis

Fig 42. Left: The PosturalSpine® bench. Rigth: Case study while performing exercises on the PosturalSpine® bench

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during periods of rapid physical development, as well as the need for adaptable treatment protocols to counteract growth-related biomechanical changes. The combination of the PosturalSpine® D'Amanti method and Chêneau brace demonstrated substantial efficacy in reducing scoliotic curvature and improving postural alignment. This innovative approach underscores the potential of integrating advanced kinesiotherapy techniques with traditional bracing in scoliosis management. However, the study's results are derived from a single case, necessitating further research with larger, more diverse cohorts to validate the observed benefits and optimize protocols for long-term management. Future investigations should also explore the role of growth-phase adaptations, adherence strategies, and the interplay of genetic and environmental factors in shaping scoliosis progression and treatment outcomes.

Key words: PosturalSpine® bench, Kinesis; health; adolescent idiopathic scoliosis, posture.

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2025Pdm3 March 28 - Abstract 079

Nanotechnology and athletic performance: Taopatch and athletic excellence

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Abstract: WITHDRAW

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2025Pdm3 March 28 - Abstract 080

Application of mindfulness techniques in the treatment of stress and eating disorders in the patients with type 1 diabetes. The need to reconnect mind and body

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Eating disorders (EDs) are serious mental disorders characterized by pathological attitudes toward food, body weight, and body image. The most common forms of EDs include anorexia, bulimia, and binge eating disorder. The danger of transmission in type 1 diabetics is that they do not feel full from food. Traditional treatment methods include cognitive behavioral therapy (CBT), but in recent years, more and more attention has been paid to the integration of mindfulness techniques into therapeutic programs. The purpose of this study is to consider the effectiveness of mindfulness techniques in the treatment of EDs in the patients with type 1 diabetes (Figure 43). Mindfulness

Fig 43. Mindfulness techniques in the treatment of stress and eating disorders in the patients with type 1 diabetes.

practices can improve emotional regulation, which is especially important for people with eating disorders, who often have difficulty managing their emotions, especially in the patients with type 1 diabetes. Mindfulness can help reduce anxiety and depression, which in turn can reduce the need to use unhealthy eating habits as a coping mechanism. The integration of mindfulness techniques into the treatment of eating disorders EDs in the patients with type 1 diabetes is a promising direction that helps improve emotional regulation, reduce stress levels, normalizes glycemic levels and develop healthy well-being. Recent advancements in neuroscience and rehabilitative science underscore the critical interplay between mental and physical processes in optimizing muscle movement and overall health. The imperative to reconnect mind and body within the realm of muscle movement healthcare, arguing that an integrative approach can significantly enhance patient outcomes and rehabilitation strategies. Key words: mindfulness, eating disorders, mind and body reconnect, optimizing muscle movement.

Key words: mindfulness; eating disorders; mind and body reconnect; optimizing muscle movement.

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2025Pdm3 March 28 - Abstract 081

Biodental engineering in research and innovation of dental implants

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Biodental engineering is a novel topic in dentistry that combines dental and engineering sciences. In this publication, examples of biodental engineering applications and developments are reviewed with the focus on the dental implantology. The rapidly growing topic of biodental engineering is an example of integrated research that has enormous engineering potential for facilitating future dental applications, dental equipment, dental materials, and dental science research.[1] Biodental Engineering (BDE) aims to solidify understanding of engineering applied to dentistry as a medical specialty with unique characteristics and wide-ranging applications. Biodental engineering covers from a scientific and relevant engineering aspect, such topics including prosthetics mechanics, orthodontics, dental implantology, dental materials, dental radiography-imaging systems, dental CAD-CAM technology and dental equipments. The current most favored approach for replacing missing teeth is dental implants. To achieve successful implant treatments that enhance both aesthetics and functionality, it is crucial to ensure precise placement of the implants.[2,3] Research examining the accuracy of robot-assisted dental implant placement in relation to freehand techniques, dynamic computer-assisted implant surgery, and static computer-assisted implant surgery is compared in this publication.[4-6] Aside from the need for minimal to no dentist involvement, a completely autonomous robot should ideally incorporate artificial intelligence (AI); therefore, the arrangement, functioning, and process closely resemble those of robot-assisted implantology, but the entire implant surgery may be performed solely by autonomous dental robots in the future.

Key words: Biodental engineering; dental implants; biomaterials; artificial intelligence, robot-guided implantology.

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2025Pdm3 March 28 - Abstract 082

3D and virtual reality techniques for planning, training and education of complex anatomical disorders

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Universities face challenges in adopting advanced technologies to enhance education and collaboration. This development project focuses on integrating 3D Modelling and virtual/augmented reality (VR/AR) technologies into healthcare education. This work aims to revolutionize education, training and research, by improving accessibility and understanding anatomies from pathological and healthy cases. The project developed different training models, creating a Real Anatomy Interactive Library (RAIL) from MRI/CT data. Additionally, we built a VR-based RHAA and developed an AR environments for realistic training and simulations. The key benefits of this application are the innovative teaching paradigms introduced with RAIL, and a unique platform for interactive healthcare education.

Key Words: 3D and virtual reality techniques; planning, training and education; complex anatomical disorders.

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2025Pdm3 March 28 - Abstract 83

Virtual Muscle Histology: towards an AI characterization in healthy and pathological conditions

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Muscle tissue characterization plays a fundamental role in diagnosing and monitoring various pathological conditions, yet current methods often rely on invasive biopsies or subjective clinical assessments. In this study, we introduce Virtual Muscle Histology, an artificial intelligence-driven framework designed to classify muscle condition and establish links between imaging biomarkers and clinical conditions. By leveraging advanced machine learning techniques, we extracted and analysed radiodensitometric, textural, and morphological features from medical imaging data to distinguish between healthy and pathological muscle states, detecting cardiomyopathies with more than 85% accuracy. The developed models demonstrated high classification performance and provided insights into the underlying alterations in muscle composition associated with disease progression, adding a longitudinal prevision on muscle degeneration. Furthermore, feature importance analysis revealed key imaging biomarkers that correlate with clinical parameters, enhancing the interpretability of AI-driven predictions reporting how clinical info are usually good for a first screening and later image-based features can detect the correct pathological condition. Our findings underscore the potential of artificial intelligence in non-invasive muscle tissue assessment, bridging for more accurate and personalized diagnostic strategies in clinical practice.

Key Words: Virtual Muscle Histology; AI characterization; healthy and pathological conditions.

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2025Pdm3 March 28 - Abstract 084

3D printed patient specific anatomy of cartilage tissue

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The advancement of additive manufacturing has enabled the creation of highly customized biomedical models with precise control over geometry and material properties. This

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research focuses on developing patient-specific synthetic cartilage using innovative Digital Anatomy polymers. The objectives include: i) the design and fabrication of a synthetic 3D-printed tibial plate, complete with tibial cartilages, aimed at replicating the mechanical behavior and morphology of their biological counterparts and ii) the design and mechanical characterization of fiber-reinforced polymers that take inspiration from cartilage's native microarchitecture. This approach offers potential alternatives to traditional manufacturing methods and reduces the need for expensive in vivo experiments.[1] The synthetic tibial plateau is designed using patient-specific anatomical data and employs advanced multi-material printing technologies to mimic the complex biomechanical properties of cartilage tissues. Furthermore, the tibial plateau incorporates a gradient of properties within the model, thus rely on a combination of materials for emulating the stiffness variations across different regions of the tibial cartilages.[2] Mechanical testing validates the performance of the synthetic construct, demonstrating comparable stress distribution, stiffness, and deformation characteristics to those of a natural tibial cartilage (Figure 44).

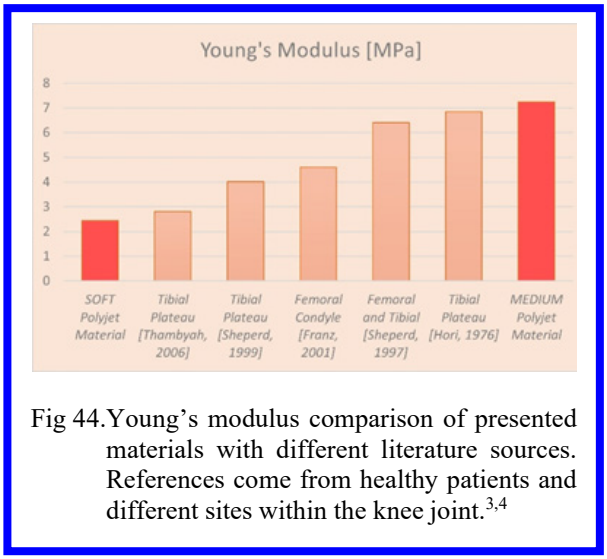

Fig 44.Young's modulus comparison of presented materials with different literature sources. References come from healthy patients and different sites within the knee joint.[3,4]

The Young's modulus values of the synthetic cartilage ranges from 2.43 MPa to 7.24 MPa,[3,4] comparable to a distribution of biological tissues' properties reported in the literature. In the second part, CAD design is utilized to create fiber-reinforced samples that imitate the layered micro-architecture of biological cartilage tissue, allowing for the study of fibers' contribution to the mechanical properties of the composite. This work showcases the transformative power of 3D printing in producing anatomically accurate and biomechanically functional synthetic models, offering invaluable tools for preclinical testing, surgical training, and implant development.

Key Words: Knee; cartilage; 3D printing; mechanical testing.

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2025Pdm3 March 28 - Abstract 085

Cohort studies using 3D-CT are needed to assess whether "home Gym-Bed" exercises are beneficial against sarcopenia,

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Abstract: WITHDRAW

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2025Pdm3 March 28 - Abstract 086

Innovative approaches in Adolescent Idiopathic Scoliosis: from neurophysiology to Artificial Intelligence

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Adolescent Idiopathic Scoliosis (AIS) is a three-dimensional spinal deformity with a significant impact on quality of life.[1] Recent research has explored not only the biomechanical and structural aspects but also the neurophysiological factors involved in AIS progression. [2] Additionally, artificial intelligence (AI) is emerging as a promising tool for predicting curve progression and optimizing therapeutic decisions, including brace prescription.[3] The aim of this study was to investigate the latest advancements in neurophysiology and artificial intelligence applied to the treatment and management of

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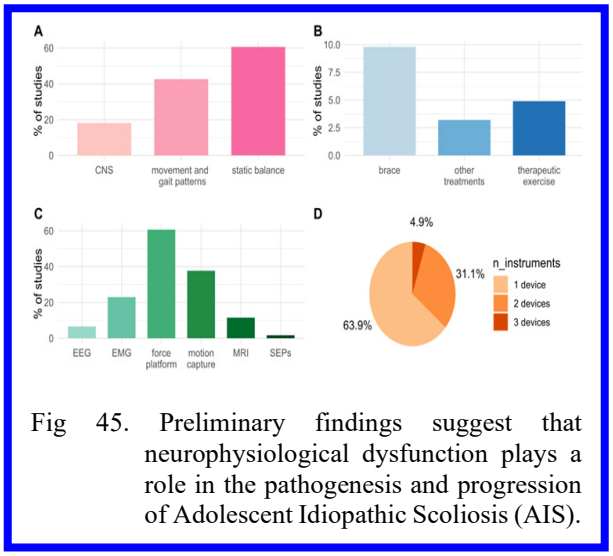

Fig 45. Preliminary findings suggest that neurophysiological dysfunction plays a role in the pathogenesis and progression of Adolescent Idiopathic Scoliosis (AIS).

AIS. The analysis was based on a review of recent neurophysiological studies, with a particular focus on balance and motor control deficits in AIS patients. Additionally, a predictive model developed using machine learning techniques on a database of AIS patients is presented, aimed at identifying early risk factors for progression and optimizing conservative treatment choices. Preliminary findings suggest that neurophysiological dysfunction plays a role in the pathogenesis and progression of AIS (Figure 45). Furthermore, the AI model demonstrates high accuracy in predicting scoliotic curve progression and optimizing brace prescription. The integration of neurophysiological approaches and AI represents an innovative frontier in AIS management. Developments in these fields could lead to more personalized and effective protocols, improving treatment adherence and reducing the need for invasive interventions.

Key-words: rehabilitation; spine; balance; scoliosis; brace.

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2025Pdm3 March 28 - Abstract 087

Quantitative 3D-CT Imaging for Sarcopenia Mitigation and Muscle Symmetry Restoration in an Elderly Subject: A Longitudinal Case Study (2014-2024)

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Sarcopenia, characterized by the progressive loss of muscle mass and function, represents a significant challenge for the elderly population, particularly in individuals with pre-existing musculoskeletal asymmetries due to trauma. This study analyzes the long-term impact of the Full-Body In-Bed Gym (FBBG) program on muscle symmetry, volume, and radiodensity in elderly subjects with a history of

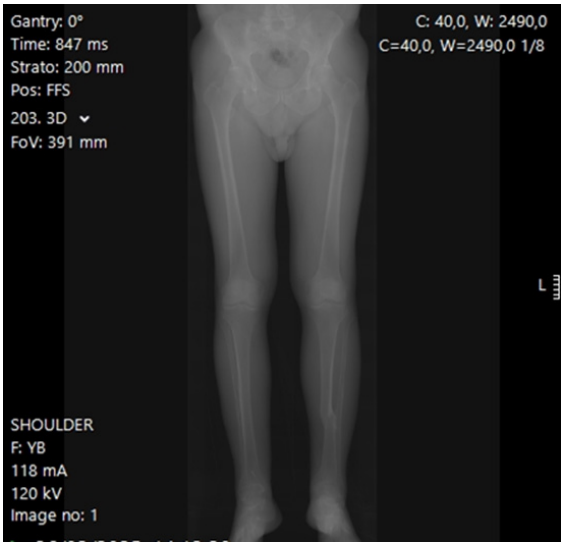

Fig 46. 2D coronal CT scan of the lower limbs with X-ray-like reconstruction.

