Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

Abstracts of the 2023 Padua Days of Muscle and Mobility Medicine (2023Pdm3) to be held March 29 - April 1 at the Galileian Academy of Padua and at the Petrarca Hotel, Thermae of Euganean Hills, Padua, Italy

Sandra Zampieri (1,2,3,4), Marco V. Narici (1,2), Paolo Gargiulo (5,6), Ugo Carraro (1,2,3)

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Abstract

At the end of the 2022 Padua Days of Muscle and Mobility Medicine (Pdm3) the next year's meeting was scheduled from 29 March to 1 April 2023. Despite the worsening evolution of the crisis in Eastern Europe, the program was confirmed in autumn 2022 with Scientific Sessions that will take place over three full days in the *Aula Guariento* of the Galileian Academy of Arts, Letters and Sciences of Padua (March 29, 2023) and then at the Conference Room of the Hotel Petrarca, Thermae of Euganean Hills (Padua), Italy. Collected during autumn and early winter, many titles and abstracts where submitted (about 100 Oral presentations are listed in the preliminary Program by January 31, 2023) confirming attractiveness of the 2023 Pdm3. The four days will include oral presentations of scientists and clinicians from *Austria, Bulgaria, Canada, Denmark, France*, *Georgia, Germany, Iceland, Ireland, Italy, Mongolia, Norway, Russia, Slovakia, Slovenia, Spain, Switzerland, The Netherlands and USA*. Together with the preliminary Program at January 31, 2023, the Collection of Abstracts is e-published in this Issue 33 (1) 2023 of the European Journal of Translational Myology (EJTM). You are invited to join, submitting your Last Minute Abstracts to ugo.carraro@unipd.it by March 15, 2023. Furthermore, with the more generous deadline of May 20, 2023, submit please "Communications" to the European Journal of Translational Myology (SCOPUS Cite Score Tracker 2023: 3.2 by January 5, 2023) and/or to the 2023 Special Issue: "Pdm3" of the Journal *Diagnostics*, MDPI, Basel (I.F. near to 4.0) with deadline September 30, 2023. Both journals will provide discounts to the first accepted typescripts. See you soon at the Hotel Petrarca of Montegrotto Terme, Padua, Italy.

For a promo of the 2023 Pdm3 link to: https://www.youtube.com/watch?v=zC02D4uPWRg

Key Words: Padua Days of Muscle and Mobility Medicine (Pdm3); European Journal of Translational Myology and Mobility Medicine, PAGEpress, Pavia, Italy; *diagnostics*, MDPI, Basel; Program and Abstracts.

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The meetings on biology, physiology, medicine and rehabilitation of skeletal muscle, called Padua Muscle Days (PMDs), started more than 30 years ago, specifically to provide advice on Translational Myology and Mobility Medicine. Always the interest was on implementing basic research and clinical trials to prevent, manage and rehabilitate young adults and elderly persons suffering with mobility disorders. As the final event of the 2022 Padua Days of Muscle and Mobility Medicine (Pdm3, the new nickname of the series) the next year meeting was planned to be held from March 29 to April 1, 2023. Despite the worsening evolution of the East-Europe crisis, the program was confirmed in autumn 2022 with Scientific Sessions to occur over four full days

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at either the Galilean Academy of Arts, Letters and Sciences of Padua *Guariento Hall* (March 29, 2023) and then in the Conference Hall of the Hotel Petrarca, Thermae of Euganean Hills (Padua), Italy. Collected during autumn and early winter, titles and abstracts of about 100 Oral presentations were submitted and are listed in the preliminary Program by January 31, 2023, confirming attractiveness of the 2023 Pdm3. The four days will include oral presentations of senior and junior scientists and clinicians from *Austria, Bulgaria, Canada, Denmark, France, Georgia, Germany, Iceland, Ireland, Italy, Mongolia, Norway, Russia, Slovakia, Slovenia, Spain, Switzerland, The Netherlands* and *USA*. Together with the preliminary Program at January 31, 2023, the Collection of Abstracts is e-published in this Issue 33 (1) 2023 of the European Journal of Translational Myology (EJTM). In the following Collection there are some empty Abstracts (only names and affiliations of authors). Some of them are just unsubmitted abstracts from high-level speakers who don't bother publishing conference abstracts, but meanwhile underestimate their value to educate young readers. Most have been decisions by speakers to do not publish in this Issue their original results deserving full articles in prestigious journals. We found the latter a strong evidence of the relevance of 2023 Pdm3 that attracted speakers and presentations of detailed original results from top labs in muscle and mobility medicine.

Sponsors of the 2023 Pdm3, March 29 – April 1, Padua and Thermae of Euganean Hills, Padua, Italy

We apologize to the readers for having decided to keep these speakers in the Program of the 2023 Pdm3.

Readers are invited to join the 2023 Pdm3, submitting Last Minute Abstracts to ugo.carraro@unipd.it up to March 15, 2023.

Furthermore, with the more generous deadline of May 20, 2023, Speakers are invited to submit a "Communication" to European Journal of Translational Myology (SCOPUS Cite Score Tracker 2023: 3.2 by January 5, 2023) and/or to 2023 Special Issue: "Pdm3" of the Journal *Diagnostics*, MDPI, Basel (I.F. near to 4.0) with deadline September 30, 2023. Both journals will provide discounts to the first accepted papers.

The Collection of Abstracts is here e-published in the European Journal of Translational Myology (EJTM), 33 (1) 2023, together with the Program that ends late on Saturday April 1, 2023 with invitation to join the 2024 Pdm3, March 27 – 30 at the Thermae of Euganean Hills (Padua), Italy.

See you in the late afternoon of March 28, 2023 for an aperitive at the Hotel Petrarca of Montegrotto Terme Euganean Hills, Padua, Italy.

For a promo of the 2023 Pdm3 link to: https://www.youtube.com/watch?v=zC02D4uPWRg

We are sure that 2023 Pdm3 will be even more successful than the successful events of the last years.[1-7]

List of acronyms

EJTM - European Journal of Translational Myology
MDPI - Molecular Diversity Preservation International
Pdm3 - Padua Days on Muscle & Mobility Medicine
PMD – Padua Muscle Days

Acknowledgments

The authors thank Organizers, Chairs, Speakers, and Attendees for their scientific and personal financial contributions to the success of the Pdm3.

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E-publishing is supported by the Armando & Carmela Mioni-Carraro Foundation for Translational Myology Padua, Italy, and the Institute of Biomedical and Neural Engineering, Reykjavik University, Reykjavik, Iceland.

Conflict of Interest

The authors disclose no conflicts of research and

publication interest or any specific endorsements of the products referenced in this manuscript.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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References

1. Zampieri S, Stecco C, Narici M, Masiero S, Carraro U. 2023 On-site Padua Days on Muscle and Mobiliy Medicine: Call for speakers. Eur J Transl Myol. 2022 Dec 13. doi: 10.4081/ejtm.2022.11071. Online ahead of print. PMID: 36511885 Free article.
2. Carraro U, Bittmann F, Ivanova E, Jónsson H Jr, Kern H, Leeuwenburgh C, Mayr W, Scalabrin M, Schaefer L, Smeriglio P, Zampieri S. Post-meeting report of the 2022 On-site Padua Days on Muscle and Mobility Medicine, March 30 - April 3, 2022, Padua, Italy. Eur J Transl Myol. 2022 Apr 13;32(2):10521. doi: 10.4081/ejtm.2022.10521. PMID: 35421919; PMCID: PMC9295170.
3. Sweeney HL, Masiero S, Carraro U. The 2022 On-site Padua Days on Muscle and Mobility Medicine hosts the University of Florida Institute of Myology and the Wellstone Center, March 30 - April 3, 2022 at the University of Padua and Thermae of Euganean Hills, Padua, Italy: The collection of abstracts. Eur J Transl Myol. 2022 Mar 10;32(1):10440. doi: 10.4081/ejtm.2022.10440. PMID: 35272451; PMCID: PMC8992680.
4. Carraro U, Yablonka-Reuveni Z. Translational research on Myology and Mobility Medicine: 2021 semi-virtual PDM3 from Thermae of Euganean Hills, May 26 - 29, 2021. Eur J Transl Myol. 2021 Mar 18;31(1):9743. doi: 10.4081/ejtm.2021.9743. PMID: 33733717; PMCID: PMC8056169.
5. Carraro U. 30 Years of Translational Mobility Medicine: 2020 Padua Muscle Days go virtual from Euganean Hills, November 19th to 21st. Eur J Transl Myol. 2020 Nov 17;30(4):9437. doi: 10.4081/ejtm.2020.9437. PMID: 33520146; PMCID: PMC7844408
6. Carraro U. Thirty years of translational research in Mobility Medicine: Collection of abstracts of the 2020 Padua Muscle Days. Eur J Transl Myol. 2020 Apr 1;30(1):8826. doi: 10.4081/ejtm.2019.8826. PMID: 32499887; PMCID: PMC7254447
7. Carraro U. Thirty years of translational research in Mobility Medicine: Collection of Abstracts of the 2020 Padua Muscle Days. Eur J Transl Myol 2020;30:3-47. Doi: 10.4081/ejtm.2019.8826.

Disclaimer

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2023 Pdm3, March 29 - April 1, 2023 - Thermae of Euganean Hills, Padua (Italy)

University of Padua &Thermae of Euganean Hills (Padua, Italy)

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

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Organizers: Elisabeth R. Barton, Ines Bersch-Porada, Ugo Carraro, Marcus Coplin, Raffaele De Caro, Paolo Gargiulo, Elena P. Ivanova, Helmut Kern, Nathan K. LeBrasseur, Christiaan Leeuwenburgh, Alessandro Martini, Stefano Masiero, Marco V. Narici, Rosanna Piccirillo, Riccardo Rosati, Marco Sandri, Piera Smeriglio, Carla Stecco, H. Lee Sweeney, Sandra Zampieri

PROGRAM

WEDNESDAY March 29, 2023

08:00 AM ***Complimentary Bus Transfer to Padua***

Guariento Hall, Galilean Academy of Arts and Science of Padua, Italy

09:00 AM ***Openings*** **Raffaele De Caro, Marco V. Narici, Ugo Carraro:** Greetings and thanks to lecturers, speakers, audience and sponsors

09:20 AM ***Lecture of Carlo Reggiani, University of Padua, Italy:*** **Single muscle fibers as a tool in aging research**

10:00 AM ***Session I: Adaptations to Physical Exercise in Aging: from cell to functioning***

Marco V. Narici, Roberto Bottinelli, Chairs

10:00 AM ***Russell T. Hepple, University of Florida, USA*****: Skeletal muscle plasticity to resistance training in pre-frail/frail elderly women**

10:20 AM ***Julian Alcázar Caminero, Universidad de Castilla-La Mancha, Toledo, Spain:*** **Improving muscle power through exercise in old age**

10:40 AM ***Simone Porcelli, University of Pavia, Italy*****: Home-based aerobic exercise training improves skeletal muscle oxidative metabolism in old people**

11:00 AM ***Martino Franchi, University of Padua, Italy:*** **Differential muscle adaptations to concentric and eccentric resistance training in older people**

11:20 AM ***Marco V. Narici, University of Padua, Italy:*** **The neuroprotective effects of exercise in older age**

11.40 AM ***Gianni Biolo, University of Trieste, Italy:*** **Nutrient-exercise interaction on muscle mass and function in aging**

12:00 AM ***Maria Chiara Maccarone, Barbara Ravara, Walter Giuriati, Stefano Masiero, Ugo Carraro, University of Padua, Italy:*** **Combating muscle weakness in bed-ridden eldery with Home-based Full-Body in-Bed Gym (hbFBiBG): Basics, Implementation and Preliminary Results of the Padua Initiative**

12:20 AM ***Ugo Carraro, University of Padua, Italy:*** **Blood contamination a lucky chance to analyze non-invasively Myokines in mouth fluids**

12:30 AM ***Ester Tommasini, Daniela Tavian et al., Milan, Italy*****: Irisin and sarcopenia: salivary irisin is induced by strenuous exercise and correlates with circulating irisin**

12.45 AM ***Lunch in Piazza Duomo, Padua, Italy***

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WEDNESDAY March 29, 2023

Guariento Hall, Galilean Academy of Arts and Sciences of Padua, Italy

02:00 PM SESSION II: ***Skeletal Muscle Epigenetics and the dark side of the genome***

Piera Smeriglio, Marco Sandri, Chairs

02:00 PM ***Marco Sandri et al., University of Padua, Italy:*** **Discovering novel longevity genes by looking at the dark side of the genome**

02:20 PM ***Chiara Lanzuolo, National Institute of Molecular Genetics, Milan, Italy***: **Chromatin conformation of muscle stem cells in physiological and pathological muscular aging**

02:40 PM ***Isabella Scionti, INMG, Lyon, France:*** **Epigenetic modifiers role in modulating muscle stem cell plasticity**

03:00 PM ***Piera Smeriglio, Sorbonne Université, Paris, France:*** **Understanding epigenetics in spinal muscle atrophy: how the yin and yang of genomic regulation contribute to the disease**