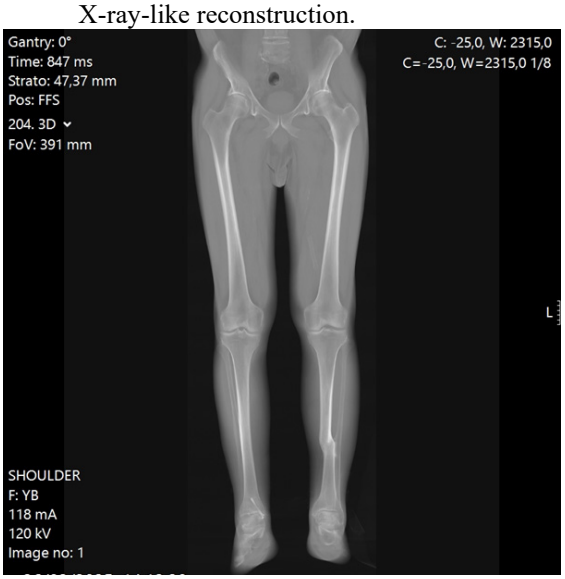

Fig 47. 3D CT scan of the lower limb bones.

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bilateral lower limb fractures. A longitudinal study was conducted on an 81-year-old man who suffered fractures in both legs in 1969. Three CT scans were performed: in 2014 (baseline), in 2023 (after 9 years of FBBG), and in 2024 (after an additional year of intensified training). The analysis included 3D volumetric segmentation and radiodensitometry to evaluate changes in muscle mass and quality over time. Muscle asymmetry was measured to determine the compensatory effects of the exercise intervention (Figure 46, 47, 48).

Between 2014 and 2023, the total muscle volume of the left leg increased by 15% and that of the right leg by 6%, with particularly significant growth in the Tibialis Anterior and Soleus muscles. Radiodensity decreased by 12-17 HU over the same period, but at a slower rate than the normal aging-related decline.

- The volumetric asymmetry between the fractured left leg and the right leg decreased from 10% (2014) to 6-8% (2023) and subsequently to 4-5% (2024) after one year of intensified training.
- The last year of more intense training contributed to nearly 40% reduction of the overall asymmetry, suggesting that higher training loads could be more effective in the later stages of rehabilitation.
- Muscle function in the left leg improved, with greater stability during standing and walking, potentially reducing the risk of falls.
- Radiodensity slightly decreased by 2 HU between 2023 and 2024, but muscle quality remained above expected sarcopenic trends.

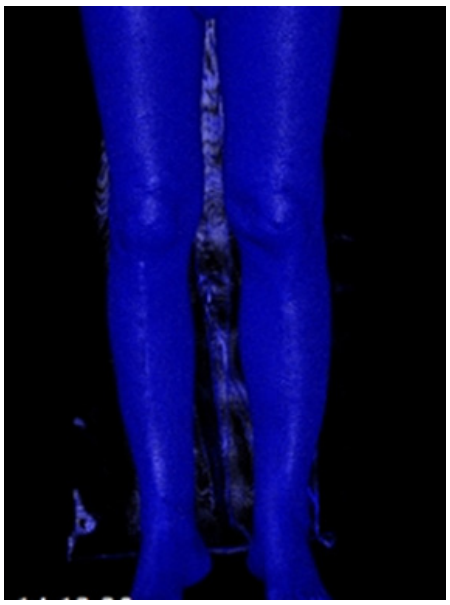

Fig 48.2D coronal CT scan of the lower limbs with X-ray-like reconstruction.

The Full-Body In-Bed Gym protocol contributed to a progressive recovery of lower limb muscle asymmetry, with functional improvements and compensation of muscle mass in the previously injured leg. These results suggest that long-term home-based exercise programs can counteract post-traumatic muscle loss and prevent sarcopenia in the elderly. Furthermore, the use of 3D computed tomography proves to be a highly effective method for monitoring muscle adaptation over time. Studies on larger cohorts will help determine whether exercise can improve muscle performance not only in the leg muscles but also in other anatomical districts.

Key words: Sarcopenia; 3D-CT Imaging; Lower Limb Fractures; Full-Body In-Bed Gym; Aging Rehabilitation.

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2025Pdm3 March 28 - Abstract 088

Innovative method for diagnosis and treatment of cranio-mandibular disorders

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At present the main study in dentistry is interdisciplinary approach for diagnosis and treatment and innovative

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technologies development in the healthcare system. Medical position of dentists according holistic approach to the full body treatment require a deeper understanding of relations between postural, joints, neuromuscular condition and right functional occlusion (Figure 49). The unique algorithm

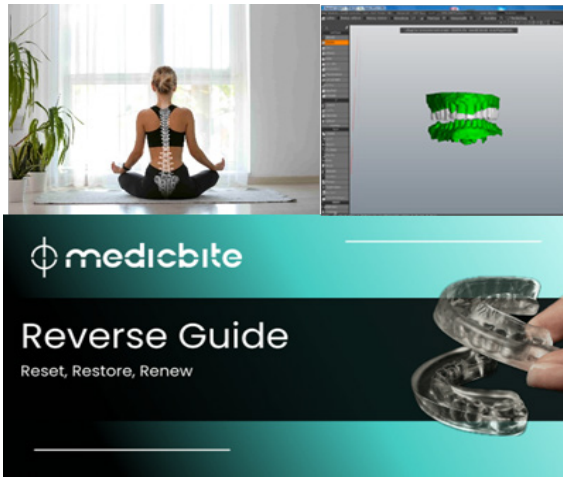

Fig 49. Preliminary findings suggest that neurophysiological dysfunction plays a role in the pathogenesis and progression of Adolescent Idiopathic Scoliosis (AIS).

determines the optimal distribution of force and the position of the lower jaw to the upper jaw. Our goal is to achieve pressure relief in the cranial sutures, head nerves, brainstem, and jaw muscles. This biomechanical principle is integrated into the guides, which through their precise and large-scale design, provide immediate relief and balance to the cranial joints during swallowing and biting. The specially designed and globally unique guides "reverse - sport – sleep" lead to a harmonious sense of well-being and an immediate increase in strength. The upper and lower jaw guides correct physical asymmetries and lead them to their orthopedic and functional starting position. The reverse guide resets all regulatory systems and corrects a variety of issues, such as physical misalignments and health complaints. The sport guide optimizes performance enhancement and shortens recovery time after training or injuries. The sleep guide improves sleep quality and reduces stress.

Key words: interdisciplinary approach, functional diagnosis and treatment; functional occlusion; cranio-mandibular disorders

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Bruxism and oral mucosa; new relationships to investigate?

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The term "bruxism" defines parafunctional clenching and/or grinding of teeth caused by involuntary rhythmic or spasmodic nonfunctional contraction of the masticatory muscles.[1,2] It is believed that daytime and nighttime bruxism are diseases,[3] the consequences of which cover all structures of the masticatory apparatus. Epidemiological studies indicate that between 8 and 31% of the total population exhibit clinical symptoms of bruxism.[4,5] The aim of this study - to establish the changes in the oral mucosa in patients suffering from bruxism by the method of autofluorescence. The study included 190 patients with bruxism aged 35-65

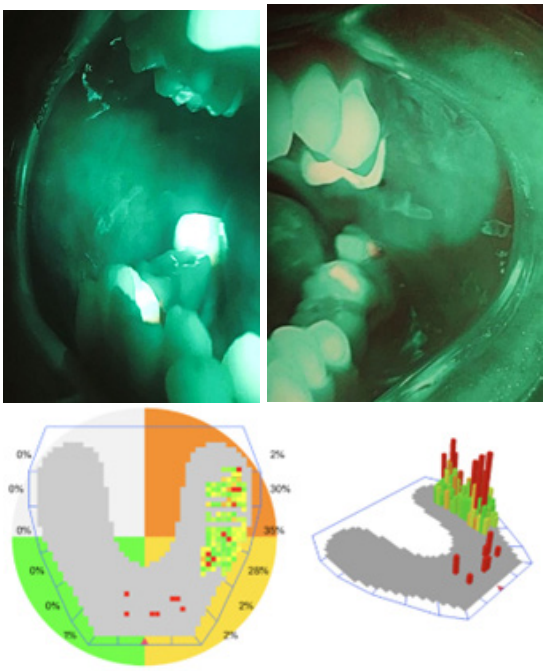

Fig 50.Areas with increased keratinization and unbalanced occlusion. Pictures from the article M. Dimova-Gabrovska and L. Maksimovskaya 2021.[5]

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years, the study was carried out at the Department of Prosthetic Dentistry, Faculty of Dental Medicine, Medical University - Sofia, Bulgaria. The deviations in static and dynamic occlusion are proven by a diagnostic computer systems T-Scan (Tekscan, USA) and OccluSense® (Bausch, Germany). For registration of the changes in the oral mucosa, the Stomatoscop AFS device is used. The occlusal analysis shows an imbalance in the distribution on occlusal force and the presence of preliminary contacts. The study of changes in the oral mucosa using the autofluorescence method allows for the objective identification of hyperkeratotic changes in the buccal mucosa in most patients with bruxism (Figure 50). Hyperkeratosis of the buccal mucosa is observed, which is characterized with increased keratinization along the length of the occlusal plain.

Key words: bruxism; oral mucosa; occlusal analysis; autofluorescence.

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2025Pdm3 March 28 - Abstract 090

New perspectives in the myofascial pain treatment

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Abstract: WITHDRAW

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2025Pdm3 March 28 - Abstract 091

Morpho-functional safety of the stomatognathic system during sports performance: indications of the Italian Society of Sports Dentistry

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Milan, Italy

Abstract: WITHDRAW

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2025Pdm3 March 28 - Abstract 092

Masticatory muscles sEMG reliability in TMD patients: Preliminary results

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Temporomandibular disorders (TMD) are a cause of non-dental orofacial pain, with complex biopsychosocial factors contributing to their development. These disorders can lead to chronic symptoms that affect patients' quality of life. Diagnosis involves clinical assessment and tests to evaluate muscle and joint pain, mobility and sound. Surface electromyography (sEMG) of the masticatory muscles provides quantitative data on muscle function and symmetry with minimal discomfort. The aim of this study was to assess the repeatability of EMG assessments of the masticatory muscles in both healthy subjects (HS) (control group) and patients with TMD (study group). Each participant completed two sessions (t0 and t1) separated by 10 days. 21 patients were recruited (3 boys and 18 girls). 12 in the control group and 9 in the study group. 17 completed the protocol. The sEMG signal was standardised by maximum

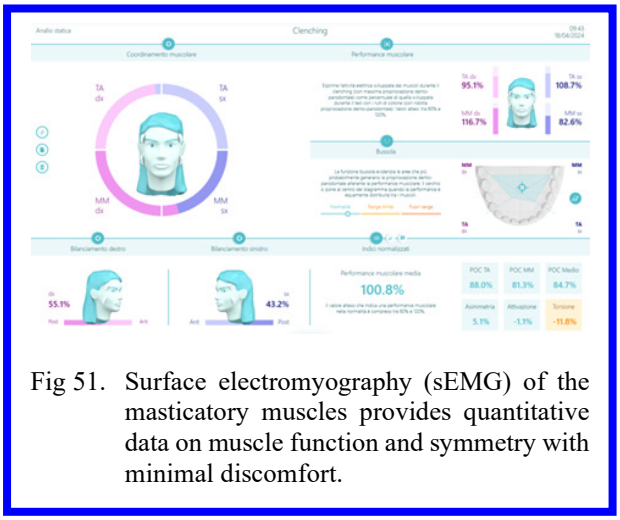

Fig 51. Surface electromyography (sEMG) of the masticatory muscles provides quantitative data on muscle function and symmetry with minimal discomfort.

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voluntary contraction (MVC) on cotton rolls. 2 tests were performed: MVC on teeth for 5 seconds and chewing gum on the right and left side for 15 seconds. Preliminary results have shown that there are significant differences between the 2 tests in TMD patients, but not in HS. In particular, during MCV in TMD subjects POC temp, Asim and Torque values are significant, while during chewing, the number and frequency of chews and recruitment on the balancing side are significant (Figure 51). We can state that repeated tests in TMDs show greater variability than in HS, who show better test repeatability.

Key words: Surface electromyography reliability; masticatory muscles adaptability; temporomandibular disorders patterns.