03:20 PM ***Giuseppina Caretti, et al., Milan University, Italy:*** **Epigenetic targeting of BET proteins rewire metabolism in the aged skeletal muscle**

03:40 PM ***Silvere M. van der Maarel, Leiden University Medical Center, The Netherlands: Facioscapulohumeral Dystrophy: Incomplete Repression of the Cleavage Stage Transcription Factor DUX4 in Skeletal Muscle***

04:00 PM ***Break***

04:00 PM SESSION III: ***Adaptations in Aging: from molecules to functioning***

Amber L. Pond, Rosanna Piccirillo, Chairs

04:00 PM ***Amber L. Pond, Southern Illinois University School of Medicine in Carbondale, IL, USA:*** **The HERG K+ channel increases intracellular calcium in myotubes by modulation of Calsequestrin**

04:20 PM ***Hans Hoppeler, University of Bern, Switzerland:*** **Fascia, Facts and Fantasies**

04:40 PM ***Rosanna Piccirillo, et al., IRCCS - "Mario Negri", Milan, Italy***: **MyoRep: a novel reporter system to detect early muscle atrophy in vivo**

05.00 PM ***Paolo Grumati, Telethon Institute of Genetics and Medicine, Naples, Italy:*** **Selective autophagy and ER dynamics during muscle differentiation**

05:15 PM ***Bert Blaauw, University of Padua, Italy***: **The role of Akt-mTORC1 signaling in regulating muscle mass and function**

05:30 PM ***Stefano Schiaffino, University of Padua, Italy:*** **Who is Terje Lømo, a 88-year-YOUNG scientist still fully active!**

05:40 PM ***Lecture of Terje Lømo, University of Oslo, Norway:*** **Body temperature regulation by muscle tone**

06:30 PM ***Complimentary Bus Transfer to Hotel Petrarca, Thermae of Euganean Hills (Padua), Italy***

08:00 PM *Dinner in Hotel Petrarca*

THURSDAY March 30, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:00 AM SESSION IV: FES managements of acquired muscle diseases

Ines Bersch-Porada, Helmut Kern, Chairs

09:00 AM ***Winfried Mayr, University of Vienna, Austria:*** **Electrical stimulation in lower motoneuron lesions, from scientific evidence to clinical practice: a successful transition – The Engineer perspectives**

09:20 AM ***Ines Bersch-Porada, Functional Electrical Stimulation Center, Notwill, Switzerland***: **Electrical stimulation in lower motoneuron lesions, from scientific evidence to clinical practice: a successful transition - The Physiotherapist experienceand researcher perspective**

09:40 AM ***Ashraf Gorgey, School of Medicine, Virginia Commonwealth University, Richmond, VA, USA: To be announced***

10:00 AM ***Giovanna Albertin, University of Padua, Italy***: **Skin improvements by home-based FES**

10:20 AM ***Ugo Carraro, University of Padua, Italy***: **40 years of basic and applied myology for hbDDM FES in 20 slides**

10:40 AM ***Break***

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THURSDAY March 30, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

11:00 AM ***Lecture of H. Lee Sweeney, University of Florida, Gainesville, FL, USA*: Improving upon AAV.micro-dystrophin gene therapy for DMD**

11:40 AM ***SESSION Va: Genetic muscle diseases*** *- Elisabeth R. Barton, H. Lee Sweeney, Chairs*

11:40 AM ***Kay Ohlendieck, Maynooth University, Maynooth, Co. Kildare, Ireland:* Proteomic profiling of reactive myofibrosis in the aged and dystrophic diaphragm**

12:00 AM ***Marina Bouchè DAHFM, Sapienza University of Rome, Italy:* To unravel immune response in Duchenne Muscular Dystrophy**

12:20 AM ***Philippe Perrin et al., Development, Adaptation and Handicap, University of Lorraine, France:* Postural control impairments in Fabry disease**

THURSDAY March 30, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

02:00 AM ***SESSION Vb: Genetic muscle diseases*** *- Capucine Trollet, H. Lee Sweeney, Chairs*

02:00 AM ***Elisabeth R. Barton, University of Florida, Gainesville FL, USA:* Novel role of store operated Ca2+ entry in Limb-Girdle Muscular Dystrophy 2A**

02.20 AM ***Capucine Trollet, Sorbonne Université, INSERM, Myology Institute, Paris, France:* Cell and molecular actors of fibrosis in muscle diseases**

02.40 AM ***Massimo Ganassi, King's College London, London, UK:* Investigating pathogenic mechanisms in FSHD myogenesis**

03:00 PM - SESSION VI: Twenty Years of AIM *– Daniela Tavian, Corrado Angelini, Chairs*

03:00 PM ***Gabriele Siciliano, University of Pisa, Italy*: Phenotype variabilities of laminopathies**

03:15 PM ***Alberto Benetollo, et al., DSB, University of Padua, Italy:* Pharmacological profile of the most promising CFTR corrector for sarcoglycanopathy treatment**

03:30 PM ***Francesco Dalla Barba, et al., DSB, University of Padua, Italy:* Zebrafish and sarcoglycanopathies: Characterization of models suitable for phenotype-based screening of drugs**

03:45 PM ***Sara Missaglia, Elena Pennisi, Daniela Tavian et al., Milan, Italy*: Exploring triheptanoin as treatment for neutral lipid storage disease with myopathy**

04:00 PM ***Gulia Ricci, et al., University of Pisa, Italy:* New avenues for treatment of facioscapulohumeral MD**

04:15 PM ***Giovanna Cenacchi, et al., Alma Mater Studiorum University of Bologna, Italy:* Two plasma circulating-miRs for the diagnosis of idiopathic inflammatory myopathies**

04:30 PM ***Roberta Costa, et al., Alma Mater Studiorum University of Bologna, Italy:* Morpho-functional characterization of Transportin3 in myogenic differentiation of a cell model of LGMD D2**

04:30 PM ***Giosuè Annibalini, et al., University of Urbino Carlo Bo, Urbino, Italy:* N-glycosylation inhibition impairs C2C12 and L6 myoblast differentiation and IGF-1 signalling**

04:45 PM ***Daniela Tavian, Ester Tommasini, et al., Milan, Italy*: Irisin and sarcopenia: salivary irisin is induced by strenuous exercise and correlates with circulating irisin**

05:00 PM ***Massimiliano Filosto, NeMO-Brescia Clinical Center for Neuromuscular Diseases, University of Brescia, Italy*: Clinical and genetic characterization of Neutral lipid storage disease with myopathy (NLSDM)**

05:15 PM ***Fabiola Moretti et al., Catholic University of Rome, Roma, Italy:* Estrogens recover muscle regeneration impaired by the pathogenic gene DUX4 in orthotopic human xenograft**

05:30 PM ***Abbass Jaber, et al., Evry University, Inserm, Evry, France:* Perturbations of cholesterol metabolism in the dystrophic muscle in DMD**

05:45 PM ***Michele Guescini, et al., University of Urbino Carlo Bo, Italy: Modulation of vesicles' secretion by EPS in an in vitro muscle model***

06:00 PM ***Alessia Geremia, et al., University of Padua, Italy:* Activation of muscle-specific Akt1 reverts cancer-dependent muscle wasting and reduces tumor mass**

06:15 PM ***Lecture of Jonathan Jarvis, Liverpool John Moores University, UK: Transcriptomic and growth responses to programmed resistance training in mouse, rat and human***

07.30 PM ***Dinner***

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FRIDAY March 31, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09.00 AM **Lecture of Simona Boncompagni, University of Chieti, Italy*: Skeletal muscle electron microscopy, still a mandatory approach in muscle rejuvenation research***

09:30 AM SESSION VII: Senescence & Rejuvenation

Nathan K. LeBrasseur, Christiaan Leeuwenburgh, Chairs

09:30 AM ***Nathan K. LeBrasseur, Mayo Clinic, Rochester, MN, USA*: Cellular senescence as a driver of skeletal muscle aging**

09:50 AM ***David Hood, York University, Canada*: Impact of age and sex on lysosomes and mitophagy during muscle use and disuse**

10:10 AM ***Christiaan Leeuwenburgh, University of Florida, Gainesville, FL, USA:* Inflammation, mitochondrial dysfunction senescense in skeletal muscle with aging and in peripheral artery disease**

10:30 AM ***Agnese De Mario, et al., University of Padua, Italy:* Pharmacological modulation of MCU in skeletal muscle**

10:40 AM ***Maira Rossi, et al., University of Pavia, Italy:* Nitrate supplementation promotes an anabolic response and attenuates neuromuscular alterations in 24-months old male mice**

10:50 AM ***Nicola Fiotti, et al., University of Trieste, Italy:* Insulin resistance modification during bed rest: relationship with circulating and muscular MMP and TIMPs**

FRIDAY March 31, 2023

ROOM B, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:30 AM Practical Course on functional analysis of the stomatognathic system

Claudia Dellavia, Riccardo Rosati, Chairs

***09:30-11.00: Riccardo Rosati, Milan, Italy:* Instrumental evaluations of the stomatognathic apparatus: static tests**

***11:15-12:30: Claudia Dellavia, Milan, Italy*: Instrumental evaluations of the stomatognathic apparatus: dynamic tests,**

For dentists who want to review/expand the functional analysis protocols of the stomatognathic system developed at the Laboratory of Functional Anatomy of the Stomatognathic Apparatus (LAFAS) of the University of Milan, Italy

FRIDAY March 31, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

11:00 AM SESSION VIII: Muscle Fascia, biology and pathology - *Carla Stecco, Alessandro Martini, Chairs*

11:00 AM ***Carla Stecco, University of Padua, Italy:* Fascia and aging**

11:20 AM ***Alessandro Martini, University of Padua, Italy*: Tensor Tympani and Stapedius: two unknown muscles**

11:40 AM ***Carmelo Pirri, et al., University of Padua, Italy*: Ultrasound imaging and fasciae**

11:50 AM ***Caterina Fede, et al., University of Padua, Italy*: How sex hormones can affect the fasciae: Implication for pain**

12:00 AM ***Giovanna Albertin, et al., University of Padua, Italy*: Lymphatic vessels detection in subcutis and superficial fascia**

12:10 AM ***Lucia Petrelli, et al., University of Padua, Italy*: Innervation and vascularization of the superficial fascia**

12:20 AM ***Lorenza Bonaldi, et al., University of Padua, Italy:* Biomechanical properties of the fascial system**

12.30 AM ***Ilaria Fantoni, et al., Orthopedics and Orthopedic Oncology, Department of Surgery, Oncology and Gastroenterology (DiSCOG), University of Padua, Italy*: Fascia Lata alterations in hip osteoarthritis: An observational cross-sectional study**

12:45 PM ***Lunch***

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02:*00 PM Lecture of Paolo Gargiulo, University of Rejkyavik, Iceland*: 3D Quantitative Muscle Color Computed Tomography

02:40 PM SESSION IX: Non-invasive Assessments in Myology - *Paolo Gargiulo, Ugo Carraro, Chairs*

02:40 PM ***Riccardo Forni, et al., University of Rejkyavik, Iceland:*** **Virtual cardiac histology: a densitometric characterisation of left ventricular tissue**

02:50 PM ***Debora Jacob, et al., University of Rejkyavik, Iceland:*** **Assessing early-stage Parkinson's Disease using a moving platform (BioVRSea)**

03:00 PM ***Valentina Betti, et al., University of Rejkyavik, Iceland*: An in silico 3d approach to evaluate bone remodelling after total hip arthroplasty: a six years longitudinal study**

03:10 PM ***Federica Ciliberti, et al., University of Rejkyavik, Iceland:*** **Novel strategies for cartilage assessment, interplay between bone and muscles**

03:20 PM ***Carlo Ricciardi, Alfonso Maria Ponsiglione, University of Federico II, Naples, Italy:*** **Interplay between the age and the asymmetry of NTRA in elderly people**

03:30 PM ***Magnus Gislason, et al., University of Rejkyavik, Iceland:*** **Time shift of peak activation levels in quadriceps and hamstrings after ACL reconstruction during single leg jump**

03:40 PM ***Ettore Rocchi, et al., University of Urbino Carlo Bo, Urbino, Italy:*** **Exploring myofibrillar alignement in muscular tissue**

03:50 PM ***Break***

FRIDAY March 31, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

04:00 PM SESSION X: Muscle Rehabilitation in Dentistry, *Riccardo Rosati, Elena P. Ivanova, Chairs*

04:00 PM ***Gaia Pellegrini, University of Milan, Italy:*** **Standardised protocols for sEMG of the masticatory muscles in oral rehabilitation**

04:15 PM ***Elena P. Ivanova, Rehabilitation and Balneology Center, Moscow, Russia:*** **Innovative methods of full dental rehabilitation**

04:30 PM ***Francesca Ferrante, et al., University of Pavia, Italy*: Electromyographic analysis of masticatory muscles before and after rapid palatal expansion**

05:00 PM ***Roberto Rongo, University of Naples Federico II, Italy*: Masticatory muscles pain management**

05:15 PM ***Mauricio Gonzalez Balut, Centro Ortodoncico Especializado, Mexico City, Mexico: Definite Orthodontic treatment for patients with Temporomandibular Joint problems and* Craniomandibular Dysfunctions**