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2025Pdm3 March 28 - Abstract 093

Ultrasound evaluation of masseter thickness in a cohort of subjects not affected by MH: A proof of concept study

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Masseter hypertrophy (MH) is a rare condition characterized by the benign enlargement of the masseter muscle, occurring either unilaterally or bilaterally. Clinically, MH presents as an asymmetric swelling in the mandibular angle region, which is typically painless and feels firm upon palpation when the patients clench their teeth. The exact etiology of MH remains unknown, though it is generally associated with grinding habits.[1] Management options for MH include botulinum toxin type A injections, physiotherapy, and surgery.[2] To monitor muscle response to treatment, ultrasonography serves as a crucial noninvasive tool for measuring masseter thickness. However, ultrasonography is known to be an operator-dependent technique.[3] The aims of this study were i) to evaluate the intra- and inter-operator repeatability of masseter thickness measurements using ultrasonography in a cohort of subjects not affected by MH ii) to assess the difference in masseter thickness between contraction and resting stata, as well as between male and female subjects. Healthy young subjects with no systemic conditions, craniofacial anomalies, or evident MH were enrolled in the study. Subjects reporting bruxism, dental clenching and temporo-mandibular pain were excluded. Before the examination, participants were required to fast for at least two hours. A specific skin point was identified at the intersection of the Gonion-Exocanthion and Stomion-Tragus lines. The ultrasonography assessments were performed using an ultra-high-frequency linear scanner (CLARIUS L20 HD3, 8–20 MHz), with a depth of 2.5 cm and a 25 mm field of view on B mode (Figure 52). The probe was positioned parallel to the mandibular ramus, gently touching the identified skin point with the probe reference marker, without applying pressure. Masseter thickness measurements were obtained tracing a distance line between the upper point of anechoic mandibular line and the line delimitating the superficial masseteric fascia. Masseter muscles of each side were acquired twice with a one-minute rest period between acquisitions, and their thickness was measured (Cap1 and Cap2), both at rest and during muscle contraction. Acquisitions and measurements were conducted by two previously calibrated operators: Operator 1 (Op 1) and Operator 2 (Op 2) at t0. Additionally, Operator 1 repeated the examination six months later (t1). The t-tests, Dahlberg ‘s error and the Mean Absolute Deviation (MAD)

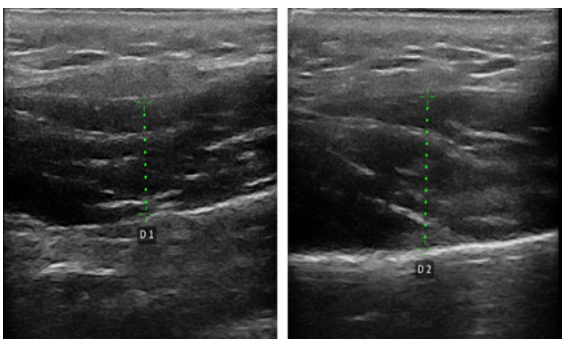

Fig 52. Ultrasonographic image showing the masseter muscle in both a resting position (A) and during contraction (B).

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	Right Masseter Rest	Right Masseter Contracted	Left Masseter Rest	Left Masseter Contracted
Op1: t0 vs t1	0,66	0,89	0,88	0,83
Op1 vs Op2	0,55	0,73	1,14	0,94

Tab. 1 Dahlberg's error intra-operator (Op1: t0 vs t1) and inter-operator (Op1 vs Op2).

	Right Masseter Rest	Right Masseter Contracted	Left Masseter Rest	Left Masseter Contracted
Op1: t0 vs t1	0,13	0,13	0,12	0,13
Op1 vs Op2	0,14	0,12	0,15	0,14

Tab. 2 Mean absolute deviation values.

	Right Masseter Rest	Right Masseter Contracted	Left Masseter Rest	Left Masseter Contracted
FEMALES	10,55 mm ± 1,18	12,19 mm± 1,78	10,65 mm± 2,39	12,14 mm± 1,97
MALES	10,94 mm± 2,21	12,67 mm± 2,55	12,04 mm± 2,07	13,54 mm±2,50

***T*ab. 3 Mean values of masseter thickness at rest and during contraction for male and female subjects.**

were calculated to evaluate the inter- and intra-operator repeatability. A multifactorial analysis of variance for Independent Samples were performed considering sex, masseter side (right/left) and the muscular status (contraction/rest). Forty-four healthy subjects were enrolled in the present study, 24 were excluded because they reported the history of bruxism, teeth clenching or temporo-mandibular pain. Ten females and 10 males, with a mean age of 25,47 years (ranging from 19 to 42) were examined. Student t-test did not show any statistically significant difference among the measurements computed by the same operator and among different operators ($p>0.05$ for all the comparisons). The Dahlberg's error test indicated lower variability in intra-operator measurements compared to inter-operator ones (Table 1). Meanwhile, the MAD showed low data dispersion relative to the average values obtained by Op1 across the two time points and between Op1 and Op2 (Tab.2). All subjects exhibited a significant difference in masseter thickness during contraction compared to the resting position (Tab. 3) with $p<.0001$. A significant difference was also found when comparing measurements between female and male subjects ($p=0.04$). In conclusion, Masseter thickness resulted significantly larger in males than in females and increased significantly from the rest position to the contraction status.

These preliminary data showed that ultrasonography may be a repeatable method for measuring masseter thickness when performed by the same operator. However, inter-operator repeatability was lower, though it remained within an acceptable range. These findings highlight the importance of using well-defined anatomical marker points to ensure measurement consistency.

Key Words: Ultrasound evaluation; masseter thickness; proof of concept study.

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2025Pdm3 March 28 - Abstract 094

Treatment of Idiopathic Recurrent Parotitis associated with masseter muscle hypertrophy: a pilot study

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Idiopathic recurrent parotitis (IRP) is an inflammatory condition of the parotid gland that can be triggered by various factors. Patients typically experience recurrent, sudden, and unilateral swelling of the parotid region, particularly during meals and chewing, especially in the morning. In some cases, IRP may be associated with masseter hypertrophy. The therapeutic use of botulinum toxin injections for masseter hypertrophy is currently under investigation; however, robust evidence in the literature remains limited. This pilot study aimed to investigate the effects of botulinum toxin injection into the masseter muscle on the neuromuscular pattern of masticatory muscles and related clinical manifestation in patients with IRP associated with masseter hypertrophy, using standardized surface electromyography (ssEMG). Patients affected by IRP associated with uni/bilateral masseter hypertrophy and

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	Patient 1		*Patient 2*	
Cotton/clench	**T0**	**T1**	**T0**	**T1**
POC TA	76.62%	83.55%	84.25%	85.90%
POC MM	83.58%	84.94%	85.47%	85.02%
Asymmetry	13.49%	-5.75%	4.66%	-0.35%
Activation	10.59%	7.04%	0.53%	-7.75%
Torque	3.70%	-1.63%	5.71%	1.72%

Tab 1. Cotton/clench parameters in the two patients at T0 and T1. In a red colour abnormal values are highlighted (TA= Anterior Temporalis, MM= masseter muscle).

	Patient 1		*Patient 2*	
Clinical parameters	***T0***	***T1***	***T0***	***T1***
Swelling	*yes*	*no*	*yes*	*reduced*
Unassisted mouth opening without pain	*38 mm*	*39 mm*	*48 mm*	*52 mm*
Unassisted mouth opening with pain	*38 mm*	*39 mm*	*48 mm*	*52 mm*
Maximum mouth assisted opening	*38 mm*	*40 mm*	*48 mm*	*52 mm*
VAS SCALE in the last 30 days	*7*	*3*	*8*	*0*
Pain frequency in the last 30 days	*Always*	*10 days*	*6 days*	*0*
Pain during chewing	*yes*	*no*	*yes*	*no*

Tab. 2. Clinical parameters evidenced in the two patients in T0 and T1.

referring pain were enrolled. Patients with parotitis associated with intrinsic salivary pathologies (stones, ductal dilations, autoimmune diseases, lymphadenopathy or serious craniofacial diseases) were excluded after being evaluated clinically by an otolaryngologist and through a sialo-magnetic resonance imaging (sialo-MRI) (Figure 53). Participants were further assessed gnathologycally using the International Diagnostic Criteria for Temporomandibular Disorders (IDCTD) questionnaire (1) and the neuromuscular pattern was recorded through ssEMG (T0), with key parameters computed for both the masseter and temporalis muscles, including the Activation Index, Torque Coefficient, Impact Coefficient, Asymmetry Index, and Percentage Overlapping Coefficient (POC%). These measurements were taken during a cotton roll/clench acquisition. Additionally, masticatory repeatability parameters were analysed over a 15-second mastication task (Figure 54). After reading and signing the informed consent, patients underwent 40 U of botulinum toxin type A injection in 2 points of the hypertrophic masseter, under electromyographic guide. Patients were re-evaluated 40 days after the injection through IDCTD and ssEMG (T1). Two female patients, aged 49 (Patient 1) and 20 years (Patient 2), were enrolled after an otolaryngologic evaluation and sialo-MRI. At T0, both patients presented with swelling of the left hemi-face and reported frequent pain, assigning high scores on the Visual Analog Scale (VAS). Both were diagnosed with myalgia according to IDCTD. The ssEMG clenching parameters were altered in Patient 1, while they were normal in Patient 2 (Tab.1).

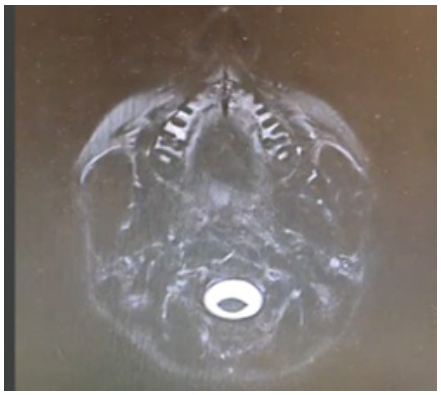

Fig 53.Sialo-MRI shows Stensen's ducts as a tubular hyperintense (white) structures. The presence of parenchymal, ductal anomalies or compression is excluded.

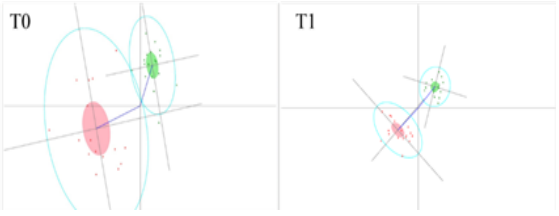

Fig 54.Lissajous plot describing the chewing test in patient 1 as confidence ellipses of the simultaneous differential left–right masseter (MM, x-coordinate) and temporalis (TA, y-coordinate) activities. In green: right-side mastication, in red: left-side mastication. The ellipses resulted downsized from T0 to T1, indicating a contraction repeatability with an improved muscular coordination

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Masticatory evaluation for both resulted uncoordinated and not repeatable. In conclusion, the present pilot study highlights that botulin toxin injection in masseter muscle in patients affected by IRP associated to MH could lead to an improvement in terms of pain and of the neuromuscular pattern of the masticatory muscles.

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2025Pdm3 March 28 - Abstract 095

Differential diagnosis of salivary gland and surrounding muscle disorders: A handbook for dentists

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Recurrent parotitis is primarily caused by salivary stones, strictures, autoimmune diseases and ab estrinseco compression.[1] Notably, the role of bruxism associated to masseter muscle hypertrophy is becoming increasingly evident in our clinical practice.[2] Among the radiological examinations typically employed in the characterization of recurrent parotitis, MR sialography is particularly valuable since it allows the evaluation of the salivary ductal system dynamically, after the stimulation with lemon juice.[3] Aim of the present work is to analyze the morphological relations existing between Stensen duct and the masseter muscle to further investigate the ethiopathogenesis of recurrent parotitis secondary to masseter muscle hypertrophy. This retrospective, monocentric study included 55 patients with recurrent parotitis with unilateral (46 patients) and bilateral (9 patients) enrolled at the ENT department of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan between January 2017 and January 2025. All patients had undergone power Doppler ultrasonography, MR sialography and a diagnostic sialendoscopy to exclude stones and duct anomalies and blood examinations to exclude immune and autoimmune disorders. The parotid glands of the included patients were analyzed separately. For controls, 33 patients with submandibular sialadenitis, who had no history of parotid symptoms and had undergone an MR sialography, were enrolled. All sialendoscopies revealed an acute angle in the region where Stensen's duct surmounts the masseter muscle. Patients with unilateral recurrent parotitis showed significantly larger diameters of the Stensen's duct in the affected gland compared to the contralateral parotid ($p<0.05$). Furthermore, in males only, the main ducts of the parotids in patients with recurrent sialadenitis were statistically longer that those in the controls ($p<0.05$). No significant differences were found in the diameters of the masseter muscles among patients with recurrent parotitis, nor in the angles formed by Stensen's duct along its pathway. In conclusion, the present study underscores the correlations between recurrent parotitis and the anatomy of Stensen's duct, namely its diameter and length. Further studies with larger sample sizes are necessary for confirmation of these preliminary data [4]. Nonetheless, our results suggest that patients with recurrent parotitis may exhibit a dysfunction of the masticatory muscles, that seems to involve not only masseter but also other muscles such as the buccinator. Therefore, an orthognathic evaluation and an electromyographic analysis of the masticatory muscle should be integrated in the diagnostic-therapeutic work-up of patients affected by recurrent parotitis

Key words: Recurrent Parotitis; Stensen duct; MR sialography; masseter muscle.

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Functional Anatomy Research Center (FARC) history and results.

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Restoring a patient's dental anatomy, which refers to the static and dynamic relationships of bones and teeth, may be necessary for various reasons. Common situations requiring reconstruction of dental and/or skeletal relationships include severe tooth wear, crowding, loss of chewing units, and oncologic surgical resections. Any procedure that alters the dental anatomy or tooth position could potentially affect dental and periodontal proprioception. González-Gil et al. (1) reported that the tactile threshold with dental prostheses (complete dentures and implant-supported restorations) is reduced compared to dentate, healthy individuals, but it remains lower than 0.06 millimeters. It is highly likely that

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dental treatments involving occlusal surfaces could alter oral proprioception, leading to neuromuscular adaptations. It has been clearly shown that dental afferents play a role in the recruitment of masticatory muscles. Occlusal changes could affect the overall contraction intensity of masticatory muscles, as well as their functional relationships, as demonstrated by Wang et al. (2) and Pumklin et al. (3). Muscle imbalances may arise from various factors, including an increased number of contacts, interference on the working or balancing side, and loss of posterior vertical support (4). Additionally, it has been shown that proprioceptive dental changes due to iatrogenic occlusal disturbances (200 µm thick) may also require functional adaptations of neck muscles (5). The role of occlusal-related functional abnormalities in the pathophysiology of Temporomandibular Disorders remains unclear; currently, no widely accepted, evidence-based scientific conclusions exist (6). The relationship between abnormal muscle recruitment and symptoms such as pain or signs of dysfunction, like movement limitation, does not appear linear, indicating that many individuals have a high degree of functional adaptability. The absence of clinical symptoms (mainly pain) following an occlusal intervention does not directly correspond to a procedure free from imperfections and/or anomalies. The adaptability of muscles and nervous system to new oral conditions (without causing symptoms such as pain) (7) could "mask" changes in other structures, such as teeth, bones, and joints. Occlusal proprioception requiring (asymptomatic) muscle adaptations could lead to changes in the distribution of occlusal forces, causing the following major complications:

a. Functional: The ability to adapt varies among individuals (some patients may develop symptoms due to altered muscular conditions) and over time.
b. Biological: Mechanical forces act on bone biology; bone apposition and resorption mechanisms are triggered by chemical processes initiated by mechanical stimuli. It has been verified that bone modifies to support functional loading needs.
c. Biomechanical: The reliability of prosthetics (crowns and implants) depends on the tension developed in artificial products.