05:30 PM ***Bazar Amarsaikhan, Mongolia:*** **Chewing hard food and its importance for general health**

05:45 PM ***Avtandil Bakradze, Tbilisi State Medical University, Tbilisi, Georgia:*** **Peculiarities of the chewing muscles electrophysiological activity in mouth breathing individuals**

06:00 PM ***Marieta Karadjova, et. al., Department of Neurology, Medical University-Sofia, Bulgaria:*** **Improvement of gait, balance and coordination after application of Taopatch® device**

06:15 PM ***Giuseppe Messina, et al., University of Palermo, Italy*: Intra-articular ultrasound-guided injection with Hyaluronic Acid and corticosteroid in retrodiscal tissue for Temporomandibular disorders**

06:30 PM ***Francesco Mantia, et al., University of Palermo, Italy*: Effects of Platelet-Rich-Plasma injection in association with therapeutic exercise in the management of medial epicondylitis**

06:50 PM **Lecture of Feliciano Protasi University of Chieti, Italy*: Mechanisms underlying exercise-dependant remodelling of the sarcotubular system: the role of temperature and pH***

07:30 PM *Dinner*

09:00 PM ***AFTER DINNER ACTIVITIES***

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SATURDAY April 1, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:00 AM Session XI: LBI workshop on muscle rehabilitation - from mouse to elderly

Sandra Zampieri, Feliciano Protasi, Chairs

09:00 AM ***Feliciano Protasi, University of Chieti, Italy:*** **Mimicking disuse and rehabiliation in a mouse model**

09:30 AM ***Antonio Musarò, University Sapienza of Rome, Italy*****: Molecular biological basis and effects of immobility and training in young and aging**

10:00 AM ***Sandra Zampieri, University of Padua, Italy*****: C-Terminal Agrin Fragment as a biomarker of muscle wasting and weakness in aging and disuse**

10:**30 AM** **Break**

10:40 AM ***Jan Cvecka, University of Bratislava, Slovakia*****: Exercise intervention in elderly: a novel system within the Centre of Active Aging in Bratislava**

11:00 AM ***Nejc Sarabon, University of Primorska, Slovenia*****: Relationship between 24-hour movement behaviour and physical performance in older adults: A cross-sectional insight into the Centre of active ageing data**

11:20 AM ***Stefan Loefler, Helmut Kern, LBI Rehabilitation Research, Vienna, Austria*****: AMB-REMOB – results of an early outpatient rehabilitation program**

11:40 AM ***Vincent Grote, Michael Fischer, LBI Rehabilitation Research, Vienna, Austria:*** **Outcomes of early rehabilitation in elderly patients**

12:**00 AM** **General discussion**

12.30 AM ***Lunch***

SATURDAY April 1, 2023

12:30 AM ***Complimentary Transfer to Medical Hotel Ermitage*** **(restricted to 15 Attendees)**

Medical Hotel Ermitage, Thermae of Euganean Hills (Padua) Italy

12:45 PM ***Practical Actitvities on European Medical Thermalism*** *- Stefano Masiero, Chair*

12:45 PM ***Working Lunch in Medical Hotel Ermitage***

01:15 PM ***Marco Maggia, Director of the Medical Hotel Ermitage:*** *Balneotherapy, Mud and Physiotherapies for Prevention & Rehabilitation in the Medical Hotel Ermitage, a pioneering 15-year successful example*

02:00 pM ***Complimentary Transfer to Hotel Petrarca Thermae of Euganean Hills (Padua) Italy***

SATURDAY April 1, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

02:30 PM **Lecture of Helmut Kern, LBI Rehabilitation Research, Vienna, Austria*****: Underwather physiotherapy after knee replacement***

03:00 PM SESSION XIIa: European Medical Thermalism and the World Federation Hydrotherapy (FEMTEC)

- Marcus Coplin, Umberto Solimene, Chairs

03:00 PM ***Marcus Coplin, Balneology Association of North America, Naturopathic Healthcare, Pagosa Springs, Colorado, USA:*** **A case study of balneotherapy in Fibromyalgia**

03:20 PM ***Umberto Solimene, Center Integrative Medicine, State University Milan, Italy:*** **World Thermal Clusters**

03:40 PM ***Maria Chiara Maccarone, Ugo Carraro, Stefano Masiero, University of Padua, Italy*****: Balneology and Health Resort Medicine and rehabilitation in the Euganean Hills Thermae: building the future**

04:00 PM ***Daniele Coraci, et al., University of Padua, Italy:*** **Technological transition of different rehabilitation approaches: challenges and answers**

04:**20 PM** **Break**

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SATURDAY April 1, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

04:40 PM SESSION XIIb: European Medical Thermalism and the World Federation Hydrotherapy (FEMTEC)

Stefano Masiero, Elena P. Ivanova, Chairs

04:40 PM ***Anna Mihaylova, Medical University of Plovdiv, Bulgaria:*** **Balneotherapy - prospects for the development of health tourism in Bulgaria**

05:00 PM ***Andrey Rachin, Rehabilitation and Balneology Center, Moscow, Russia*: Modern methods of neuro-rehabilitation**

05:20 PM ***Maxim Yu. Yakovlev, et al., Rehabilitation and Balneology Center, Moscow, Russia:*** **Correction of increased meteosensitivity of obese patients when using Terrainkur, taking into account the bioclimatic characteristics during stay in health resorts**

05:40 PM ***Kirill V. Terentev, et al., Moscow regional research clinical institute named after M.F. Vladimirsky, Moscow, Russia:*** **Video analysis of patients' gait during Terrainkur in obese people**

06:00 PM ***Irina A. Grishechkina, Rehabilitation and Balneology Center, Moscow, Russia:*** **Outcomes of rehabilitation programs in patients with post-COVID-19 syndrome**

06:20 ***Stefano Masiero, University of Padua, Italy:*** **Final remarks**

06:45 PM ***Ugo Carraro: Adijo, Adiós, Arrivederci, Auf Wiedersehen, Au revoir, Goodbye to the 2024 Padua Days on Muscle and Mobility Medicine – Padua, Italy, March 13-16, 2024***

07:30 PM *Dinner*

09:00 PM ***AFTER DINNER ACTIVITIES***

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ABSTRACTS of the2023 Pdm3

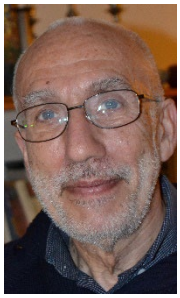
WEDNESDAY March 29, 2023
Aula Guariento, Galilean Academy of Arts, Letters and Science, Padua, Italy

2023Pdm3 March 29 - Abstract 1

LECTURE

Single fibers as a tool in aging muscle research

Carlo Reggiani



Department of Biomedical Sciences, University of Padova, Italy; ZRS, Koper, Slovenia.
Email: carlo.reggiani@unipd.it

Skeletal muscle is a highly heterogeneous tissue, composed of a variety of cells and different myofiber types, mostly classified as slow and fast, the latter divided in two subgroups fast 2A and fast 2X. The functional properties of a muscle are determined not only by its myofibers with their contractile and metabolic features but also by all cellular components. With aging, progressive alterations of all cellular and molecular components lead to skeletal muscle atrophy and loss of performance. Although the final functional output of a muscle depends on many factors from neural drive to metabolic support, muscle fibers are the only component able to generate force and movement. The study of the structural, molecular and physiological characteristics of individual single fibers can provide important clues to understand which changes are more relevant to the age-dependent impairment of muscle function and, to some extent, to design possible countermeasures aimed to slow down the aging process
Key Words: aging; skeletal muscle; fiber types; force generation; fiber size regulation.

References

1. Murgia M, Toniolo L, Nagaraj N, Ciciliot S, Vindigni V, Schiaffino S, Reggiani C, Mann M. Single Muscle Fiber Proteomics Reveals Fiber-Type-Specific Features of Human Muscle Aging. Cell Rep. 2017 Jun 13;19(11):2396-2409. doi: 10.1016/j.celrep.2017.05.054. PMID: 28614723
2. Aas SN, Breit M, Karsrud S, Aase OJ, Rognlien SH, Cumming KT, Reggiani C, Seynnes O, Rossi AP, Toniolo L, Raastad T. Musculoskeletal adaptations to strength training in frail elderly: a matter of quantity or quality? J Cachexia Sarcopenia Muscle. 2020 Jun;11(3):663-677. doi: 10.1002/jcsm.12543. Epub 2020 Feb 24. PMID: 32091670; PMCID: PMC7296272
3. Venturelli M, Saggin P, Muti E, Naro F, Cancellara L, Toniolo L, Tarperi C, Calabria E, Richardson RS, Reggiani C, Schena F. In vivo and in vitro evidence that intrinsic upper- and lower-limb skeletal muscle function is unaffected by ageing and disuse in oldest-old humans. Acta Physiol (Oxf). 2015 Sep;215(1):58-71. doi: 10.1111/apha.12524. Epub 2015 May 28. PMID: 25965867; PMCID: PMC4516639.
3. Rejc E, Floreani M, Taboga P, Botter A, Toniolo L, Cancellara L, Narici M, Šimunič B, Pišot R, Biolo G, Passaro A, Rittweger J, Reggiani C, Lazzer S. Loss of maximal explosive power of lower limbs after 2 weeks of disuse and incomplete recovery after retraining in older adults. J Physiol. 2018 Feb 15;596(4):647-665. doi: 10.1113/JP274772. Epub 2018 Jan 19. PMID: 29266264; PMCID: PMC5813607.
4. Marcucci L, Reggiani C. Increase of resting muscle stiffness, a less considered component of age-related skeletal muscle impairment. Eur J Transl Myol. 2020 Jun 17;30(2):8982. doi: 10.4081/ejtm.2019.8982. PMID: 32782762; PMCID: PMC7385684.

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Session I: Adaptations to Physical Exercise in Aging: from cell to functioning
Marco V. Narici, Roberto Bottinelli, Chairs

2023Pdm3 March 29 - Abstract 2

Skeletal muscle plasticity to resistance training in pre-frail/frail elderly women

Russell T. Hepple, *University of Florida, USA*

Pdm3 March 29 - April 1, 2023

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2023Pdm3 March 29 - Abstract 3

Improving muscle power through exercise in old age

Julian Alcázar Caminero (1,2)

(1) GENUD Toledo Research Group, Universidad de Castilla-La Mancha, Toledo, Spain; (2) CIBER of Frailty and Healthy Aging, Instituto de Salud Carlos III, Madrid, Spain.
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Muscle power is defined as the rate at which mechanical work is performed or the product of force and velocity. Notably, muscle power is one of the first capabilities declining with age, making the loss of muscle power an

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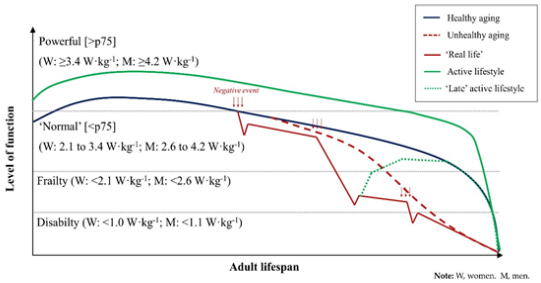

Functional trajectories according to relative muscle power

important hallmark of aging. The loss of muscle power with age is also one of the main determinants of impaired functional ability in older people. Specifically, relative muscle power (i.e., normalized to body mass) has been found to be more strongly associated to physical performance in older people in comparison with absolute muscle power, handgrip strength and sarcopenia. This would be due to most of the activities of daily living being weight bearing tasks (e.g., walking, chair rising or stair climbing). Nevertheless, the lack of feasible tests and normative data for older people has prevented the widespread testing of muscle power in older people in the past. Recently, a feasible test to evaluate relative lower-limb muscle power in older people has been validated: the sit-to-stand muscle power test (1). In addition, normative data, cut-off points and an operational algorithm to diagnose low relative muscle power in older people has been provided (2). Importantly, older people having low relative muscle power presented a higher risk of mobility limitations, frailty, disability, hospitalization, and all-cause mortality. Fortunately, power-oriented resistance training performed throughout a relative wide range of loads has been provided as an effective treatment to revert low muscle power in older people (3). With the advent of increasingly aging societies, and with main healthy aging goal of maintaining functional ability, the monitoring and treatment of low relative muscle power through exercise in older people should be a public health priority. Finally, and with this purpose, a free-cost smartphone app (PowerFrail App®) that integrates the sit-to-stand muscle power test is available.

Key Words: Mechanical power; aging; power training; functional ability; sarcopenia.