In this context, the use of instrumental evaluations of masticatory function (before and after therapies that modify dental occlusion) is proposed to help clinicians quantify the impact of occlusal changes on oral biology. Biomechanical studies show that each muscle has its own specific action vectors (or more than one, providing redundancy features to the stomatognathic system) and that alterations in muscle force distribution cause changes in mechanical stresses on hard structures (8).

At the Functional Anatomy Research Center of the University of Milan, standardized electromyographic protocols are developed to measure the effects of dental occlusion on masticatory muscle recruitment (9), allowing inter- and intra-subject comparisons. Such an evaluation may not only prevent the onset of symptoms but also ensure greater reliability and durability of oral rehabilitations under uniform stress.

Key words: dental occlusion; masticatory muscle; standardized electromyographic measurement.

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2025Pdm3 March 28 - Abstract 097

Maintenance and restoration of masticatory muscle function in everyday dentistry

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2025Pdm3 March 28 - Abstract 098

Functional and non-functional parafunctions: what role in TMDs?

Rosaria Bucci, Roberto Rongo

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Abstract: WITHDRAW

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2025Pdm3 March 29 - Abstract 099

Standardized electromyographic examination of the masticatory muscles: technical and clinical suggestions to reduce the learning curve

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The muscles responsible for mandibular, tongue, hyoid, soft palate, and lip movements generate mechanical forces that stress the hard tissues (bones, temporomandibular joint, teeth). Several muscle groups are involved and coordinated by the central nervous system under the influence of peripheral inputs. Surface electromyography (sEMG) is a low-cost, non-invasive method usable in dental clinical practice and scientific research for the quantitative and qualitative analysis of head and neck muscles1. At the FARC (Functional Anatomy Research Center) of the University of Milan, a standardization protocol for the sEMG examination (ssEMG) has been developed, based on the differentiated analysis of tests performed with and without information from the dento-periodontal receptors (respectively clenching teeth in maximum intercuspation and with cotton rolls placed between the dental arches)2. This method reduces the technical and biological variability of the sEMG examination3, but a learning curve is necessary for the novice examiner. Based on the experience in the field of instrumental analysis of the masticatory muscles developed at the FARC, we can suggest the following objectives hierarchy to reduce the ssEMG operators' learning period:
A) Focus on obtaining repeatable acquisitions: a) Ensure the patient is free from pain at rest and can clench his/her teeth comfortably, without experiencing pain/discomfort or gag reflex. b) Obtain at least three calibrations with cotton rolls and evaluate the coherence of the myoelectric signal amplitude between acquisitions. Repeat if they are not coherent; c) Remember that clenching the teeth is not an easy exercise to perform; take care to allow the patient to become familiar with maximal clenching before performing the instrumental recordings.
B) Consider that the EMG exam is not a morphological exam of a static object but a functional exam with the aim of analyzing behaviors: a) Obtain at least two clenching acquisitions and evaluate their coherence; if they are not coherent, acquire additional ones and evaluate the trend; b) If interim dental prostheses should be modified to re-establish muscular performance, consider that the patient often needs time to find a new motor pattern (adaptation) for the new occlusion. Repeat the tests a few days after the prosthetic occlusion change.
C) Start analyzing asymptomatic subjects: a) Train to perform repeatable recordings in asymptomatic subjects with normal ssEMG coordination values; b) Reversibly modify (with paper shims between the dental arches) the patient's dental occlusion to evaluate his/her adaptation modalities to the altered morphological conditions. Identify patients with poor/medium/high functional response to the occlusal stimulus; c) If the occlusion of asymptomatic patients must be altered for prosthetic/rehabilitative reasons, start using ssEMG with the aim of maintaining the initial functional condition after prosthetic treatment. Based on the Authors' experience and recent evidence4,5, ssEMG improves the understanding of patients' chewing physiology. The consequences of dental treatment on masticatory muscle biology could be objectively assessed daily in research and clinical settings, but correct operator training must be performed to ensure high-quality measurements.

Key words: Masticatory muscles sEMG; instrumental evaluation; chewing physiology

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The impact of exercise and nutrition therapy on measures for sarcopenia in patients with rheumatoid arthritis: A systematic review

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The risk of sarcopenia is high (with a prevalence of ≥25%) in individuals with rheumatoid arthritis (RA).[1] The aim of this systematic review was to analyse the existing evidence on the efficiency of exercise and nutrition therapy on parameters of sarcopenia among patients with RA.[2] We included randomized controlled trials (RCTs) assessing the effect of physical exercise and dietary supplementation on muscle mass, muscle strength and physical performance in subjects with RA. We used the electronic databases Medline, Embase, Clinical Trial Register, and Cochrane Trial Register in accordance with the PRISMA guidelines,[3] and identified 25 studies published up to December 2023 including 2603 eligible patients aged 55 years and over. Study selection and data extraction were performed by two independent reviewers. Studies were heterogeneous in terms of protocols for physical exercise and dietary supplementation (proteins, essential amino acids, creatine, β-hydroxy-β-methylbuthyrate, vitamin D, and omega-3 fatty acids). Exercise programs, whether focused on resistance or aerobic training and neuromuscular electrical stimulation improved measures for sarcopenia, including hand grip strength (15/22 RCTs), 1-repetition maximum of upper and lower limbs (6/8 RCTs), physical performance (6/10 RCTs), and body composition (3/4 RCTs).Nutritional interventions showed additional benefits on some of the parameters (i.e., handgrip strength, lean body mass) in a small number of studies (3/5 RCTs). In conclusion, physical exercise has a positive impact on muscle mass and function in patients with RA. However, the additional effect of dietary supplementation has only been reported in a limited number of studies. Healthcare providers should incorporate exercise and nutrition in the management of RA to achieve the best possible patient outcomes.

Key words: Rheumatoid arthritis, exercise, nutrition, muscle, sarcopenia, systematic review.

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Performance score T2D – a new way to look at rehabilitation outcomes of post COVID patients

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Evaluating the effectiveness of rehabilitation interventions using patient-reported and clinician-reported outcome measures is critical for the management and prognosis of patients. As post COVID (PC) patients face unique rehabilitation challenges, careful consideration of individual baseline values must be considered for reliable evaluation of health-related quality of life and physical performance. The T2D performance score allows correction of baseline

Table 1. Rehabilitation Outcomes by Diagnostic Group.

Score	Indication	Admission	Discharge	Difference	T2D [z]	Cohen's d, p
EQ5D-5L	Post–COVID	0.77 ± 0.17	0.79 ± 0.17	0.021	0.08	0.14*
	Other Pulmonary Diagnosis	0.80 ± 0.16	0.84 ± 0.16	0.036	0.48	0.27**
	Other Indication	0.84 ± 0.15	0.87 ± 0.14	0.031	0.33	0.25**
6MWT	Post–COVID	500 ± 111	557 ± 103	56.5	0.81	0.68**
	Other Pulmonary Diagnosis	481 ± 132	526 ± 126	45.6	0.46	0.55**
	Other Indication	515 ± 111	563 ± 115	47.8	0.67	0.84**

Diagnosis, ICD-10 Code: Post–COVID (U09.9) n=207, Other Pulmonary diagnosis (J44, J45, C34) n=149, Other Indication (M16, M17, M54, I21, I25, E11, E66) n=458; * p < .05, ** p <.01

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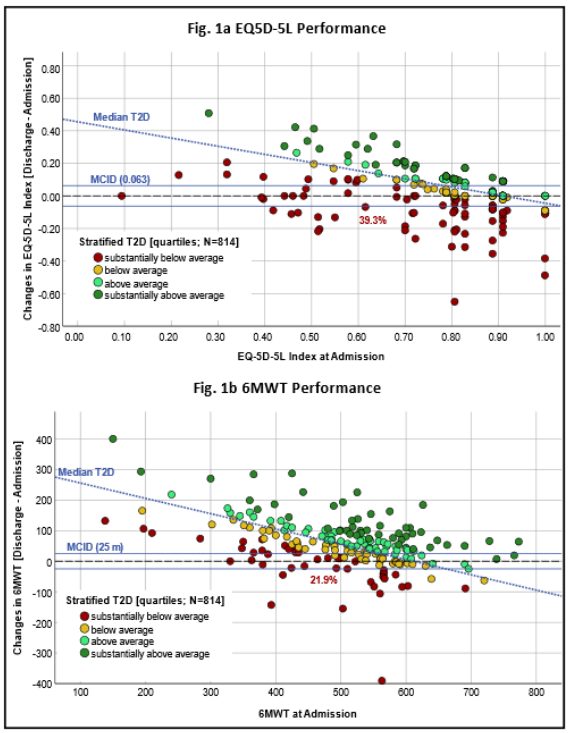

Fig. 55. Performance of Post COVID-19 Patients stratified by T2D.

differences, avoiding issues like mathematical coupling or regression effects and allowing a reliable evaluation of treatment outcomes.[1,2] This study aims to compare rehabilitation outcomes of post COVID-19 (PC) patients with those of other cohorts, utilizing the T2D performance score to adjust for baseline differences. Monocentric data of 814 patients (51 ± 12 years; 54.2% female) with pulmonological, cardiovascular, metabolic, or musculoskeletal diagnoses, including 207 with PC, who underwent outpatient rehabilitation in 2023 were used to compare PC patients with other pulmonary diagnosis and other indications. Outpatient rehabilitation was conducted following the Austrian guidelines,[3] utilizing a multidisciplinary and interprofessional approach that incorporated strength training, endurance training, physiotherapy, as well as psychological and nutritional interventions.[4] Health-related quality of life (EQ5D-5L) and physical performance (six-minute walk test, 6MWT) were measured at admission and discharge. Differences in groups were examined using T2D performance score to stratify outcomes by baseline values. All patient groups showed significant improvements, with comparable effect sizes (see Table 1). Patients with PC were notably younger (44.7 ± 12.6, $p<0.001$) and predominantly female (76%) compared to the other groups. At admission, PC patients had significantly lower EQ5D-5L scores compared to those with other indications (Cohen's $d = 0.45$; $p < .001$) and tendential lower than other pulmonary diagnosis (Cohen's $d = 0.18$; $p < .093$). At discharge, PC patients demonstrated modest gains in EQ5D-5L, with an improvement of 0.021 points (Cohen's $d = 0.14$, $p<0.05$), though their scores remained significantly lower than those of the other pulmonary patients (Cohen's $d = 0.30$; $p < .005$) and other indications (Cohen's $d = 0.53$; $p < .001$). In contrast, they demonstrated significant improvement in the 6MWT of 56.5 meters from admission to discharge (Cohen's $d = 0.68$, $p < .01$), scoring significantly higher at discharge that other pulmonary patients (Cohen's $d = 0.27$, $p = .011$) Stratifying by T2D quartiles highlighted this discrepancy in PC patient's performance in health-related quality of life and physical performance, with 39% in the lowest-performing quartile for EQ5D-5L (Figure 55a) but only 22% in the lowest quartile for 6MWT (Figure 55b), compared to 25% overall. In conclusion, while outpatient rehabilitation was effective across patient groups, leading to significant improvements, particularly in functional exercise capacity, PC patients differed markedly, showing substantial progress in physical performance while remaining poor in health-related quality of life scores. These findings underscore the importance of adjusting for baseline values, as done with T2D, to better understand differential rehabilitation outcomes.

Key words: Post COVID-19 Syndrome; Physical Performance; Health-Related Quality of Life; Rehabilitation Research.

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Which factors influence the success of rehabilitation? A mixed-methods study on patients and healthcare professionals

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The success of rehabilitation is influenced by a number of factors. This study seeks to determine the extent to which patients and healthcare professionals can accurately assess health status and rehabilitation outcomes based on patient records, and to identify the factors that impact these evaluations. The study cohort comprised 23 patient-researchers and 24 healthcare professionals, of whom 78.7% were female. Both groups evaluated the health status of anonymised rehabilitation patients at admission and discharge, as well as rehabilitation outcomes, utilising a five-point rating scale based on patient documentation. Each participant analysed records from six individual cases from the historical cohort. The self-assessments of rehabilitation outcomes were compared with objective classifications (poor, moderate, good) using standardised outcome assessments (PROMs and CROMs). The potential moderating critical factors influencing rehabilitation outcomes were examined through both open-ended and structured questions. Furthermore, the influence of evaluators' epistemic trust (1) on external assessments was analysed in greater detail. Additionally, patients provided self-assessments of their personal rehabilitation progress during a three-week inpatient orthopedic rehabilitation program. The most crucial factors for successful rehabilitation, as identified by all participants, were physical activity and general health status. However, patient-researchers placed significantly greater emphasis on psychosocial elements, including optimism, self-efficacy, self-care, mindfulness, social relationships, and medication ($p < .05$) compared to healthcare professionals. In terms of their own rehabilitation success, patients identified activities, participation and environmental factors as key elements, emphasising the importance of active engagement in therapy and effective communication with healthcare professionals (Figure 56). Additionally, notable discrepancies were identified in the evaluations of rehabilitation progress made by patients and healthcare professionals. Healthcare professionals assigned significantly more favourable ratings to patients' health status at admission ($p < .001$, $\eta^2_p = 0.069$) and displayed greater confidence in their assessments of rehabilitation success ($p < .001$, $\eta^2_p = 0.049$). The external evaluations of rehabilitation success by healthcare professionals were more closely aligned with objective classifications, showing a 54.5% agreement ($\kappa = 0.30$, $p < .001$), compared to a 47.7% agreement by patient-researchers ($\kappa = 0.18$, $p < .001$). Higher levels of epistemic trust were associated with more positive assessments of rehabilitation outcomes ($B = -0.45$, $p = .042$), with a greater degree of this relationship observed among healthcare professionals (27.63 ± 0.80 vs. 25.61 ± 3.76; $p = .031$). However, no clear relationship was established between epistemic trust and the accuracy of outcome assessments.