References

1. Alcazar J, Losa-Reyna J, Rodriguez-Lopez C, Alfaro-Acha A, Rodriguez-Mañas L, Ara I, García-García FJ, Alegre LM. The sit-to-stand muscle power test: An easy, inexpensive and portable procedure to assess muscle power in older people. Exp Gerontol. 2018 Oct 2;112:38-43. doi: 10.1016/j.exger.2018.08.006. Epub 2018 Sep 1. PMID: 30179662..
2. Alcazar J, Alegre LM, Van Roie E, Magalhães JP, Nielsen BR, González-Gross M, Júdice PB, Casajús JA, Delecluse C, Sardinha LB, Suetta C, Ara I. Relative sit-to-stand power: aging trajectories, functionally relevant cut-off points, and normative data in a large European cohort. J Cachexia Sarcopenia Muscle. 2021 Aug;12(4):921-932. doi: 10.1002/jcsm.12737. Epub 2021 Jul 3. PMID: 34216098; PMCID: PMC8350203.
3. Rodriguez-Lopez C, Alcazar J, Sanchez-Martin C, Baltasar-Fernandez I, Ara I, Csapo R, Alegre LM. Neuromuscular adaptations after 12 weeks of light- vs. heavy-load power-oriented resistance training in older adults. Scand J Med Sci Sports. 2022 Feb;32(2):324-337. doi: 10.1111/sms.14073. Epub 2021 Oct 16. PMID: 34618979.

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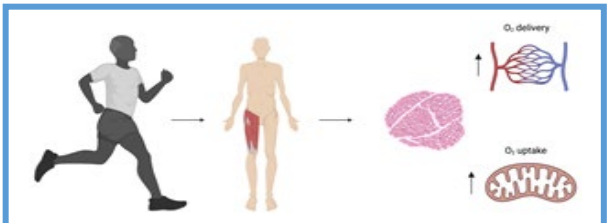
2023Pdm3 March 29 - Abstract 4

Home-based aerobic exercise training improves skeletal muscle oxidative metabolism in old people

Simone Porcelli (1,2), Mauro Marzorati (2), Lucrezia Zuccarelli (3), Roberto Bottinelli (1,4) Bruno Grassi (4).

(1) Department of Molecular Medicine, University of Pavia; (2) Institue of Biomedical Technologies, National Research Council; (3) Department of Medicine, University of Udine; (4) Interdepartmental Centre of Biology and Sport Medicine, IRCCS Mondino Foundation.
Email: simone.porcelli@unipv.it

The world population is ageing, and adults more than 65 years old are expected to double in number to about 1.5 billion in 2050. Although the rate of change is heterogeneous, the human ageing is characterized by inevitable and progressive reduction of physiological functions leading to exercise intolerance, defined as the incapacity to produce/maintain adequate muscle force or power to accomplish activities of daily living. In aged adults slower gait speed, lower muscle strength and changes in muscle quality have been correlated to impaired skeletal muscle oxidative capacity. Elderly, compared to young, show lower O2 consumption at peak



Schematic representation about how endurance exercise can prevent skeletal muscle impariments by improving microvascular O2 delivery and mitochondrial respiratory function.

exercise (V'O2peak) and impaired submaximal muscle oxidative function as well as decreases in mitochondrial content and reduced function in mitochondrial respiration and mitochondrial enzymatic activities. High-level of habitual physical activity and exercise training may slower V'O2peak decline and preserve mitochondrial function in elderly. This presentation will focus on methods and tools capable to objectively identify and quantify, noninvasively, changes in O2 delivery and O2 uptake within skeletal muscle in response to endurance training when home-based aerobic training sessions are prescribed to older adults and patients with metabolic myothaties. The importance of exercise intensity for individualized training prescription will be also highlighted together with potential pitfalls of prescribing exercise at home based on specific heart rate (HR) values as textbook and guidelines suggest.

Key Words: Activities of daily living; metabolic myopathies; chronic heart failure; NIRS; high-resolution respirometry.

References

1. Harridge SD, Lazarus NR. Physical Activity, Aging, and Physiological Function. Physiology (Bethesda). 2017 Mar;32(2):152-161. doi: 10.1152/physiol.00029.2016.
2. Gonzalez-Freire M, Scalzo P, D'Agostino J, Moore ZA, Diaz-Ruiz A, Fabbri E, Zane A, Chen B, Becker KG, Lehrmann E, Zukley L, Chia CW, Tanaka T, Coen PM, Bernier M, de Cabo R, Ferrucci L. Skeletal muscle ex vivo mitochondrial respiration parallels decline in vivo oxidative capacity, cardiorespiratory fitness, and muscle strength: The Baltimore Longitudinal Study of Aging. Aging Cell. 2018 Apr;17(2):e12725. doi: 10.1111/acel.12725.
3. Cartee GD, Hepple RT, Bamman MM, Zierath JR. Exercise Promotes Healthy Aging of Skeletal Muscle. Cell Metab. 2016 Jun 14;23(6):1034-1047. doi: 10.1016/j.cmet.2016.05.007. PMID: 27304505; PMCID: PMC5045036.
4. Porcelli S, Marzorati M, Morandi L, Grassi B. Home-based aerobic exercise training improves skeletal muscle oxidative metabolism in patients with metabolic myopathies. J Appl Physiol (1985). 2016 Sep 1;121(3):699-708. doi: 10.1152/japplphysiol.00885.2015. Epub 2016 Jul 21. PMID: 27445303.
5. Zuccarelli L, Porcelli S, Rasica L, Marzorati M, Grassi B. Comparison between Slow Components of HR and V˙O2 Kinetics: Functional Significance. Med Sci Sports Exerc. 2018 Aug;50(8):1649-1657. doi: 10.1249/MSS.0000000000001612. PMID: 29570539.

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2023Pdm3 March 29 Abstract 5

Differential muscle adaptations to concentric and eccentric resistance training in older people

Martino Franchi,
University of Padua, Italy

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

Pdm3 March 29 - April 1, 2023

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2023Pdm3 March 29 Abstract 6

The neuroprotective effects of exercise in older age

Marco V. Narici,
University of Padua, Italy

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

Pdm3 March 29 - April 1, 2023

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2023Pdm3 March 29 Abstract 7

Nutrient-exercise interaction on muscle mass and function in aging

Gianni Biolo,
University of Trieste, Italy:

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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2023Pdm3 March 29 - Abstract 8

Combating muscle weakness in bed-ridden eldery with Home-based Full-Body in-Bed Gym (hbFBiBG): Basics, Implementation and Preliminary Results of the Padua Initiative

Maria Chiara Maccarone (1), Barbara Ravara (2,3,4,5), Walter Giuriati (2), Stefano Masiero (1,3), Ugo Carraro (2,3,5)

(1) Physical Medicine and Rehabilitation School, Department of Neuroscience, University of Padua, Italy, (2) Department of Biomedical Sciences, University of Padua; (3) CIR-Myo - University of Padua; (4) Department of Neuroscience, Section of Rehabilitation, University of Padua, Italy; (5) A-C M-C Foundation for Translational Myology, Padua, Italy.
E-mail: mariachiara.maccarone@phd.unipd.it

Mobility-impaired subjects, either very old or younger but suffering with systemic neuromuscular disorders or chronic organ failures, spend small amounts of time for daily physical activity, contributing to aggravate their poor mobility by resting muscle atrophy.[1,2] Among these

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patients at risk of developing muscle atrophy and skeletal muscle weakness, also patients suffering from COVID-19 syndrome or Long Covid outcomes can be included.[3] In addition to the management of psychological symptoms, it is mandatory to offer to these patients physical rehabilitation approaches easy to learn and to self-manage at home. Inspired by the proven capability to recover skeletal muscle contractility and strength by home-based volitional exercises and functional electrical stimulation, we suggest a 10-20 min-long daily routine of easy and safe physical exercises that can activate, and recover from weakness, skeletal muscles employed in every-day mobility activities. Most of these exercises can be performed in bed (Full-Body in-Bed Gym) and hospitalized patients can learn this light training before leaving the hospital, representing an extension of the traditional cardiovascular-respiratory rehabilitation training.[1-5] We started collecting preliminary data from patients enrolled in the Full-Body in-Bed Gym program at the Rehabilitation Section of the University of Padua, Italy. Blood pressure readings demonstrated a transient decrease in peripheral resistance due to the increased blood flow in the main activated muscles. Patients' good compliance to the treatment and satisfaction were also collected. Preliminary data suggest that Full-Body in-Bed Gym, performed regularly and continued over time, may help maintaining independence of frail subjects, including patients suffering from COVID-19 pandemic outcomes. We hope that our preliminary experience in the future will be extended with further results from an international clinical trial. Interested colleagues are invited to join our project.

Key Words: Skeletal muscle weakness; home-based Full-Body in-Bed Gym; older olds; mobility impaired persons

References

1. Gava P, Kern H, Carraro U. Age-associated power decline from running, jumping, and throwing male masters world records. Exp Aging Res. 2015;41(2):115-35. doi: 10.1080/0361073X.2015.1001648.
2. Carraro U, Gava K, Musumeci A, Baba A, Piccione F, Marcante A. Safe Antiaging Full-Body In-Bed Gym and FES for Lazy Persons: Home In-Bed Exercises for Fighting Muscle Weakness in Advanced Age. In: Rehabilitation Medicine for Elderly Patients, Masiero S, Carraro U, Eds., pag. 43-52. ISBN 978-3-319-57405-9 ISBN 978-3-319-57406-6 (eBook). doi 10.1007/978-3-319-57406-6.
3. Carraro U, Marcante A, Ravara B, Albertin G, Maccarone MC et al. Skeletal muscle weakness in older adults home-restricted due to COVID-19 pandemic: a role for full-body in-bed gym and functional electrical stimulation. Aging Clin Exp Res. 2021;33(7):2053-2059. doi:10.1007/s40520-021-01885-0
4. Carraro U, Gava K, Baba A, Marcante A, Piccione F. To Contrast and Reverse Skeletal Muscle Atrophy

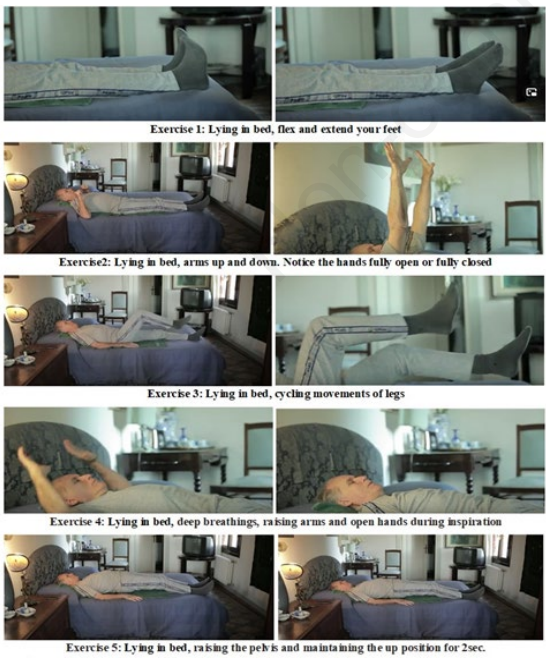

Fig 1. The routine will sequentially contract all major skeletal muscles, alternating exercises mobilizing arms, legs, spine, neck, diaphragm and other ventilation muscles.

Fig 2. The routine will sequentially activate major skeletal muscles, alternating exercises mobilizing arms, legs, spine, neck, diaphragm and other ventilation muscles.

by Full-Body In-Bed Gym, a Mandatory Lifestyle for Older Olds and Borderline Mobility-Impaired Persons. Adv Exp Med Biol. 2018;1088:549-560. doi: 10.1007/978-981-13-1435-3_25.
5. Berger D, Bloechlinger S, von Haehling S, Doehner W, Takala J, Z'Graggen WJ, Schefold JC. Dysfunction of respiratory muscles in critically ill patients on the intensive care unit. J Cachexia Sarcopenia Muscle. 2016. Sep;7(4):403-12. doi: 10.1002/jcsm.12108. Epub 2016. Mar 9.

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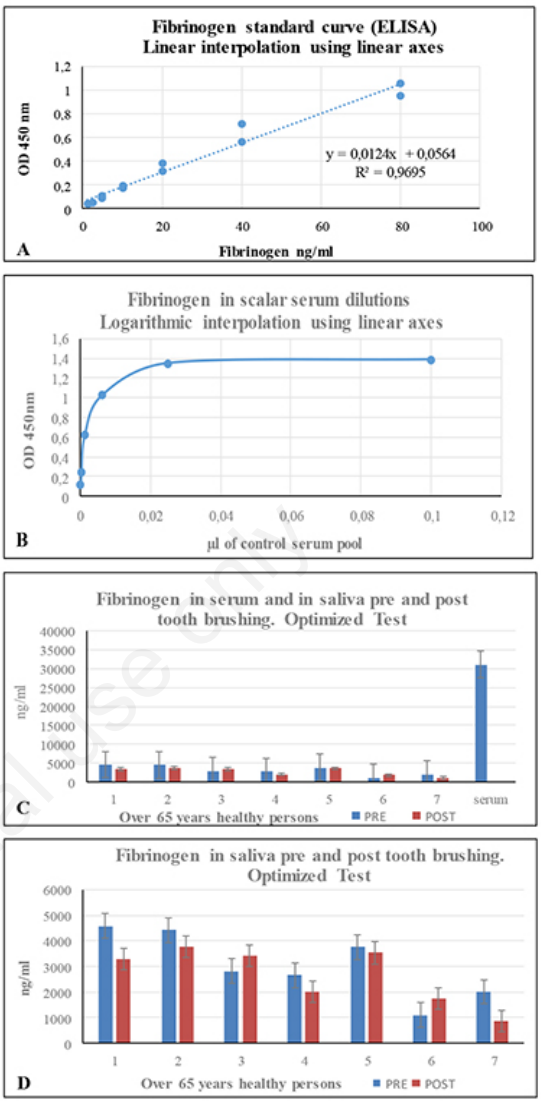
2023Pdm3 March 29 - Abstract 9

Blood contamination, a lucky chance to analyze non-invasively Myokines in mouth fluids

Ugo Carraro (1,2,3,5)

(1) Department of Biomedical Sciences, University of Padua; (2) CIR-Myo - University of Padua; (3) A-C M-C Foundation for Translational Myology, Padua, Italy.
Email: ugo.carraro@unipd.it

Use of saliva in clinical studies are increasing to identify methods less invasive than blood sampling in search for systemic changes of biomarkers related to physical activity, aging, late aging and rehabilitation. The consensus is that the diagnostic value of whole saliva is compromised by the presence of blood, but we are looking at the contamination as a major opportunity for non-invasive analyses of serological biomarkers. The aim of this preliminary study was to evaluate the presence of serum in mouth fluids of healthy seniors and the eventual changes after a modest trauma, i.e., tooth brushing. Seven heathy persons, aged more than 65 years, drooling saliva in a test tube provided the fluids for the analyses. After low speed centrifugation, small aliquots of supernatants were frozen in liquid nitrogen and stored at -80° until use. Aliquots were thawed and used for quantification by the Lowry method of total proteins and by colorimetric ELISA of serum albumin, fibrinogen and lysozyme. Hemoglobin content was quantified by Spectrophotometry. Adjustment of saliva dilution, after a preliminary test, increased the homogeneity of the analytes' content determined by colorimetric ELISA. The control reference to judge the quantity of serum in saliva was a pool of sera from age-matched healthy persons. Saliva collected from the seven healthy elderly person before and after tooth-and-gum, brushing presented measurable amount of the analytes, including fibrinogen, a minor component of the pooled sera. Tooth brushing did not induced statistically significant difference in analytes' contents, suggesting that a measurable blood contamination is a frequent event in elderly persons. In conclusion, fibrinogen analysis in saliva is a promising approach to quantify serological biomarkers by a non-invasive procedure that will increase acceptability and frequency of analyses during follow-up in aging and rehabilitation



Fibrinogen contamination of saliva in aged persons

Key Words: Saliva; blood contamination; fibrinogen; non-invasive analyses of plasm proteins.

References

1. Ravara B, Zampieri S, Kern H, Carraro U. Blood contamination, a problem or a lucky chance to analyze non-invasively Myokines in mouth fluids? Eur J Transl Myol. 2019 Dec 10;29(4):8713. doi: 10.4081/ejtm.2019.8713. PMID: 31908751; PMCID: PMC6926435.
2. Kang JH, Kho HS. Blood contamination in salivary diagnostics: current methods and their limitations. Clin Chem Lab Med. 2019 Jul 26;57(8):1115-1124. doi: 10.1515/cclm-2018-0739. PMID: 30511922
3. Parkin GM, Kim S, Mikhail A, Malhas R, McMillan L, Hollearn M, Granger DA, Mapstone M, Yassa

MA, Thomas EA. Associations between saliva and plasma cytokines in cognitively normal, older adults. Aging Clin Exp Res. 2023 Jan;35(1):117-126. doi: 10.1007/s40520-022-02292-9. Epub 2022 Nov 1. PMID: 36319939

4. Forcina L, Miano C, Scicchitano BM, Musarò A. Signals from the Niche: Insights into the Role of IGF-1 and IL-6 in Modulating Skeletal Muscle Fibrosis. Cells. 2019 Mar 11;8(3):232. doi: 10.3390/cells8030232. PMID: 30862132; PMCID: PMC6468756.

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2023Pdm3 March 29 Abstract 10

Salivary irisin is induced by strenuous exercise stimulus and correlates with circulating irisin

Ester Tommasini (1,2)*, Sara Missaglia (1,3), Paola Vago (1,3), Claudio Pecci (4), Christel Galvani (2), Andrea Silvestrini (5), Alvaro Mordente (5), Daniela Tavian (1,3)

(1) Department of Psychology, Università Cattolica del Sacro Cuore, Milan, Italy; (2) Exercise & Sport Science Laboratory, Università Cattolica del Sacro Cuore, Milan, Italy; (3) Laboratory of Cellular Biochemistry and Molecular Biology, CRIBENS, Università Cattolica del Sacro Cuore, Milan, Italy; (4) Human Performance Laboratory, MAPEI Sport Research Centre, Olgiate Olona (VA), Italy; (5) Department of Basic Biotechnological Sciences, Intensivological and Perioperative Clinics, Università Cattolica del Sacro Cuore, Rome, Italy.
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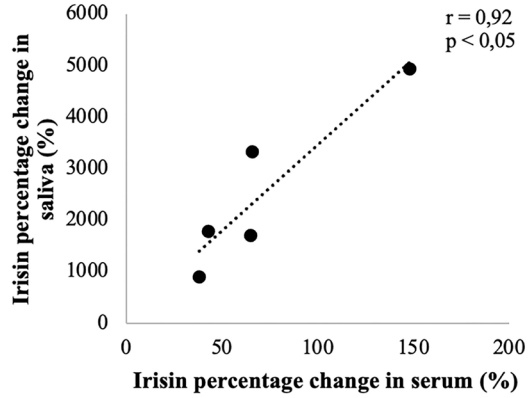
Physical activity can increase the circulating level of irisin, fostering several beneficial effects on health.[1,2] This exercise-induced myokine is generally analyzed in blood, but its collection is invasive and exposes to potential risks. Substitution of saliva sample for blood would represent a less invasive method for irisin detection. However, a limited number of studies evaluated the amount of irisin in saliva samples.[3,4] Our purpose was to verify whether saliva could represent an alternative sample in which detecting irisin changes induced by an exogenous stimulus. Five active healthy adults (age: 29±14yrs; mean body mass index: 22,9±3,7kg/m^2; mean peak oxygen uptake 54,0±16,5ml/kg/min) performed an incremental exercise until exhaustion on a cycle ergometer and their blood and saliva samples were collected before the exercise, 15min, 24h, 48h post-exhaustion. Irisin levels were determined using ELISA Assay Kit (#EK-067-29). Incremental exercise has determined consistent changes in irisin levels. Indeed, serum and salivary irisin levels (baseline: 9,77±2,87ng/ml, 0,06±0,05ng/ml; 15min: 10,80±2,48ng/ml, 0,35±0,45ng/ml; 24h: 15,93±2,42ng/ml, 1,71±1,87ng/ml; 48h: 9,72±2,75ng/ml, 0,20±0,33ng/ml, respectively) increased from baseline to 24h post-exercise, and then returned to basal level after 48h of rest. A significant difference of serum irisin levels at 15min ($p \leq 0,01$) and 24h ($p \leq 0,001$) compared to baseline was found. Moreover, a significant correlation ($r=0,92$, $P<0,05$) was found between irisin percentage change in serum and saliva from baseline to 24h post-exercise.[5] The findings, while preliminary, indicate that collecting saliva samples represents a valid and sensitive method of detecting irisin level changes in response to exercise.



Correlation between irisin percentage change in saliva and serum from baseline to 24 h postexercise in 5 subjects. Reproduced with permissions from Reference[5].

Key Words: irisin; saliva sample; serum sample; physical exercise.

References:

1. Liu S, Cui F, Ning K, Wang Z, Fu P, Wang D, Xu H. Role of irisin in physiology and pathology. Front Endocrinol. 2022; 13:962968. doi: 10.3389/fendo.2022.962968.
2. Bao JF, She QY, Hu PP, Jia N, Li A. Irisin, a fascinating field in our times. Trends Endocrinol Metab. 2022; 33(9):601-613. doi: 10.1016/j.tem.2022.06.003.
3. Aydin S, Aydin S, Kobat MA, Kalayci M, Eren MN, Yilmaz M, Kuloglu T, Gul E, Secen O, Alatas OD, Baydas A. Decreased saliva/serum irisin concentrations in the acute myocardial infarction promising for being a new candidate biomarker for diagnosis of this pathology. Peptides. 2014; 56:141-145.doi: 10.1016/j.peptides.2014.04.002.
4. Khan SU, Ghafoor S, Khaliq S, Syed AR. Salivary Irisin and periodontal clinical parameters in patients of chronic periodontitis and healthy individuals: A novel salivary myokine for periodontal disease. J Pak Med Assoc. 2022; 72(1):27-33.doi: 10.47391/JPMA.01367.

5. Missaglia S, Tommasini E, Vago P, Pecci C, Galvani C, Silvestrini A, Mordente A, Tavian D. Salivary and serum irisin in healthy adults before and after exercise. European Journal of Translational Myology. 2023. https://doi.org/10.4081/ejtm.2023.11093

Pdm3 March 29 - April 1, 2023

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WEDNESDAY March 29, 2023

Guariento Hall, Galilean Academy of Arts and Sciences of Padua, Italy

SESSION II: Skeletal Muscle Epigenetics and the dark side of the genome

Piera Smeriglio, Marco Sandri, Chairs

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2023Pdm3 March 29 - Abstract 11

***Marco Sandri** et al., University of Padua, Italy: Discovering novel longevity genes by looking at the dark side of the genome*

On-site presentation of unpublished results. The authors denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

Pdm3 March 29 - April 1, 2023

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2023Pdm3 March 29 - Abstract 12

Chromatin conformation of muscle stem cells in physiological and pathological muscular aging

Philina Santarelli (1) , Emanuele di Patrizio Soldateschi (2), Federica Lucini (3), Margherita Mutarelli (4), Valentina Rosti (2), Cristiano Petrini (3), Elisa Salviato (3), Francesco Ferrari (3), Chiara Lanzuolo (1,2)

(1) Istituto Nazionale Genetica Molecolare (INGM), Milan; (2) CNR Institute of Biomedical Technologies (ITB), Milan; (3) IFOM, the FIRC Institute of Molecular Oncology, Milan; (4) CNR Institute of Applied Sciences and Intelligent System, Pozzuoli (ISASI); (5) CNR Istituto di Genetica Molecolare
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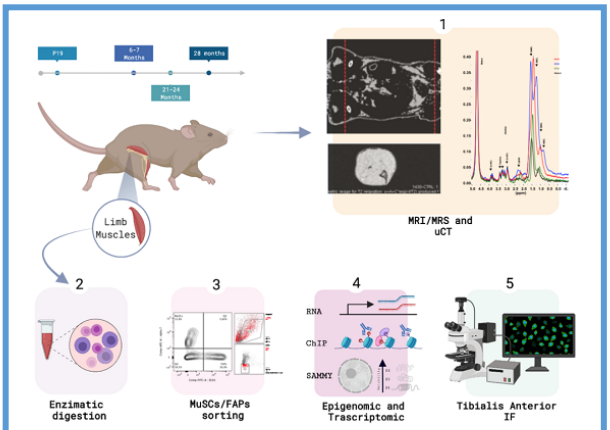

Experimental Design: Mice of different ages were subjected to MRI/MRS and µCT (1). Limb muscles were excised and enzymatically digested to obtain a cell suspension (2). The cell suspension was then stained and FACS-sorted to obtain two cell populations, MuSCs and FAPs (3). These populations were further divided to perform ChIP-seq (4). The tibialis anterior was embedded in OCT and flas-frozen for immunofluorescence analysis (5). This schematic representation was creted with BioRender.com

The correct 3D organization of the genome is known to influence the spatiotemporal expression of lineage-specific genes during stem cell differentiation and aging processes. We introduce a novel evolution of the SAMMY-seq technique to precisely map genomic regions separated by their biochemical properties. This single-handedly technique enables the identification of heterochromatic and euchromatic domains and their compartmentalization in the nuclear space. Crucial practical advantages of this method include: its applicability on as little as 10K cells; reduced costs; few manipulation steps and short execution time. In postnatal Muscle Stem Cells (MuSCs) we observed a reproducible distribution of euchromatic and heterochromatic genomic domains, in line with known epigenetic signatures. Our findings highlight how MuSCs over life exhibit a global steady chromatin organization, accompanied by solubility changes that favour processes such as MuSCs activation but may become obstacles during aging for proper pool maintenance. Still, we describe environmental alterations of the muscle niche, emphasizing a supportive population of MuSCs, namely FAPs, which exhibit dramatic transcriptional alterations during aging. Our extensive characterization of the environment and chromatin organization in MuSCs expands our understanding of quiescence, activation and aging processes, laying the groundwork for the study of the role of the epigenome in pathological conditions.

Key Words: Muscle stem cells; epigenetics; chromatin compartments; muscle aging.

References

1. Rosti V., Gorini F., Santarelli P., Sarnicola M. L., Magnani S. and Lanzuolo C "Polycomb bodies detection in murine fibromuscular stroma from skin, skeletal muscles and aortic tissues" Methods Mol Biol. In press.