In conclusion, patients and healthcare professionals both identify physical activity and general health status as key factors for rehabilitation success, establishing a shared foundation for evaluation. However, patients emphasize a more personalized approach to their own rehabilitation, focusing on active involvement and supportive interactions, while considering broader psychosocial factors when assessing others. Healthcare professionals demonstrate more valid assessments, closely aligned with objective measures, supported by higher levels of epistemic trust. Although trust is linked to more positive evaluations, its relationship with assessment accuracy remains complex. While subjective insights offer valuable perspectives on individual needs, consistent use of objective outcome measures is crucial for evidence-based practice. The creation of a trusting environment and the identification of critical success factors through collaboration can enhance rehabilitation outcomes.

Key words: Critical Success Factors; Epistemic Trust; Orthopaedic Rehabilitation.

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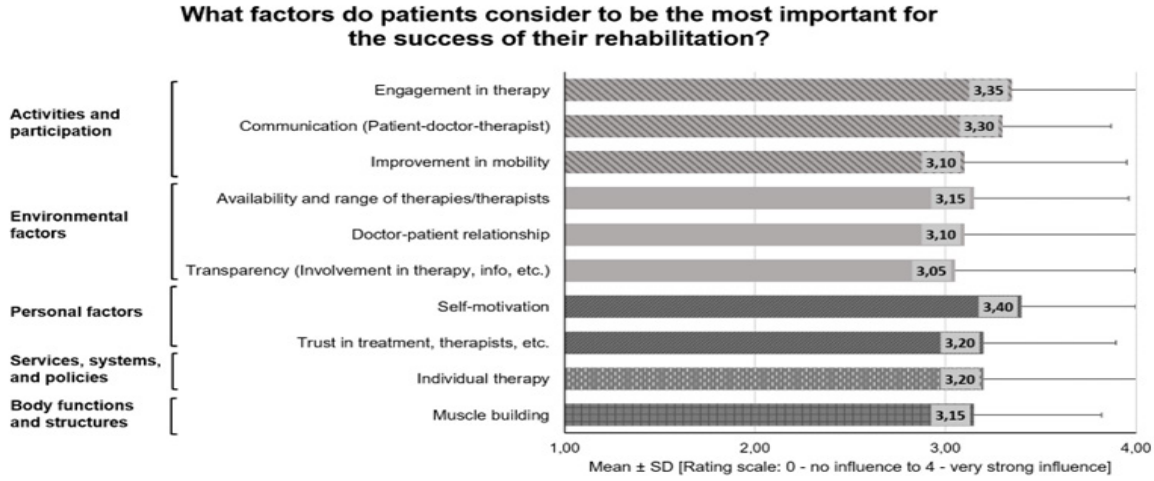

Fig 56. Key factors identified by patients as critical for their own rehabilitation success

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Effectiveness of a digital intervention to promote physical activity after oncological rehabilitation in breast cancer patients: a protocol for a randomized controlled trial

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Physical activity and regular exercise can improve cancer patients' quality of life (QoL) and symptoms related to their underlying disease or cancer treatment, such as sleep quality, pain, anxiety, fatigue, cardiopulmonary, immune, and muscle function.[1] In addition, meta-analyses suggest that depression in cancer patients is alleviated by aerobic exercise, and that in certain types of cancer (e.g., breast or colorectal), survival rates are improved while the risk of recurrence is reduced.[2,3] Therefore, medical exercise therapy, which includes strength and aerobic endurance training, plays a central role in oncological rehabilitation, along with psycho-oncological support. Previous research has shown that inpatient oncological rehabilitation (OR) improves quality of life, function, symptoms and psychological distress in several tumour types.[1] However, designing exercise programmes that are tailored to cancer survivors is essential to optimize adherence and health outcomes.[5] To improve adherence to exercise and training after inpatient rehabilitation, we propose a randomized clinical trial using a digital intervention for structured training at home with a modification of the 'aktivplan' application originally developed for cardiac rehabilitation (Figure 57). Approximately 70 breast cancer patients at the Austrian Rehabilitation Centre St. Veit im Pongau will be randomized to either (a.) a control group, which will receive regular treatment for three weeks according to the Austrian guidelines for Phase II rehabilitation, or (b.) an intervention group, which will receive additional supervised training for 12 weeks after their stay. In addition, patients in the intervention group will be counseled during their inpatient stay to develop a personalized plan for healthy physical activity through shared decision-making, with the aim of selecting appropriate exercises and activities and setting personally meaningful goals. At the end of their inpatient stay, patients will have access to their personalized exercise plan through the app interface. They will be able to report their activities, review their performance or access additional resources, including contact with the study physiotherapist. At three time points, namely t0 (start of the inpatient rehabilitation programme), t1 (end of the programme) and after 12 weeks of participation in the study (t2), patients in both the intervention and control groups will complete questionnaires using electronic patient-reported outcome measures (ePROMs), These include the Godin-Shephard Leisure-Time Physical Activity Questionnaire, the QLQ-C30 and QLQ-C30, which are standard quality of life questionnaires developed by the European Organization for Research and Treatment of Cancer Quality of Life Group (EORTC-QLG), and the Hospital Anxiety and Depression Scale (HADS) (see Figure 57). The primary objective is to test whether the use of the 'aktivplan-OR' app in combination with the associated support after a phase II rehabilitation intervention significantly improves adherence to exercise and training for at least 12 weeks. A further aim is to investigate whether the ePROM indicates an improvement in quality of life, somatic and emotional functions, symptoms caused by cancer or cancer treatment, and psychological distress in cancer survivors. In addition, a multivariate analysis will identify critical success factors for sustainable improvement of patients' health. In conclusion, if this digital intervention can improve adherence to physical activity after the end of rehabilitation,

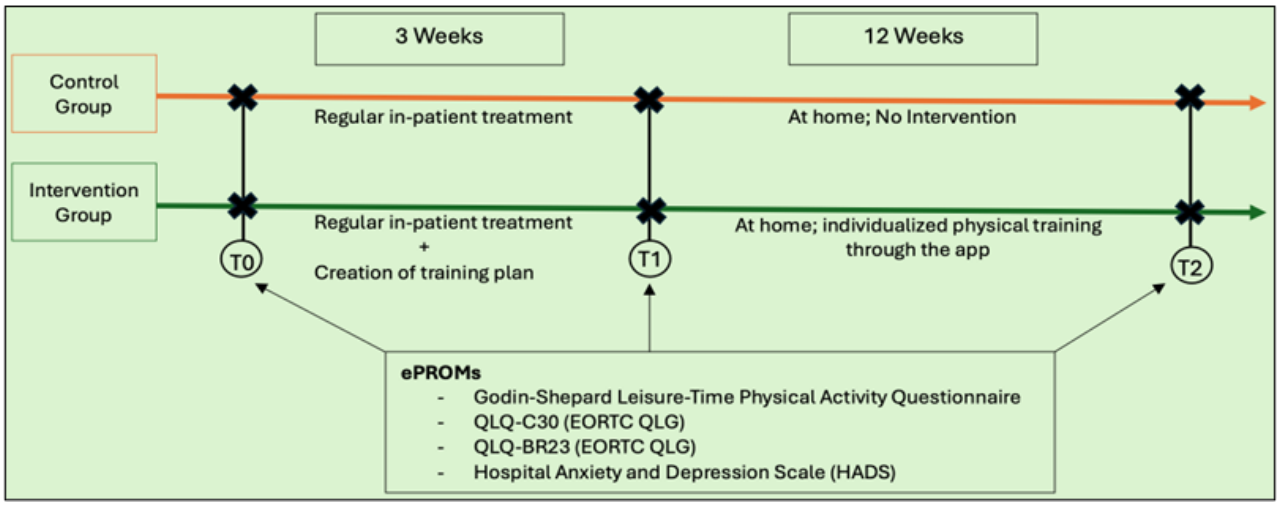

Fig 57. Planned course of study and methods.

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it may be suitable for wider application to improve QoL and prognosis in cancer patients.

Key words: Physical activity; oncological rehabilitation; secondary prevention; mHealth.

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Gastrointestinal disorders and neurological diseases

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Gastrointestinal disorders are problems that affect the quality of life of many patients with mobility problems. Swallowing alterations, dysphagia, dyspepsia, constipation or incontinence are recurrent disorders in patients suffering from neurological diseases and often contribute to negative outcomes due to a reduction in the ability to eat or isolation that induce socially unacceptable symptoms. The study and treatment of gastrointestinal disorders in neurological pathologies and motor disorders has acquired great interest in recent years, focused on the bidirectionality of the relationship between the central nervous system and the intestine. Functional bowel symptoms cataloged in the Rome IV criteria system are frequently present in the general population without apparent neurological causes. while the same disorders when present in subjects suffering from Parkinson's disease, multiple sclerosis, muscular dystrophies or dermatomyositis can lead to the clinical suspicion of neuropathic gastrointestinal pathologies. The bidirectional relationship is conceptually evident due to the possibility that the intestine represents the gateway for pathogenic substances at the nervous level, hypothesized for pathologies such as encephalopathy or Alzheimer's.[1-2] Head trauma and ischemic pathologies involving the cranial nerves can alter the function of swallowing so much as to lead to the establishment of alternative routes to the oropharyngeal one for feeding these patients.[3] Psychiatric pathologies such as anxiety and depression are frequent causes of irritable bowel syndrome. Recent evidence increasingly highlights the role that the intestinal microbiota can play in the interrelationship in question. Complex interactions link the enteric neuromuscular system, light sensitivity, epithelial integrity, and immune response.[4] The recent development of technologies that allow the identification of the different bacterial strains that compose it have highlighted the alterations most frequently present in the intestine of patients suffering from neurological and psychiatric pathologies to the point of demonstrating in guinea pigs the induction of neurological disorders with the transplantation of faeces from pathological patients.[5] The techniques for evaluating the activity of myenteric fibers have allowed the classification and diagnosis of the most serious motility disorders such as: esophageal achalasia, gastroparesis, abdominopelvic dyssynergia and Hirschsprung. Today we have not only advanced tools for the study of gastrointestinal pathologies but also treatments that directly influence visceral neurological and muscular components.

KeyWords: Gastrointestinal Symptoms; Gut-brain Interaction; Microbiota; Neurological Diseases.

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Sacral neuromodulation for bowel dysfunction

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Sacral neuromodulation (SNM) is an established therapeutic option for individuals with bowel dysfunction, particularly those with conditions such as fecal incontinence, chronic constipation, or bowel-related disorders that are refractory to conservative treatments. This technique involves the stimulation of the sacral nerve roots, which play a crucial role in regulating the muscles of the pelvic floor and bowel function. Between January 2023 and October 2024, a total of 21 patients underwent treatment at our center. Among these, 12 patients presented with both fecal and urinary incontinence, 6 patients had isolated fecal incontinence, and 3 patients suffered from constipation associated with chronic pelvic pain. A total of 21 first-stage SNM procedures were performed, followed by 17 permanent implants. The primary outcomes assessed during follow-up included: a reduction of at least 50% in episodes of fecal incontinence (FI) and/or urinary incontinence (UI); a reduction of at least 50% in symptoms of constipation and chronic pelvic pain (CPP) for the respective patient subgroup. The secondary outcome for all patients was the overall satisfaction with symptom relief and improvement in quality of life. With a median follow-up of 12 months (range: 6–24 months), all 12 patients (100%) with mixed fecal and urinary incontinence reported significant improvement in their symptoms, with a substantial reduction in leakage episodes. Among the 6 patients with isolated fecal incontinence, 3 (50%) demonstrated clinical improvement, while the remaining 3 did not achieve significant symptom relief following the first-stage SNM procedure, leading to device removal. Regarding the 3 patients with constipation and chronic pelvic pain, 2 (67%) reported complete resolution of pain symptoms and a marked improvement in bowel function, achieving regular bowel movements.With respect to the secondary outcome, all 17 (100%) patients who underwent permanent implantation reported satisfaction with symptom relief and an overall improvement in quality of life. These highly satisfactory outcomes can be attributed to a rigorous preoperative selection process to identify suitable candidates for SNM, as well as systematic post-procedural follow-up. Additionally, continuous parameter adjustments tailored to individual patient needs have likely contributed to the overall success of the procedure. However, the limited sample size of this study does not allow for the identification of the optimal patient subgroup that would benefit most from this intervention. Further studies with larger cohorts are necessary to refine patient selection criteria.

Key Words: Constipation; Electric stimulation; Fecal incontinence; Sacral nerve stimulation; Sacral neuromodulation.