2. Sebestyén E, Marullo F, Lucini F, Petrini C, Bianchi A, Valsoni S, Olivieri I, Antonelli L, Gregoretti F, Oliva G, Ferrari F, Lanzuolo C. SAMMY-seq reveals early alteration of heterochromatin and deregulation of bivalent genes in Hutchinson-Gilford Progeria Syndrome. Nat Commun. 2020 Dec 8;11(1):6274. doi: 10.1038/s41467-020-20048-9. PMID: 33293552; PMCID: PMC7722762.
3. Bianchi A, Mozzetta C, Pegoli G, Lucini F, Valsoni S, Rosti V, Petrini C, Cortesi A, Gregoretti F, Antonelli L, Oliva G, De Bardi M, Rizzi R, Bodega B, Pasini D, Ferrari F, Bearzi C, Lanzuolo C. Dysfunctional polycomb transcriptional repression contributes to lamin A/C-dependent muscular dystrophy. J Clin Invest. 2020 May 1;130(5):2408-2421. doi: 10.1172/JCI128161. PMID: 31999646; PMCID: PMC7190994.

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2023Pdm3 March 29 - Abstract 13

Isabella Scionti, *INMG, Lyon, France:* ***Epigenetic modifiers role in modulating muscle stem cell plasticity***

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2023Pdm3 March 29 - Abstract 14

Piera Smeriglio, *Sorbonne Université, Paris, France:* ***Understanding epigenetics in spinal muscle atrophy: how the yin and yang of genomic regulation contribute to the disease***

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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2023Pdm3 March 29 - Abstract 15

Epigenetic targeting of BET proteins rewire metabolism in the aged skeletal muscle

Lorenzo Nevi (1), Cinzia Bottino (1), Ummu Guven (1), Giulio Pavesi (1), Marc Beltrà (2), Fabio Penna (2), Giuseppina Caretti (1)

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Email: giuseppina.caretti@unimi.it

Aging is associated with a progressive decline of muscle mass and strength that is observed among healthy adults, with an acceleration in the rate of decline past middle age. The pathological loss of muscle mass associated with aging, known as sarcopenia, negatively affects the quality of life and leads to increased occurrence of falls, hospitalization, and to decreased independence. Previous reports from our group showed that the epigenetic factor bromodomain and extra-terminal domain (BET) protein BRD4 plays a role in promoting muscle wasting in experimental models of cancer cachexia and muscular dystrophy. Here, we evaluated the impact of pharmacological blockade of BET proteins in the skeletal muscle of 24-month-old mice. Mice were treated with the BET inhibitor JQ1+ (20mg/kg) or the inactive enantiomer JQ1- daily, for 24 days. During treatment, mice were weighed, and muscle performance was evaluated through the treadmill and grip tests. After sacrifice, different muscles and several tissues were isolated and collected for morphological and molecular analysis, including RNA-seq, Western Blot, and IHC. Our data show that JQ1 treatment induced weight loss in old mice and BET blockade also displayed a beneficial effect on muscle performance, and it was associated with a marked reduction in fibrosis. Following JQ1 treatment, RNA-seq assays highlighted an enrichment in the level of key transcripts involved in fatty acid oxidation in skeletal muscle. Metabolomic and immunoblot analysis revealed a reduced reliance on glycolysis and an increase in fatty acid oxidation. In conclusion, our data suggest that JQ1+ treatment ameliorates mitochondrial fatty acid metabolism in old mice, improves muscle function and it may be beneficial in the treatment of sarcopenia.

Key Words: BET proteins; sarcopenia; lipid metabolism.

References

1. von Haehling S, Morley JE, Anker SD. An overview of sarcopenia: facts and numbers on prevalence and clinical impact. J Cachexia Sarcopenia Muscle. 2010 Dec;1(2):129-133. doi: 10.1007/s13539-010-0014-2. Epub 2010 Dec 17. PMID: 21475695; PMCID: PMC3060646.
2. Segatto M, Fittipaldi R, Pin F, Sartori R, Dae Ko K, Zare H, Fenizia C, Zanchettin G, Pierobon ES, Hatakeyama S, Sperti C, Merigliano S, Sandri M, Filippakopoulos P, Costelli P, Sartorelli V, Caretti G. Epigenetic targeting of bromodomain protein BRD4 counteracts cancer cachexia and prolongs survival. Nat Commun. 2017 Nov 22;8(1):1707. doi: 10.1038/s41467-017-01645-7. PMID: 29167426; PMCID: PMC5700099.
3. Segatto M, Szokoll R, Fittipaldi R, Bottino C, Nevi L, Mamchaoui K, Filippakopoulos P, Caretti G. BETs inhibition attenuates oxidative stress and preserves muscle integrity in Duchenne muscular dystrophy. Nat Commun. 2020 Nov 30;11(1):6108. doi: 10.1038/s41467-020-19839-x. PMID: 33257646; PMCID: PMC7705749.

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Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

2023Pdm3 March 29 - Abstract 16

Facioscapulohumeral Dystrophy: Incomplete Repression of the Cleavage Stage Transcription Factor DUX4 in Skeletal Muscle

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Facioscapulohumeral dystrophy (FSHD) is characterized by progressive weakness and wasting of the facial, shoulder girdle and upper arm muscles. FSHD is caused by incomplete repression of the cleavage stage transcription factor DUX4 in skeletal muscle. A copy of this DUX4 gene is located in each unit of the D4Z4 macrosatellite repeat in the subtelomere of chromosome 4q, which adopts a repressive chromatin structure preventing DUX4 expression in somatic cells. In the population, the polymorphic D4Z4 repeat varies between 8-100 units and most often, DUX4 expression in skeletal muscle of FSHD patients is caused by D4Z4 chromatin relaxation as a consequence of a contraction of the repeat to a size of 1-10 units (FSHD1). However, with the advances in genome technologies, new genetic causes for FSHD have been uncovered over the past decade. In addition to genomic rearrangements to D4Z4 other than repeat contractions such as translocations and duplications, also mutations in chromatin factors that are necessary to establish or maintain a repressive D4Z4 chromatin structure (SMCHD1, DNMT3B and LRIF1) have been recognized to cause FSHD (FSHD2). However, rather than a dichotomy between both disease forms, FSHD1 and FSHD2 should rather be considered a continuum in which the reduced D4Z4 repeat size and a partial failure in establishing and maintaining a repressive D4Z4 chromatin structure proportionally contribute to the derepression of DUX4 in skeletal muscle.

Key Words: Facioscapulohumeal dystrophy (FSHD); D4Z4; epigenetics; chromatin; DUX4.

References

1. Tihaya MS, Mul K, Balog J, de Greef JC, Tapscott SJ, Tawil R, Statland JM, van der Maarel SM. Facioscapulohumeral muscular dystrophy: the road to targeted therapies. Nat Rev Neurol. 2023 Jan 10. doi: 10.1038/s41582-022-00762-2. Epub ahead of print. PMID: 36627512.

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WEDNESDAY March 29, 2023

Guariento Hall, Galilean Academy of Arts and Sciences of Padua, Italy

SESSION III: Adaptations in Aging: from molecules to functioning

Amber L. Pond, Rosanna Piccirillo, Chairs

2023Pdm3 March 29 - Abstract 17

The HERG K+ Channel increases Intracellular Calcium in myotubes by modulation of Calsequestrin

Amber Pond (1) , Shalini Guha (1), Emily LaVigne (2), Natalie McClure (1), Jennifer Koran (3), Gregory H. Hockerman (2).

(1) Anatomy Department, Southern Illinois University School of Medicine, USA; (2) Medicinal Chemistry and Molecular Pharmacology, Purdue University, IN, USA; (3) School of Education, Southern Illinois University-Carbondale, USA.
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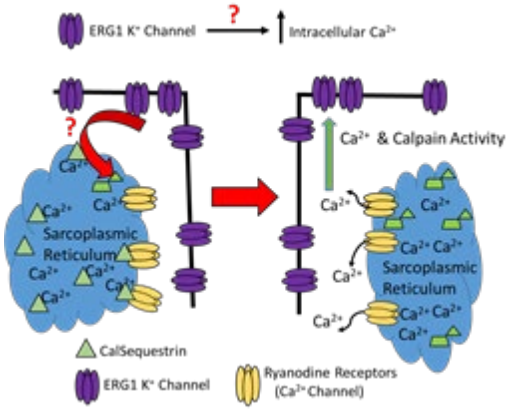
Pond AL, Whitmore C, Thimmapuram J, Hockerman GH. The ERG1A potassium channel induces expression of genes related to skeletal muscle atrophy in C2C12 myotubes**.** *FASEBJ 2021;35(S1):1.* https://doi.org/10.1096/fasebj.2021.35.S1.04316. The ERG1A K^+ channel upregulates protein degradation in skeletal muscle atrophying in response to disuse[1] and is found upregulated in muscle atrophying in response to cancer[1] and denervation[2]. We have shown that over-expression of the HERG channel increases basal intracellular calcium concentration ($[Ca^{2+}]i$) and calpain activity in C2C12 myotubes[3]; however, it is not known how HERG modulates $[Ca^{2+}]i$. Indeed, we find that L-type calcium current is not changed by HERG expression. Thus, to



HERG may increase intracellular Ca2+ concentration by decreasing abundance of the calcium binding/buffering protein CalSequestrin 1

Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

explore this mechanism, we increased [Ca^{2+}]i by depolarization with 100 mM KCl and used Fura2 dyes and immunoblot to reveal that HERG does not alter myotube calcium levels by affecting L-type calcium channels. Instead, using the SERCA blocking agent thapsigargin with our Fura2 assay, we discovered that the HERG-mediated increase in calcium occurs through modulation of intracellular calcium stores[4]. Therefore, we hypothesized that HERG may be modulating[Ca^{2+}]i by modulation of ryanodine receptor (RyR1) activity. To investigate this, we transduced myotubes in a 96-well plate with either a control or HERG-encoded adenovirus and after 48 hours loaded these with QBT Fura (Molecular Devices; San Jose, CA). At 1 hour post-loading, we treated the myotubes with either ryanodine (90 uM to block RyR1 receptors) or vehicle for 30 minutes. We then treated the cells with caffeine (5 mM) to activate ryanodine receptors and evaluated the [Ca^{2+}]i over time by fluorescence (340 and 380 excitement; 508 nm emission). The 340/380 ratios were determined and normalized to baseline. The ratios were plotted over time, the area under the curve (AUC) was calculated, and these were analyzed by ANOVA with means separated by Tukey's test. Interestingly, in response to caffeine, the significant increase in [Ca2+]i was similar in control (73.3%, $p<0.005$) and HERG-expressing (71.7%, $p<.001$) myotubes. However, when the cells were treated with ryanodine to block RyR1, the [Ca^{2+}]i increase was lower in the HERG-expressing (46.4%, $p<0.02$) relative to control (24.9%, $p<0.8$) myotubes. The data suggest that the increase in [Ca^{2+}]i in the HERG-expressing cells is, at least in part, a result of RyR1 activation. Because calsequestrin 1 (CaSeq1) is an integral part of RyR1 modulation of [Ca^{2+}]i and was reported mildly downregulated in HERG-expressing myotubes by Next Generation Sequencing,[5] we performed an immunoblot on control and HERG-expressing myotubes (n=8, 4 replicates each HERG and control), in which we detected a full length CaSeq ~63 kD protein along with ~50 kD and ~40 kD CaSeq proteins which appear to be CaSeq1 degradation products. Each protein was decreased in the HERG-expressing myotubes relative to control cells: ~63 kD decreased 47.2%, $p<0.001$; ~50 kD decreased 44.9%, $p<0.01$; and ~40 kD decreased 49.8%, $p<0.01$ (Student's t-test). CaSeq1 is known to function as a calcium buffer in skeletal muscle sarcoplasmic reticulum (SR), storing calcium when the concentration is high. Thus, we suggest that HERG expression produces a decrease in CaSeq protein, which removes this calcium binding protein and increases free calcium in intracellular calcium stores (Figure). Dysregulation of normal calcium buffering is known to contribute to pathologies in both skeletal muscle and heart. This is an exciting finding which merits further exploration.

Key Words: HERG, calcium signaling, ryanodine receptors, calsequestrin, myotubes

References

1. Wang X, Hockerman GH, Green HW 3rd, Babbs CF, Mohammad SI, Gerrard D, Latour MA, London B, Hannon KM, Pond AL. Merg1a K+ channel induces skeletal muscle atrophy by activating the ubiquitin proteasome pathway. FASEB J. 2006 Jul;20(9):1531-3. doi: 10.1096/fj.05-5350fje. Epub 2006 May 24. PMID: 16723379**.**
2. Anderson LB, Ravara B, Hameed S, Latour CD, Latour SM, Graham VM, Hashmi MN, Cobb B, Dethrow N, Urazaev AK, Davie JK, Albertin G, Carraro U, Zampieri S, Pond AL. MERG1A Protein Abundance Increases in the Atrophied Skeletal Muscle of Denervated Mice, But Does Not Affect NFκB Activity. J Neuropathol Exp Neurol. 2021 Sep 10;80(8):776-788. doi: 10.1093/jnen/nlab062. PMID: 34363662.
3. Whitmore C, Pratt EPS, Anderson L, Bradley K, Latour SM, Hashmi MN, Urazaev AK, Weilbaecher R, Davie JK, Wang WH, Hockerman GH, Pond AL. The ERG1a potassium channel increases basal intracellular calcium concentration and calpain activity in skeletal muscle cells. Skelet Muscle. 2020 Jan 16;10(1):1. doi: 10.1186/s13395-019-0220-3. PMID: 31948476; PMCID: PMC6966811.
4. Pond AL, Pratt E, Whitmore C, Rantz E, Salyer A, Carraro U, Zampieri S, Cheatwood J, Hockerman GH. 2018. Investigation of the mechanism by which the ERG1a K^+ channel increases intracellular calcium. Presented at 2018 Spring Padua Muscle Days, March 15-17; University of Padua, Italy.
5. Pond AL, Whitmore C, Thimmapuram J, Hockerman GH. The ERG1A potassium channel induces expression of genes related to skeletal muscle atrophy in C2C12 myotubes**.** *FASEBJ 2021;35(S1):1.* https://doi.org/10.1096/fasebj.2021.35.S1.04316. Presented Virtually at the 2021 Experimental Biology Conference on April 27, 2021.

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2023Pdm3 March 29 - Abstract 18

Fascia; facts and fantasies

Hans Hoppeler
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Classical anatomy of academic medicine describes bones (osteology), joints (arthrology) and muscle (myology). There is no specific category which describes "fascia" as an independent anatomical entity. Likewise, academic medicine does not recognize fascia as a pathogenetic entity other than when considered as connective tissue under the broad heading of rheumatic diseases. This is

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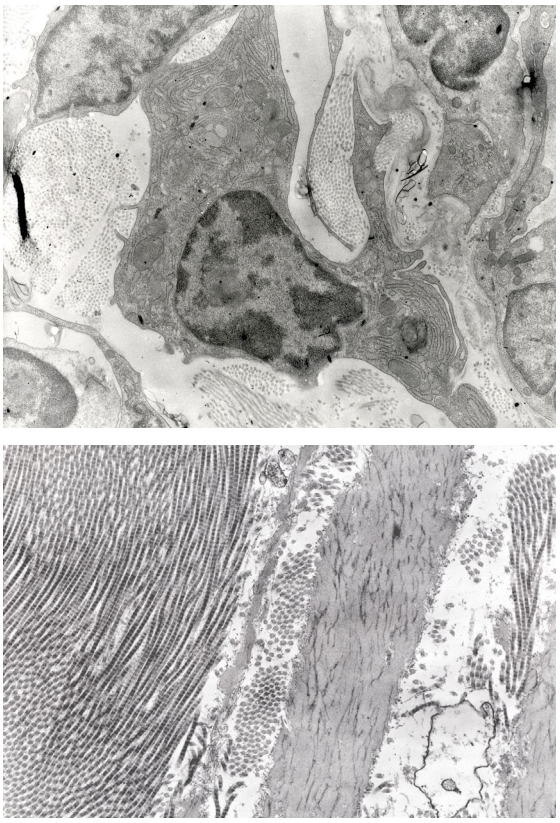

Fibrocyte (top) and collagen, elastin and hyalorunides responsible for mechanical properties of fascia (below).

different in osteopathic medicine. The founder of osteopathic medicine, Still, A.T. (1828-1917) viewed the human organism very much as a mechanical contraption that needed to be balanced to function properly. As a MD, trained by his father, he abhorred the drug medications of his time, which he (rightfully) considered dangerous. Instead, he corrected the mechanical causes for disordered bodily functions by adjusting the bony framework. For Still, the power to cure depended on the knowledge of the right or normal position and the skill to adjust bones, muscles and ligaments accordingly. As broadly speaking connective tissue (ligaments, fascia, tendons, connective interstitial tissue) is responsible for the connectivity and the positioning of the body elements in 3D space, it follows that these elements have become a major focus in osteopathic medicine today. Academic medicine sees connective tissue as composed of collagen, elastin and matrix with mechanical properties depending on the quantity and arrangement of these elements harbouring various sensory elements and important parts of the immune system and response. However, academic medicine does not see somatic dysfunctions in general related to myofascial function or dysfunction. Osteopathic medicine has a different perspective and sees fascia as a key mediator in somatic disease and pain conditions. Over the last 20 years a sizeable osteopathic literature has developed on these issues. This merits a closer look at fascia function and malleability in view of their potentially overlooked relevance for pathological processes in human disease.

Key Words: Osteopatic medicine; fascia; connective tissue; mechanical signaling.

References

1. Still AT. Osteopathy, Research and Practice. 1910, Past Masters Press, 2020, ISBN 978-1-396-31698-2.
2. Liem T, Tozzi P, Chila A. Fascia in the Osteopathic Field. 2017, Handspring, ISBN 9781909141278.

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2023Pdm3 March 29 - Abstract 19

MyoRep: a novel reporter system to detect early muscle atrophy in vivo

Andrea Re Cecconi, Nicoletta Rizzi, Mara Barone, Mara Forti, Michela Chiappa, Adriana Maggi, Paolo Ciana, Lorena Zentilin, **Rosanna Piccirillo**
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On-site presentation of unpublished results. The authors denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

Pdm3 March 29 - April 1, 2023

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2023Pdm3 March 29 - Abstract 20

Paolo Grumati, *Telethon Institute of Genetics and Medicine, Naples, Italy:* **Selective autophagy and ER dynamics during muscle differentiation**

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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2023Pdm3 March 29 - Abstract 21

Bert Blaauw, *University of Padua, Italy:* **The role of Akt-mTORC1 signaling in regulating muscle mass and function**

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

Pdm3 March 29 - April 1, 2023

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Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

2023Pdm3 March 29 - Abstract 22

LECTURE

Body temperature regulation by muscle tone

Terje Lømo (1), Arild Njå (1)

(1) Institute of Basic Medical Sciences, University of Oslo, Norway.
E-mail: terje.lomo@medisin.uio.no

Experiments were done on adult, male, Wistar rats chronically implanted with (i) EMG electrodes for recording motor unit activity, (ii) thermistors for recording core body and muscle temperatures, and (iii) a tube in the jugular vein for infusion of drugs. Each rat was placed in a climate chamber and video recorded at temperatures ranging from +4 to +34°C. Four springs supported the floor under which a force transducer recorded all movements such that each movement and the rest/sleep period that followed, could be monitored consecutively for the duration of the experiment. Previous work had shown (i) that during rest/sleep, tonic motor unit activity in several deep muscles increases linearly when the ambient temperature falls from 32°C to less than 7°C and (ii) that overt shivering first occurs when the temperature reaches about 7°C (Lømo et al., 2020). Here we show, first, that in adductor longus, a red muscle that lies close to the large femoral vein, the amount of tonic activity increases progressively when it gets colder, confirming our view that such heat-producing activity in deep muscles warms up the blood in nearby veins before it enters the body's cavities. Second, we show that iliopsoas, a large muscle that we term internal because it lies inside the abdominal and pelvic cavities, may generate substantial amounts of tonic motor unit activity during rest/sleep. But, unlike all deep external muscles that we record from, this tonic activity is independent of the ambient temperature. Furthermore, simultaneous EMG recordings from iliopsoas and different deep external muscles revealed occasional brief peaks of tonic activity in iliopsoas that coincided with similarly brief periods of no activity (atonia) in the external muscles. The duration and spacing of these peaks/troughs suggested some relationship to REM sleep, which accompanies such muscle atonia. Third, and again unexpectedly, we observed massive tonic motor unit activity in iliopsoas when the rat recovered from general anaesthesia, using ZRF i.v. (14.7 mg zolazepam, 14.7 mg tiletamine, 1.77 mg xylazine and 10 µg fentanyl per ml 0.9% NaCl). Following ZRF, all motor unit activity stopped, and the body temperature fell rapidly. During recovery, tonic activity started first in iliopsoas, then in deep external muscles, and, at about the same time, the body temperature began to rise. Only much later did the rat begin to wake up and start moving. This suggested that iliopsoas may generate heat-producing tonic activity in an emergency that threatens the body's core temperature without participating in the daily moment to moment temperature control. The results bear on the relative roles of brown adipose tissue (BAT) and tonic motor unit activity in controlling the body temperature and will be discussed. The relevant literature is confusing. Muscle tone and burst activity (overt shivering) are both described as forms of shivering, the continuous form often presented as pre-shivering tone or as a pre-stage to overt shivering. In general, these forms are not explicitly distinguished and are often treated as different expressions of the same underlying phenomenon. Although they both produce heat to protect the body against hypothermia, they should not be conflated because they arise from entirely different mechanism and cover strikingly different ambient temperature ranges (Lømo et al., 2020).

References

1. Lømo T, Njå A. Body temperature control in rats by muscle tone during rest or sleep. Acta Physiol. 2020; 228(2) e13348.
https://doi-org.ezproxy.uio.no/10.1111/apha.13348

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THURSDAY March 30, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:00 AM SESSION IV: FES managements of acquired muscle diseases –

Ines Bersch-Porada, Helmut Kern, Chairs

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2023Pdm3 March 29 - Abstract 23

Electrical stimulation in lower motoneuron lesions, from scientific evidence to clinical practice – a successful transition, a Physioterapy experience and researcher perspective

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Long pulse stimulation and its beneficial effect on lower motor neuron (LMN) damage have long been underestimated in daily rehabilitation practice in Switzerland/worldwide. The underlying reason may be the lack of knowledge about the neurophysiological changes of muscle after LMN in the acute phase after injury, the incorrect selection of stimulation parameters, namely pulse width, frequencies and amplitudes, the lack of perseverance in the application in the chronic phase

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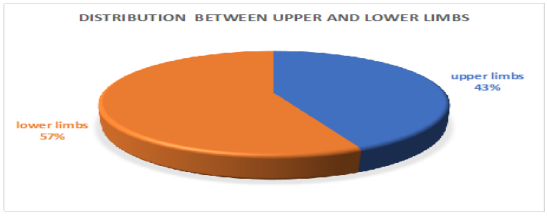

Figure 1: Distribution of upper and lower motoneuron lesions.

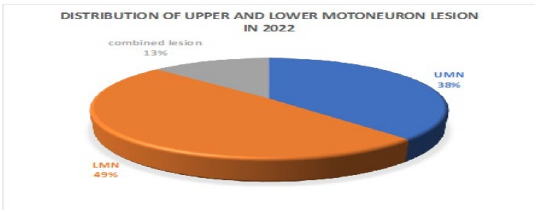

Figure 2: Distribution in stimulation between upper and lower limbs

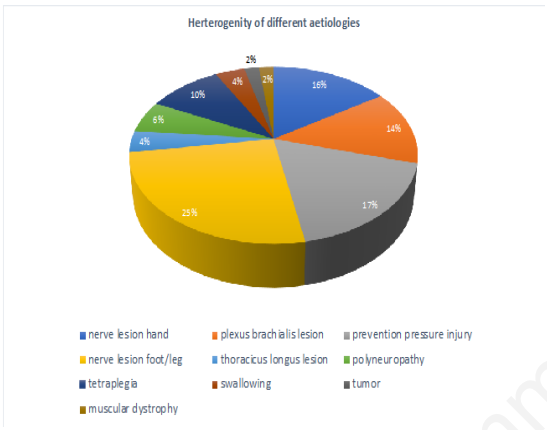

Figure 3: Etiological heterogeneity of LMN lesions

after injury or the unavailability of appropriate stimulators. In addition, the aetiology of the damage to the LMN may vary. The lesion might directly occur in the anterior horn, as it is the case in spinal cord injury (SCI), or it might result from peripheral nerve injuries, which can affect upper or lower extremities as a result of cuts, fractures or disc herniations. Due to the large heterogeneity of the aetiologies and the small population in the individual groups, the aim of the present observational study was to extract the number of patients, the type of LMN and form of stimulation from data collected in 2022 and consequently to substantiate these with the scientific evidence of the expected stimulation effect. Data collection included a pool of 128 patients seen in the year 2022. Only those who consulted the outpatient service for the first time seeking to conduct long pulse stimulation in the domestic setting were included for data analysis. The individuals were grouped in stimulation of the upper or lower extremities as well as in damage affecting the anterior horn or the peripheral nerve. 100 new patient cases were evaluated in 2022. 38% showed an upper motor neuron lesion, 49% a LMN lesion and 13% a combined lesion (Fig.1). In 57% the lower limbs and in 43% the upper limbs were affected, respectively (Fig. 2). The heterogeneity of the various types of LMN is reflected in Figure 3. Six patients that conducted long pulse stimulation at home are presented as cases with the physiological background and the illustration of their functional improvement. FES of denervated muscles is an early treatment option in temporary and potentially chronic peripheral denervation. The best effects are accomplished as long as the muscle is intact or just slightly atrophied and not yet undergoes degenerative developments.[1-4] In cases with perspective of recovery of nerve supply, the method is capable of preserving the reinnervation target in near-normal state. If denervation is permanent, FES of denervated muscle is the only option to maintain muscle tissue and metabolic functioning in the anatomical region.[5,6] This is important for prevention, e.g. pressure injuries, various degenerative developments, and eventual future novel therapy options. Long-term degeneration results in definitely irreversible conditions; nevertheless there is evidence, that even then tissue morphology and metabolic processes can be positively affected.[6] The spectrum of available stimulators is still limited. There are several handy stimulators on the market, that allow shorter “long-duration” stimuli – shorter means duration per phase of 15 to 20ms in biphasic pulses, which is a precondition to accomplish fused contractions via pulse trains with frequencies of 20 Hz or more, in principle. This is essential for building of muscle volume, force and endurance training, and functional use. A limitation of most available stimulators is in low deliverable maximum amplitude and minimum of inter-pulse pauses being longer than the pulse itself. Currently, the “Stimulette RISE”, offered by the Viennese family enterprise Schuhfried, is the only certified medical product capable of delivering stimuli with the necessary reduced inter-pulse pauses, down to 10ms, which are required for eliciting fused contractions, and an intensity reserve sufficient for activating larger muscles. What remains critical, is handling and placement of electrodes. As excessive local current density can result in skin injury, care must be taken to assure full surface skin contact with evenly distributed contact pressure and so, well distributed current density. Longstanding denervation and in particular large muscles require the use of conductive polymer electrodes in wet foam pockets or with gel as contact medium. Biphasic rectangular pulses are first choice and most effective in eliciting muscle contractions. For cases, where intact sensory nerves or motor nerves are unintentionally co-activated, ramp-shaped pulse forms can shift activation thresholds of neurons higher than those of muscle fibers, based on accommodation effects in the nerve fiber membrane with a higher excitability. In case of partly denervation of a muscle, which is seen in practice rather often, accommodating pulses can be useful for recruiting the denervated fiber population with some selectivity. This is useful for estimating the degree of denervation in

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single muscles as well as for focused conditioning of the denervated fiber population.