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First Reported Case of a Robotic Subtotal Colectomy in Slow transit constipation: a new frontier

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Slow transit constipation accounts for about 15–30% of chronic constipation and is characterized by prolonged transit time of colonic contents, abdominal distension, abdominal pain, and defecation dependent on laxatives. Non-surgical treatments such as diet adjustment, taking laxatives, increasing fiber and water intakes are the preferred treatments method. However surgical treatment seems to be the only chance to treat patients with last stages of slow transit constipation. Macha MR et al. demonstrated that it is feasible to perform minimally invasive surgery with optimal results and low morbidity for the treatment of end stage of slow transit constipation. Robotic colorectal surgery has been largely described in literature with comparable outcomes to laparoscopic surgery in terms of safety and feasibility. We report the first case in literature of a Robotic Subtotal Colectomy performed in Sant'Antonio Hospital of Padua using the Versius Robotic System in a patient with a low transit refractory constipation after failing every conservatory treatment. Surgery was performed using the Versius system from CMR surgical which consists of bedside units for each instrument and a console. The patient is a woman with long term low transit refractory constipation that was referred by our center gastroenterologist. The patient was discharged on

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postoperative day fourth postoperative day with no complications. After 9 months of follow-up, the patient is in excellent health. She reports regular bowel movements, requiring the use of osmotic laxatives only occasionally.

Key words: Constipation, slow transit constipation; Colectomy.

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Safety and Efficacy of Intermuscular Tunnelling prior selective miotomy in a young patient affected by type 2 Achalasia

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Achalasia is a major motor disorder characterized by incomplete lower esophageal sphincter (LES) relaxation and consequent Esophagogastric Junction Outflow Obstruction (EGJOO), defined as pathologic Integrated Relaxation Pressure (> 15 mmHg), and absent peristalsis, according to Chicago 4.0 classification.[1] The disease is thought to be primarily related to impairment of normal enteric neuronal function as an autoimmune process, even though a proper etiology is lacking. Unfortunately, no therapy reverses the neural injury, and all current therapeutic efforts are then focused on disrupting the LES via dilation or myotomy in order to address EGJOO and treat symptoms.[2]

Both Peroral endoscopic myotomy (POEM) and Heller-Dor laparoscopic myotomy are long-term treatment, with a dysphagia and regurgitation remission rate of about 95%1. POEM is a more recent procedure,[3] allowing a length-tailored and selective myotomy of circular layer of esophageal muscularis propria via endoscopic access in third space, with consequent preservation of EGJ anatomy. It consists of a preliminary esophageal mucosal incision, subsequent submucosal tunnelling throughout esophageal wall and beyond cardia, and selective myotomy of circular layer with a patient-based extension.[4] We present a case of a 34-year-old patient with type 2 Achalasia, naive for previous treatment, suffering from multiple aspiration pneumonia episodes, on a monthly basis, and severe weight loss. POEM was therefore performed, with an unpleasant surprise. Severe fibrosis, probably consequence of several food impactions, hampered a proper access to submucosa, forcing an intermuscular tunneling approach.(Figure 58)

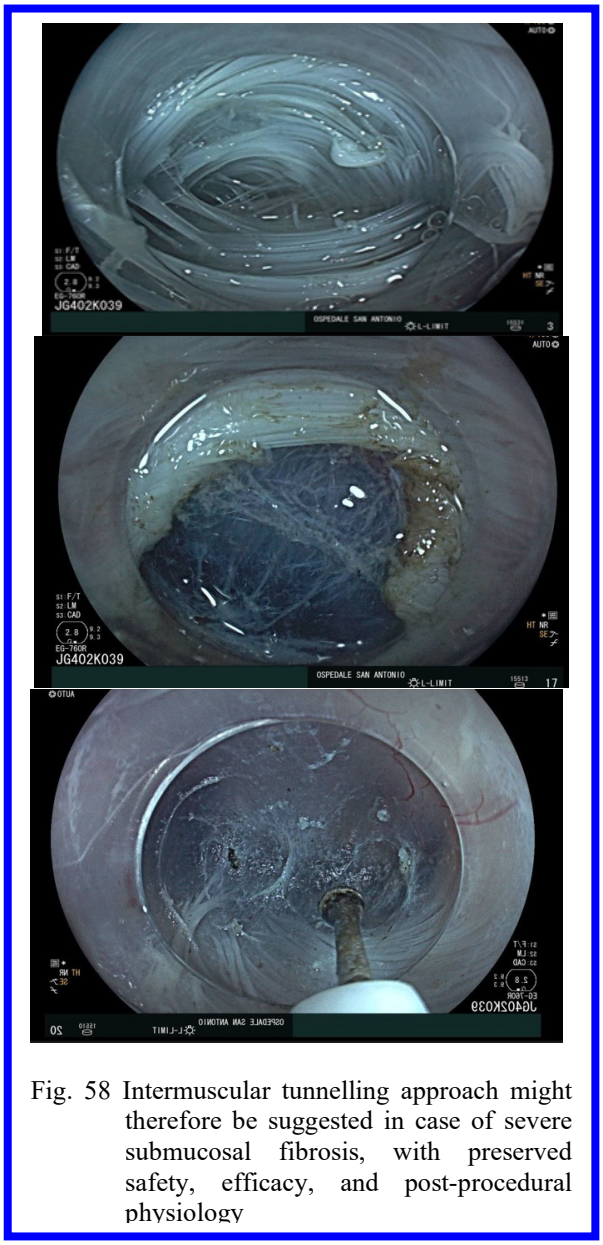

Fig. 58 Intermuscular tunnelling approach might therefore be suggested in case of severe submucosal fibrosis, with preserved safety, efficacy, and post-procedural physiology

Submucosal tunnel was finally reached up, with subsequent procedure accomplishment. The patient experienced no adverse events, except for mild, and opioids responder, post-procedural chest pain, fast discharge, and complete

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remission of symptoms. At 1 year follow-up the patents maintained full clinical remission. Neither High-resolution Manometry or upper GI endoscopy showed residual pathologic muscular activity nor blown-out myotomy (BOM) pseudodiverticulum in distal esophagus. An intermuscular tunnelling approach might therefore be suggested in case of severe submucosal fibrosis, with preserved safety, efficacy, and post-procedural physiology

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Esophageal motility disorders: from diagnosis to treatment

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Esophageal motility disorders comprehend a large variety of clinical conditions. Diagnosis is sometimes challenging, and treatment options varies from medical therapy to endoscopic or surgical strategies (Figure 59). Clinical presentation of esophageal disease could be characterized by dysphagia, food regurgitation, thoracic pain, gastro-esophageal reflux, but sometimes patients complain soft symptoms such as sialorrhea or epigastric pain. Upper GI endoscopy is the first line tool to detect esophageal disorders, in order to exclude malignancies or obstructive causes of symptoms (such as esophagitis, stenosis, etc…). Barium-swallow X-ray or Time-barium esophagogram is useful to detect esophageal morphology and the presence of hiatal or congenital hernia.1

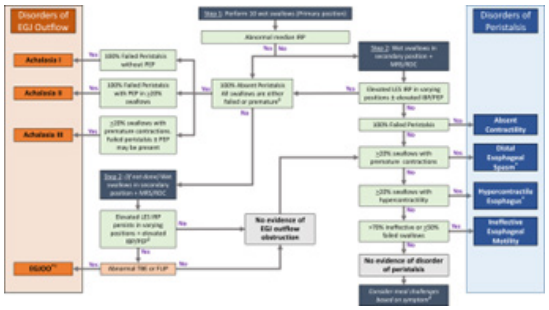

Fig. 59 The Chicago Classification v.4.0 Yadlapati R, Kahrilas PJ, Fox MR, et al. Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©. Neurogastroenterol Motil. 2021 Jan;33(1):e14058. doi: 10.1111/nmo.14058. Erratum in: Neurogastroenterol Motil. 2024 Feb;36(2):e14179. doi: 10.1111/nmo.14179. PMID: 33373111; PMCID: PMC8034247.

High-resolution manometry is mandatory to detect esophageal motility disorders according to the Chicago Classification v.4.0.2 Treatment options comprehend medical, endoscopic or surgical therapies. Esophageal motility disorders characterized by outflow obstruction symptoms often require endoscopic or surgical treatments to obtain symptoms' relief (i.e., POEM3 or laparoscopic Heller myotomy4). Those patients with GERD symptoms and evidence of ineffective/absent motility could be treated with PPi or surgical operation with optimal results.5 Patients with esophageal spasm or dysmotility need medical therapy; endoscopic or surgical treatments are sometimes used but with very low evidence.

Key Words: esophageal motility disorders; achalasia; high-resolution manometry; PPi; laparoscopic fundoplication.

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Chemokines as potential biomarkers and therapeutic targets for intestinal motility disorders in IBD

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Eotaxin and RANTES are chemokines of the CC family that have a number of functional properties, including eosinophil recruitment. They are studied as potential biomarkers of

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various gastrointestinal diseases, including those associated with intestinal motility disorders. Eotaxin is a chemokine that selectively attracts eosinophils, which play a key role in inflammatory reactions. According to a number of studies, inflammatory bowel diseases (IBD) are associated with increased eotaxin levels, which correlated with eosinophil accumulation and inflammation in the gut.[1,2] It has been established that eotaxin-mediated eosinophil activation can lead to the release of neurotoxic proteins that damage intestinal neurons, potentially altering intestinal motility. Inhibition of the eotaxin-CCR3 axis has been shown to alleviate intestinal neuropathy and restore colonic motility in animal colitis models.[1] Given its role in eosinophil recruitment and inflammation, eotaxin may also serve as a biomarker for conditions characterized by intestinal motility impairment and inflammation, such as IBD.[2] Similar to eotaxin, RANTES is involved in recruiting various immune cells, including T cells and eosinophils, to inflammation sites. CCR3 is a receptor that binds RANTES and is expressed on eosinophils, promoting their migration to inflamed intestinal tissues.[3,4] So it is of particular interest to study the expression patterns in the eotaxin - CCR3 - RANTES system in IBD with significant motility impairment. The aim of the study was to test the hypothesis about the most significant effects of cytokines and chemokines in different parts of the intestine on motility changes in individuals with IBD. Materials and methods: Patients 18-66 y.o. with newly diagnosed Crohn's disease (CD) (n=8) and Ulcerative colitis (UC) (n=10) were included in the study. The main laboratory data included CRP, fecal calprotectin, ANCA, ASCA, White Blood Cells (WBC) count. All patients were performed with ileocolonoscopy and biopsy histological assessment. In our work, we analyzed the immunological profile of various intestinal regions (ileum, sigmoid colon) of patients with IBD (n=18): UC (10) and CD (8) with varying degrees of intestinal motility disorders, which was confirmed by stool frequency as a surrogate marker. Results: When clustering based on cytokine groups, the most interesting results in the data set were found for chemokines, including the most stable data for eotaxin and RANTES. Increased expression of these chemokines significantly correlated with higher stool frequency for these patients. It is also noteworthy that the composition of patients in the cluster with a high concentration of chemokines for the sigmoid colon differed from the composition of patients compared to the ileum data. These differences can be explained by different location of the process (Figure 60). Conclusion: Previously, other authors demonstrated the possibility of influencing the eotaxin-CCR3 axis in experimental models to reduce inflammation and normalize intestinal motility in IBD [1; 2].

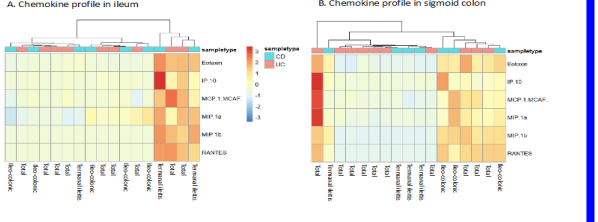

Fig 60. Chemokine profile in ileum and sigmoid colon in IBD patients.

The data obtained in the work allow to consider the potential for targeted therapeutic action on the eotaxin-CCR3-RANTES axis. These chemokines are also among the potential biomarkers of impaired motility and severity of inflammation in IBD.

Key words: Inflammatory bowel disease (IBD); eotaxin; CCR-3; RANTES; motility.

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Gut microbiome - SCFA - motility disorders dynamic system as the target for correction

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The dynamic system involving gut microbiota, short-chain fatty acids (SCFAs), and motility disorders presents a promising target for correcting in inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS). Both conditions are associated with dysbiosis, a microbial imbalance that affects gut health and function. Dysbiosis is a common feature in both IBD and IBS, characterized by reduced microbial diversity and altered microbial

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composition.[1,2] SCFAs, produced by gut microbiome, play a crucial role in maintaining intestinal health and modulating gut motility, which is often disrupted in IBD and IBS. SCFAs are also associated with gut microbiome composition and inflammation. Dysmotility can alter microbial composition, leading to increased inflammation and susceptibility to colitis.[3] This suggests that SCFAs may influence IBD not only by directly affecting motility but also by modulating the gut microbiome. Certain microbial genera, such as Clostridium and Ruminococcus, are involved in SCFA production and are found in altered amounts in IBD patients. These changes may affect the overall SCFA profile and contribute to disease progression.[4] This study tested the hypothesis about the relationship between 16s rRNA sequencing data and changes in the level of total bile acids and SCFA composition in individuals with altered intestinal motility in IBD and IBS. Patients 18-66 y.o. with IBD (n=15) and IBS (n=14) and clinical dysmotility were included in the study. All patients were performed with 16s rRNA sequencing, total bile acids level and SCFA, including acetic, propionic and butyric acid. In our work, we analyzed the correlation between the increasing level of total bile acids, SFCA composition changes and 16s rRNA sequencing data with varying degrees of intestinal motility disorders, which was confirmed by stool frequency as a surrogate marker. In terms of alpha diversity, the groups do not differ from each other (Figure 61). The patterns of change in the representation of

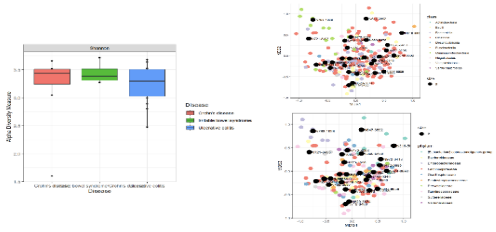

Fig 61. Alpha-diversity, class and phylum distribution in IBD and IBS patients..

the Clostridia class - Roseburia inulivoraus, Roseburia interstinalis, Rumminococcus torques, correlated with changes in the SCFA composition with a significant predominant change in butyric acid and the level of total bile acids. The revealed changes may be pathogenetically associated with changes in gut motility. Assessing the composition of the microbiota and understanding the role of SCFAs in gut motility may underline therapeutic strategies for the treatment of IBD. Targeting this system could offer novel therapeutic strategies for these disorders. Modulating SCFA levels through microbiome therapy or their effects on motility may help manage symptoms and improve gut health in patients with IBD and IBS.

Key words: gut microbiome; SFCA; bile acids; motility.

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2025Pdm3 March 29 - Abstract 111

Neurophenomenological interview as a method of studying psychosomatic balancing in the process of adaptation to learning (by ZOOM)

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A first-year university student encountered with a fast pace of learning, rigorous requirements of the institution and interactions with university teachers. The acquisition of professional knowledge and skills, psychological and social well-being depend on adaptation to new conditions, the ability to respond adequately and work in a team.
The psycho-emotional state has an impact on a motivation and behavior in tight situations. Adaptation is a process of active development and accommodation to the environment and life.[1] According to the biopsychosocial model, long-term stress causes psychological and physiological changes that lead to chronic physical diseases. Physical symptoms of stress and mental health-related illnesses significantly reduce quality of life, escalate a burden of symptoms and increase health care utilization.[2] Psychological outcomes of stress include anxiety, depression, and burnout,[3] with burnout defined as emotional exhaustion, cynicism, and decreasing of personal effectiveness.[4] Such states are called somatization. The purpose of this study was to determine the connection between somatization and psychophysiological

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indicators in the process of adaptation to studying at a university between male and female first-year university students. The respondents of the study were 48 first-year university students of pedagogical specialties (83.3% female and 16.7% male). All participants of the experiment entered university for the first time after graduating from school. The experiment included several stages. On the first stage we delivered the assessment of the psychological state using a psychodiagnostic method, including the following tests: "The Assessment of Students Adaptability in the Higher Educational Establishment" (author T. D. Dubovitskaya); "The State-Trait Anxiety Inventory, STAI" (author C. Spielberger, adaptation by Yu. L. Khanin); "The Giessen Somatic Complaints Questionnaire" (adapted from NIPNI); "The Dutch Four-Dimensional Symptoms Questionnaire, 4DSQ" (author B.Terluin et al., adapted by A. B. Smulevich et al.). On the second stage of the experiment, students were shown videos of stressful situations during adaptation to studying at a university with recording of the electrical activity of the brain and an interview based on the results of viewing each video. After watching each video, the respondents answered interview questions, which included questions of the mental plan, meaning, questions of content and qualitative coverage of the event, and character questions. While the experiment participants' watched videos and answered interview questions, the electrical activity of the brain (EEG) was recorded using the Encephalan-EEG-19/26 device to assess the relationship between general brain activity and intellectual comprehension with the level of somatization among students. To evaluate the electroencephalographic study, the Encephalan software by LLC Medicom was used. To check the distribution of data according to the studied parameters we used graphical methods and conducted calculations of asymmetry and kurtosis. The obtained results showed that the distribution corresponds to normal and is within the acceptable values for a normal distribution (from -1 to +1).

Using correlation analysis and the Pearson coefficient, a significant correlation was found between the "somatization" indicator and the following parameters: "adaptability to the study group" ($r = 0.483$, $p \leq 0.05$); "alpha rhythm power during viewing of the first video" ($r = -0.495$, $p \leq 0.05$); "alpha rhythm power during answering questions after the second video" ($r = -0.528$, $p \leq 0.01$); "alpha rhythm power during answering questions after the third video" ($r = -0.516$, $p \leq 0.05$). Moreover, an inverse relationship between somatization and alpha power was found while watching the second video and answering questions after the second and third videos. Analysis of correlations and average values of the alpha rhythm and beta rhythm in groups with expressed and unexpressed somatization (division was delivered according to the norms of the 4DSQ: 0-13 points - low level of somatization (30 respondents), 14-24 - average level of somatization (8 respondents), 25-32 - high level of somatization (10 respondents)) indicated that the group with a low level of somatization has a lower alpha rhythm. A similar pattern can be observed in the beta rhythm indicators, which is confirmed by outcome results of discriminant analysis. Probably this trend may indicate that the participants of the experiment are actively involved in the process. Apparently, students with high levels of somatization do not experience cognitive load while watching videos of stressful situations and answering following questions. At the same time, the beta rhythm while watching the video and answering questions of the participants with low levels of somatization had high rates. It can relate to the fact that they participated more actively in the experiment and controlled the events that took place.

During the study, brain activity indicators and psychodiagnostics results were analyzed using the Wilks' Lambda distribution. This allowed us to identify key indicators that can be used for predicting the level of somatization within first-year university students. As a result of discriminant analysis, a classification function was obtained, which allow us to divide students into two groups depending on the expression of somatization:

somatization= -0.033a+0.171b-0.377c+0.054d-0.076e-0.046f-7.147, where

a is situational anxiety ("STAI" (C. Spielberger);

b – anxiety (questionnaire 4 DSQ);

c – distress (questionnaire 4 DSQ);

d – alpha rhythm power when watching the second video;

e – alpha rhythm power when answering interview questions on the second video;

f – beta rhythm power when answering interview questions on the second video

Research findings allow us to conclude that the level of somatization is directly related to how well a person adapts to a study group. Among all the stressful situations that can lead to somatization, the most significant is the situation of failure in studies and interpersonal relationships. It can be assumed that this situation is associated with both factors that are important for adaptation - educational activities and relationships in the group. This can be a source of significant mental stress for first-year university students, both male and female. Situational anxiety and anxiety that a person experienced during the last 30 days before the experiment are important for determination of somatization expression. Moreover, an important indicator of distress is a state of reduced adaptation during steady stress, accompanied by feelings of anxiety, discomfort, depression and helplessness. The absence of a persistent feeling of anxiety - "distress" - may refers to unconscious processes where the tension is not recognized by the individual.[5] Further studies in this research area are needed. Potentially, participants with a high level of somatization also have signs of alexithymia, which determines their insensitivity to internal mental processes and states. As was mentioned above, students with expressed somatization demonstrate high rates of adaptation to learning when answering the questions of the subjective questionnaire "The Assessment of Students Adaptability in the Higher Educational Establishment". These patterns can be explained by the mechanism of psychosomatic balancing. Students with expressed somatization do not realize the presence of neuropsychic tension, therefore they do not display the first and second levels of defense - "confrontation" and "distress". Instead, somatization occurs at the third level. These findings are supported by measures of brain activity. During the study, we focused on two main rhythms - alpha and beta. A decrease in alpha rhythm is directly related to a high level of somatization and high adaptation to the study group. According to results of discriminant analysis, students with low expression of the beta rhythm shown the absence of cognitive assessment of a difficult situation during adaptation to the university. The results of this study require further researches of the phenomenon of somatization within first-year students during the period of adaptation to the university

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environment.

Key words: somatization; adaptation; EE; mechanism of psychosomatic balancing; neurophenomenological interview.

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2025Pdm3 March 29 - Abstract 112

Prognosis of movement disorders in patients with cardioembolic stroke on the background of anticoagulant therapy (by ZOOM)

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Anticoagulant therapy is used in patients at high risk of cardiac thromboembolism to prevent the recurrent cerebrovascular accidents.[1,2] Heparins bind to acute phase proteins, including fibrinogen, fibronectin, as well as von Willebrand factor (vWF), thereby inhibiting their interaction with platelet receptors GPIb-V-IX and αIIbβ3, potentially improving cerebral microcirculation and reducing neurological deficits.[3,4] The aim of this study was to investigate the interaction between vWF and movement impairment in acute cardioembolic stroke (CES) on the background of heparins. All patients on the 2-3 days and 7-10 days after ischemic stroke underwent clinical analysis: NIHSS, MRC muscle and modified Rankin scales (MRS). vWF was evaluated using aggregometer ALAT-2 (Biola, Russia). Blood samples were collected from 30 patients with CES, of whom 15 patients were treated with unfractionated heparin (UFH) and 15 with low-molecular-weight heparin (LMWH), as well as 15 patients with noncardioembolic stroke (nCES) who did not receive heparins. The present study was approved by the Local Ethics Committee. In CES patients, the NIHSS scale was 9 (4-10) points pre-treatment and 6 (3-8) points post-treatment ($p<0,001$). During the follow-up period, there was a significant improvement in muscle strength according to the MRC scale: on paretic arms proximally ($p=0.001$) and distally ($p<0.001$), on paretic legs proximally ($p<0.001$) and distally ($p=0.002$), indicating moderate regression of motor symptoms and adequate anticoagulation. MRS scores before and after treatment were 4 (3-4) and 3 (2-3) points, respectively ($p<0,001$). There was a nonsignificant trend towards lower vWF levels during follow-up (115,7% (90,9-129,9) pre-treatment and 106,4% (83,7-120,7) post-treatment, $p=0,225$). The pre-treatment vWF is correlated with the NIHSS scale ($p=0,043$, $r=0,372$). There were no statistically significant differences in NIHSS, MRC and MRS scores between UFH and LMWH treatment. Patients with nCES showed a significant change in MRS scores ($p=0.013$), but no statistical difference in NIHSS and vWF was found during the follow-up period ($p=0.101$ and $p=0.650$, respectively). In conclusion, reduction of plasma vWF levels on the background of heparins with both LMWH and UFH can be associated with a positive outcome due to regression of focal, motor neurological symptoms.

Key Words: Prognosis of movement disorders; with cardioembolic stroke; anticoagulant therapy.

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2025Pdm3 March 29 - Abstract 113

Neurokinetics of emotional motor components of behavior in adolescents in norm and pathology (by ZOOM)

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The article deals with the algorithm of neuropsychological experiment on the development of skills of self-regulation of psychophysiological indicators in the situation of public speaking, built on the principle of neurophenomenological construct of new active neuropsychology and its direction - neurokinetics. The development of new patterns of social behavior in situations of interaction is considered from the standpoint of methods of experimental psychology, neurophenomenology and biofeedback,
Key words: Adolescents; emotions; kinetics; biofeedback; neurophysiological diagnostics.

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2025Pdm3 March 29 - Abstract 114

Can the microclimatic conditions of terrainkur influence the results of treatment in patients with arterial hypertension and overweight?

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Cardiological rehabilitation and health-resort treatment of cardiological patients is a complex of measures providing secondary prevention of cardiovascular morbidity and subsequent acute coronary events.[1] Exercise therapy techniques are central to the rehabilitation of cardiac patients.[2] Terrainkur, which is a variation of exercise therapy and a combination of exercise therapy and climatotherapy, is recommended for patients with arterial

Fig 62. Characteristics of the area. At the top left is a terrainkur route mainly with darkened areas of the terrain, at the top right is a terrainkur route mainly with open areas, below is a general view of the bay on the Black Sea coast, on the shore of which the Vulan spa and resort complex is located (sky color).

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hypertension and excess body weight. The aim of this report is to evaluate effectiveness and safety of using a predictive model for meteopathic reactions (hypertensive crisis) in order to select optimal terrainkur routes for patients with arterial hypertension and excess body weight (Figure 62). A total of 95 overweight and obese patients with arterial hypertension were examined in the premises of "Vulan" health resort complex in the period between 1st April and 31st October 2023, according to the design of an open prospective interventional comparative uncontrolled study. Along with standard therapy, the patients underwent a terrainkur course of 10 procedures. The first group walked a terrainkur route in a microclimate with sparing microclimatic effects on the organism, the second group - in a microclimate with training microclimatic effects on the organism, and for the third group of patients the terrainkur route was selected with due regard to indications of the information and analytical programme to assess the risk of developing meteopathic reactions of the organism.[3] Before and after the therapy, we studied heart rate variability and hemodynamic parameters ("Zdoroviye-Express" Hardware and Software Suite, Russia), conducted analysis of body composition by bioimpedance method ("Medass" Scientific and Technical Centre LLC, Russia), assessed psychophysiological characteristics (the Luscher Color Test ("Zdoroviye-Express" Hardware and Software Suite, Russia); the WAM questionnaire (well-being, activity, mood) and the results of the 6-minute walk test. Statistical processing was performed using methods of descriptive statistics. Analysis of intergroup differences and assessment of intragroup dynamics was evaluated using the Mann-Whitney and Wilcoxon tests. The significance of differences was established at $p < 0.05$. Processing of all findings was performed using a software package Statistica 8.0, 10.0 (IBM PC, USA) and Microsoft Excel (Microsoft, USA). The most pronounced reduction in fat mass was observed in the group that underwent terrainkur, which involved the alternation of microclimatic conditions in accordance with the indications provided by the information and analytical programme.[4] In addition, the patients in this group demonstrated positive changes in heart rate variability parameters: the rate of decrease of the index of functional changes was -3,9% - decrease from 2,82 (2,35; 3,04])to 2,71 (2,47; 3,01) points (Z=2,83; p=0,005), the rate of decrease of the index of activity of regulatory systems was -28,6% - decrease from 7,0 (5,0; 8.0])to 5.0 (4.0; 6.0) points (Z=2.86; p=0.004), which is statistically significantly different from the indicators in the other two studied groups (0.17 and 0.20, respectively). In conclusion, the safest and most effective is the terrainkur with alternation of microclimatic conditions depending on the indications of information and analytical system to assess the risk of developing meteopathic reactions of the organism (hypertensive crisis).

Key Words: Cardiac Rehabilitation; Blood Pressure; Overweight; Heart Rate; Secondary Prevention.

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2025Pdm3 March 29 - Abstract 115

The paradigm of somatic intelligence in neurorehabilitation (by ZOOM),

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The article delves into the revolutionary concept of somatic intelligence, exploring its importance in various disciplines such as social psychology, psychiatry, cognitive sciences and psychodynamic approach in medicine and neurorehabilitation. Somatic intelligence, defined as the body's innate ability to process and integrate sensory, emotional and cognitive information, is presented as a key factor in understanding human behaviour, mental health and recovery processes. The authors propose a comprehensive methodological paradigm for research, emphasising the integration of neurodiagnostic tools, holistic therapeutic practices and rehabilitation strategies. This paradigm aims to bridge the gap between mind and body, offering new perspectives on the relationship between physical and psychological well-being. By focusing on somatic intelligence, the article advocates a more nuanced and interdisciplinary approach to mental health care, neurorehabilitation and the development of personalised treatment plans that take into account the person as a whole rather than isolated symptoms

Key Words: neuropsychology, neurorehabilitation, psychosomatic balancing, somatic intelligence, self-identity.

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2025Pdm3 March 29 - Abstract 116

The Effect of Calcium and Vitamin D3 on Calcium Homeostasis and Falls Incidence in Patients with Osteoporosis Undergoing Medical Rehabilitation (by ZOOM)

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Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue leading to increased bone fragility and fracture susceptibility (1). Worldwide, 23% of women and 12% of men have osteoporosis, with the prevalence increasing significantly with age (2). Bone fractures are a major health consequence of osteoporosis leading to an increased risk of mortality, disability, loss of independence and increased medical costs (3). Fall preventing and nutritional status improving are important for patients with osteoporosis undergoing physical rehabilitation to reduce the risk of fractures. The aim of the study was to evaluate the effect of long-term calcium and vitamin D3 intake on calcium homeostasis and fall's rate in patients with osteoporosis starting rehabilitation course. The study enrolled 119 men and women aged 50-80 ys. with osteoporosis who suffered low trauma fractures and had high absolute fracture probability by FRAX, entering the in-patient department for medical rehabilitation. Patients included in the study were randomized into 3 groups. Patients in group 1 (n=41) before starting a rehabilitation course were prescribed for 12 months antiresorptive therapy (bisphosphonates or denosumab) in combination with a food supplement containing calcium citrate 1000 mg and vitamin D3 600 IU daily. Patients in group 2 (n=39) before starting a rehabilitation were prescribed for 12 months only nutritional support with calcium citrate and vitamin in the same daily dosage. Patients of the group 3 made up the control group (n=39) in which patients did not receive any interventions except physical therapy procedures. All patients undergo laboratory examination, food calcium intake and fall assessment at baseline, in 6 and 12 months. Daily calcium intake in the study sample (n=119) was 782.9±243.4 mg. Vitamin D deficiency was detected in 38.4% of the examined. An increase in 25(OH)D level was noted in groups 1 and 2 after 6 and 12 months ($p<0.01$). Patients in group 1 showed an increase in serum osteocalcin and calcium levels after 6 and 12 months ($p<0.05$). In group 3, there was an increase of PTH level after 6 months ($p<0.05$) and 12 months ($p<0.01$), CTx and alkaline phosphatase after 12 months ($p<0.05$). In group 1, there was a decrease in proportion off fallen at least once patients after 6 months ($p=0.026$) and in the total falls cases after 12 months ($p=0.027$). Group 2 showed a decrease in fallen patients number after 6 and 12 months ($p=0.0034$) and in total falls number after 6 months ($p=0.0142$). The data obtained on dietary calcium intake and vitamin D insufficiency are generally consistent with the data for our country (4). As in our study, several studies have also demonstrated the effectiveness of vitamin D supplementation in increasing muscle strength and reducing the risk of falls (5). At the same time, the study Saha, S (2018) found no positive effect of vitamin D on muscle strength (6), and the work of Bislev, LS (2018) even showed that adding higher doses to meals impairs muscle strength (7). At present, the study of Shibasaki, K (2021) is the only published work, in addition to our own, that has demonstrated that participants with osteoporotic vertebral or hip fracture received anti-osteoporotic medication exhibited greater gains in functional independence after the rehabilitation than those who did not (8). In conclusion, the majority of patients aged between 50 and 80 years old with osteoporosis admitted to a rehabilitation hospital have a deficiency of vitamin D and dietary calcium intake. There is no statistically significant improvement in dietary calcium intake and an increase in vitamin D levels when dietary recommendations are taken

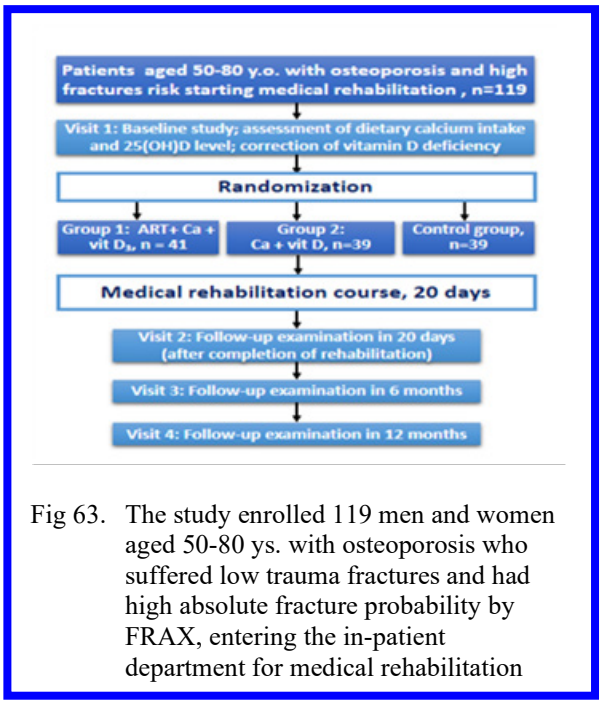

Fig 63. The study enrolled 119 men and women aged 50-80 ys. with osteoporosis who suffered low trauma fractures and had high absolute fracture probability by FRAX, entering the in-patient department for medical rehabilitation

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into account. The administration of a moderate dosage of calcium and vitamin D via dietary supplementation has been associated with an increase in serum 25(OH)D levels and the maintenance of calcium and PTH levels, and has been demonstrated to prolong the efficacy of medical rehabilitation, maintaining the achieved improvements in muscle strength and postural balance control for up to 12 months. This is associated with a decrease in falls frequency, and the effects are more pronounced when combined with antiresorptive drugs. The results justify the prescription of calcium and vitamin D supplementation as part of a comprehensive rehabilitation programme for older patients with osteoporotic fractures.

Key words: osteoporosis; medical rehabilitation; bone remodeling; vitamin D.

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2025Pdm3 March 29 - Abstract 117

Effectiveness of the Pelvic Floor Muscles Electrotherapy and Magnetic Stimulation in Preconception Programs for Women of Reproductive Age, (by ZOOM)

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The use of preconception programs for women with gynecological diseases can improve fertility rates, increase the reproductive potential and fertility of women planning a pregnancy.[1-4] The aim of the study was to optimize preconception training programs for women of reproductive age using electrotherapy and magnetic stimulation of the pelvic floor muscles. The use of electropulse therapy and magnetic field effects on the pelvic organs in programs is important due to the microcirculatory outcomes that these effects facilitate. An open randomized controlled trial in parallel groups was conducted. As a result of the initial questionnaire, collection of complaints and anamnesis, according to the inclusion/exclusion criteria, 80 patients diagnosed with chronic endometritis and pelvic organ prolapse 1st and 2nd degree aged 25-45 years were included in the study. The patients included in the study were randomized into 2 groups. The first group, the control group (n-40), received standard therapy, including a daily complex intake of vitamin and mineral preparations. The patients of the second group (n-40) underwent a complex of preconception preparation, including standard therapy in combination with electrical pulse therapy and a high-intensity.

Pulsed magnetic field on the pelvic floor area. All the patients underwent laboratory and clinical investigations before and in 3 and 6 months after the treatment. Following the intervention, there was a notable increase in the uterine arterial perfusion index in groups 1 and 2 when compared to the baseline measurement. In contrast, the control group did not demonstrate any changes. The median of this indicator in the control group did not change significantly ($p>0.05$), in the first group it increased by 2.36 times ($p<0.05$). According to ultrasound Doppler ultrasonography of uterine vessels, the frequency of visualisation of colour signals of arcuate and basal vessels of myometrium in group 2 increased by 84.3% after the exposure, and by 56.2% - of spiral vessels of endometrium, respectively. The maximum blood flow velocity and systole-diastolic ratio significantly decreased in the 2nd study group ($p<0.05$). After the treatment group 2 showed a statistically significant decrease in the value of anterior urethrovesical angle (α) during Valsalva test (before treatment 69.96±2.38, after treatment 54.31±3.16, $p<0$, 001) and the value of rotation angle α during loading (before treatment 35.23±2.75, after treatment 19.78±2.87, $p<0.001$) compared to the control group (before treatment 64.35±1.96 and 33.15±2.37, after treatment 64.14±2.06 and 33.07±2.14, $p>0.5$). When analyzing delayed results, a significant increase in pregnancy cases in the second group was revealed by 1.6 times (36.8%) compared to the control group (23%) ($p< 0.05$, chi-square test). In conclusion, preconception programs should be recommended, including methods of electrotherapy and magnetic stimulation of the pelvic floor muscles for women

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with impaired uterine blood flow and grade 1 and 2 pelvic organ prolapse. Pre-pregnancy programs improve fertility rates for women planning pregnancy.

Key words: electrotherapy, magnetic stimulation, pelvic floor muscles, preconception program.

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2025Pdm3 March 29 - Abstract 118

Effectiveness of a Rehabilitation Programme for Patients with Post-Thrombotic Syndrome including Robotic Biofeedback Training of the Calf Muscle Venous Pump (by ZOOM)

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In advanced stages of chronic venous insufficiency, the calf muscles may become dysfunctional, leading to a slowdown in blood flow in the lower extremities and an increased risk of deep vein thrombosis (DVT). It has been established that physical exercise improves venous return of blood from the lower extremities by improving the function of the gastrocnemius and plantar muscle pumps, achieved by increasing the range of motion in the ankle joint. A review of the literature reveals a lack of prior studies examining the effectiveness of robotic lower extremity muscle training with biofeedback in patients with post-thrombophlebitic syndrome (PTFS) of the lower extremities. The aim was to study the effect of a comprehensive rehabilitation program using robotic lower extremity muscle training with biofeedback on the performance of the calf muscle pump, as well as on the range of motion of the ankle joints (AROM) in patients with post-thrombophlebitic syndrome of the lower extremities.[2,3] This pilot project included 20 patients with lower limb PTFS (C3-C5 according to the CEAP classification), average age 56.12±4.9 years, disease duration 8.67±1.14 years, BMI 27.01±2.68. All patients had a documented history of an episode of DVT. The patients underwent goniometry with measurement of the range of motion in the ankle joint (dorsiflexion) in degrees and measurement of the malleolar volume (cm). The performance of the calf muscle-venous pump was assessed using isokinetic dynamometry of the lower limb muscles on a robotic biomechanical diagnostic complex with biofeedback (BFB) (CON-TREX, Physiomed, Germany). The following significant strength parameters were studied: average extension force (N), as well as total work (J). Each patient underwent measurements before and after the rehabilitation course, including intermittent pneumatic compression (IPC) of the legs No. 12, laser therapy on the vascular area of the lower extremities No. 12, as well as 12 robotic training sessions on the Leg Press Module with biofeedback (CON-TREX, Physiomed, Germany) (Figure 64).

Fig 64. Biofeedback simulator for lower extremity muscles (CONTREX, Germany)

Results. Following the completion of the rehabilitation programme, an increase in the AROM (dorsiflexion) was observed from 7.48 ± 3.42 degrees to 9.62 ± 3.56 degrees, with the age norm being 20 degrees. The isokinetic dynamometry data indicated an improvement in the average limb extension force (Newton) by 176%, and total work (J) by 144%. Additionally, a reduction in the malleolar circumference by 6.85% was observed as a consequence of IPC and laser therapy. In conclusion: Edema, decreasing AROM (dorsiflexion) and calf muscle pump dysfunction are associated with progressive severity in PTFS. Accordingly, the application of robotic biofeedback training of the lower extremity muscles in conjunction with intermittent pneumatic compression (IPC) and laser therapy results in a decrease in venous hypertension, strengthening of the ankle joints and improvement of muscle-venous pump function, which is accompanied by an improvement in the functional mobility and an overall well-being of patients with PTFS.

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Key words: post-thrombophlebitic syndrome, physical exercise, robotic training, calf muscle pump dysfunction.

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Functional asymmetry and interhemispheric interactions as predictors of mental and somatic disorders

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The persistent interest in studying individual functional asymmetry in mental activity among both healthy individuals and patients has prompted numerous scientific investigations. However, the practical application of these findings remains limited. A meta-analysis of data from various sources highlights a significant correlation between the functional asymmetry profile and the likelihood of developing specific diseases, as well as the peculiarities of their progression, particularly in psychiatric and therapeutic contexts. Notably, a research gap exists regarding this correlation, especially among cardiology patients, including those with primary arterial hypertension. In this group, the disease's pathogenesis is closely linked to autonomic nervous system dysfunction, often manifesting as sympathicotonic hyperactivity. The individual profile of interhemispheric asymmetry determines the specificity of mental functions and may serve as a predictor for the development of essential arterial hypertension. Given these findings, the inclusion of a novel screening method a rapid test for detecting left-handedness-into diagnostic protocols appears promising. This method, currently under validation, is notable for its speed, efficiency, and accessibility. It requires no specialized equipment, incurs minimal financial costs, and demands little effort from both researchers and participants, making it suitable for diverse clinical settings.

Key Words: Functional asymmetry; interhemispheric interactions, predictors of mental and somatic disorders.

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