Key words: long pulse stimulation, denervation, lower motoneuron damage

References

1. Alberty M, Mayr W, Bersch I. Electrical Stimulation for Preventing Skin Injuries in Denervated Gluteal Muscles-Promising Perspectives from a Case Series and Narrative Review. Diagnostics (Basel). 2023 Jan 6;13(2):219. doi: 10.3390/diagnostics13020219. PMID: 36673029; PMCID: PMC9857944.
2. Bersch I, Fridén J. Electrical stimulation alters muscle morphological properties in denervated upper limb muscles. EBioMedicine. 2021 Dec;74:103737. doi: 10.1016/j.ebiom.2021.103737. Epub 2021 Dec 9. PMID: 34896792; PMCID: PMC8671101.
3. Bersch I, Fridén J. Upper and lower motor neuron lesions in tetraplegia: implications for surgical nerve transfer to restore hand function. J Appl Physiol (1985). 2020 Nov 1;129(5):1214-1219. doi: 10.1152/japplphysiol.00529.2020. Epub 2020 Sep 24. PMID: 32969783.
4. Chandrasekaran S, Davis J, Bersch I, Goldberg G, Gorgey AS. Electrical stimulation and denervated muscles after spinal cord injury. Neural Regen Res. 2020 Aug;15(8):1397-1407. doi: 10.4103/1673-5374.274326. PMID: 31997798; PMCID: PMC7059583.
5. Kern H, Salmons S, Mayr W, Rossini K, Carraro U. Recovery of long-term denervated human muscles induced by electrical stimulation. Muscle Nerve. 2005 Jan;31(1):98-101. doi: 10.1002/mus.20149. PMID: 15389722.
6. Kern H, Carraro U. Home-Based Functional Electrical Stimulation of Human Permanent Denervated Muscles: A Narrative Review on Diagnostics, Managements, Results and Byproducts Revisited 2020. Diagnostics (Basel). 2020 Jul 29;10(8):529. doi: 10.3390/diagnostics10080529. PMID: 32751308; PMCID: PMC7460102.

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Home-Based Electrical Stimulation Training for SCI Persons with Lower Motor Neuron Injury

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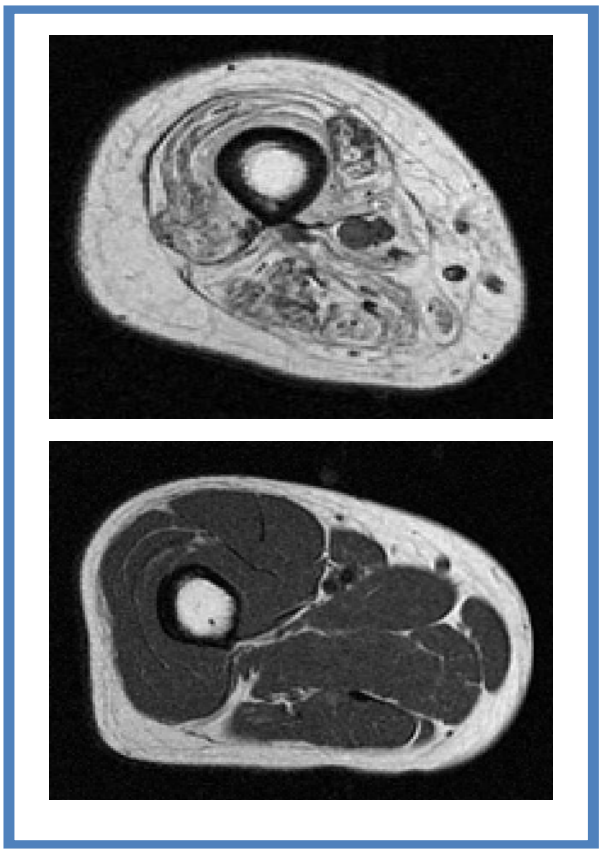
Spinal cord injury (SCI) results in skeletal muscle atrophy and dramatic changes in body composition. Lower motor neuron (LMN) injury results in denervation of the lower extremity muscles which exacerbates muscle atrophy.[1,2] Our recent unpublished work demonstrated that compared to innervated group with SCI (Figure), LMN resulted in remarkably lower cross-sectional area of the whole thigh and knee extensor muscles. This is accompanied with increased intramuscular fat and decreased leg lean mass. Furthermore, knee bone mineral density of the distal femur and proximal tibia is severely impacted following LMN. In the RISE project, long pulse width stimulation (LPWS) has shown promising outcomes in stimulation of the denervated muscles.[1,2] However, applications of LPWS are clearly limited in North America. We have previously shown that using testosterone treatment in conjunction with surface neuromuscular resistance training augmented muscle hypertrophy and enhanced metabolic profile after SCI.[3,4] We, hereby, present our preliminary evidence about conducting home-based and lab-based trial of combining TT + either short or LPWS stimulation in SCI persons with LMN. The overall goal is to increase skeletal muscle size, leg lean mass and to improve metabolic health in this sub-population with SCI https://clinicaltrials.gov/ct2/show/NCT03345576. The-12 month trial demonstrated the safety and feasibility of using LPWS with TT in restoring muscle size after chronic LMN. Furthermore, home-based approach is likely to provide an opportunity for long-term



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commitment and adherence for this population; especially during the era of COVID-19 pandemic.

Key Words: Denervation; muscle cross sectional area; intramuscular fat; long pulse width stimulation; testosterone; spinal cord injury.

References

1. Gorgey AS, Khalil RE, Alrubaye M, Gill R, Rivers J, Goetz LL, Cifu DX, Castillo T, Caruso D, Lavis TD, Lesnefsky EJ, Cardozo CC, Adler RA. Testosterone and long pulse width stimulation (TLPS) for denervated muscles after spinal cord injury: a study protocol of randomised clinical trial. BMJ Open. 2022 Oct 5;12(10):e064748. doi: 10.1136/bmjopen-2022-064748.
2. Chandrasekaran S, Davis J, Bersch I, Goldberg G, Gorgey AS. Electrical stimulation and denervated muscles after spinal cord injury. Neural Regen Res. 2020 Aug;15(8):1397-1407. doi: 10.4103/1673-5374.274326. PMID: 31997798.
3. Gorgey AS, Khalil RE, Gill R, Gater DR, Lavis TD, Cardozo CP, Adler RA. Low-Dose Testosterone and Evoked Resistance Exercise after Spinal Cord Injury on Cardio-Metabolic Risk Factors: An Open-Label Randomized Clinical Trial. J Neurotrauma. 2019 Sep 15;36(18):2631-2645. doi: 10.1089/neu.2018.6136.
4. Gorgey AS, Graham ZA, Chen Q, Rivers J, Adler RA, Lesnefsky EJ, Cardozo CP. Sixteen weeks of testosterone with or without evoked resistance training on protein expression, fiber hypertrophy and mitochondrial health after spinal cord injury. J Appl Physiol (1985). 2020 Jun 1;128(6):1487-1496. doi: 10.1152/japplphysiol.00865.2019.

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Skin improvements by home-based Functional Electrical Stimulation (hbFES)

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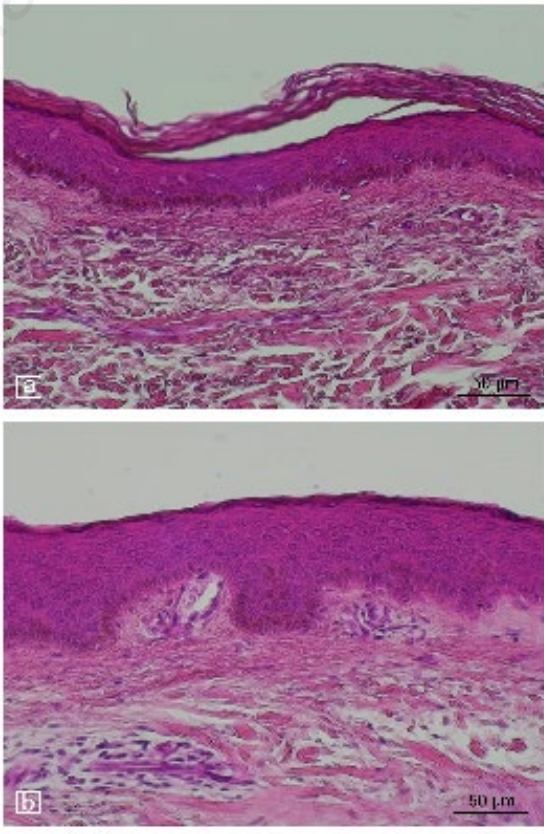
The epidermis represents the first line of defense of our body against the outside world. The skin is a complex sensory organ that protects the internal body from chemical, physical, and biological insults despite its apparently simple structure. Dermatological complications may develop after spinal cord injury (SCI) due to higher vulnerability to hypoxia, injury and infection (1). Despite the clinical relevance of dermatological complications, information on the histological changes that occur in skin of SCI persons is scarce, mainly because skin biopsies are usualy not performed except for major dermatological problems, such as pressure sore complications(2). Through the EU Program RISE (3,4), SCI patients suffering with complete conus and cauda equina syndrome (Conus-Cauda Syndrome), and thus with permanent denervation and degeneration of muscles (DDM), , were subjected to home-based functional electrical stimulation (h-bFES) of atrophic quadriceps muscles. It was observed impressive positive changes in the stimulated thigh muscles over a period of two years with use of very large electrodes in contact with the skin and a new electrical stimulator designed in Vienna. Because tissue biopsies harvested for muscle's analysis included the skin, we had extended quantitative histologic analyses of 52 skin biopsies of both legs of 13 SCI patients. We stressed that the tissue biopsies were collected only from SCI patients who did



H-E staining in skin specimens: skin sample from a SCI patient injured 5 years before (a) and after two years of h-bFES .

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not present with any local or general dermatological complications. The aim of this study was to verify the influence of h-bFES on skin. We have proven that 2 years of h-bFES reversed the process of skin atrophy and the flattening that occurs between 1 and 8 years post-SCI, that were the different period from spinal cord injury of the subjects that we have analyzed. We provided evidence that h-bFES produced an increased epidermal thickness and dermal-epidermal complexity (5), both of which are important mechanisms of skin resistance to physical, chemical and biological insult. The skin epidermis has shown an increase of thickness from 46.3 µm ± 9.6 µm before electrical stimulation to 64.3 µm ± 12.9 µm after 2 years of daily electrical stimulation . Times different from the spinal damage therefore allowed us to highlight that it was possible to act on the process of skin atrophy even though several years had passed since the spinal damage. Our results provided the evidence to justify further testing of electrical stimulation as an important contributory mechanism to prevent or manage skin disorders, in particular incoming pressure sores in SCI, metabolic diseases and late aging.

Key words: Epidermis thickness; electrostimulation; hbFES; spinal cord injury.

References

1. Marbourg JM, Bratasz A, Mo X, Popovich PG. Spinal Cord Injury Suppresses Cutaneous Inflammation: Implications for Peripheral Wound Healing. J Neurotrauma. 2017 Mar 15;34(6):1149-1155. doi: 10.1089/neu.2016.4611. Epub 2016 Oct 17. PMID: 27650169; PMCID: PMC5359642.
2. Hitzig SL, Eng JJ, Miller WC, Sakakibara BM; SCIRE Research Team. An evidence-based review of aging of the body systems following spinal cord injury. Spinal Cord. 2011 Jun;49(6):684-701. doi: 10.1038/sc.2010.178. Epub 2010 Dec 14. PMID: 21151191; PMCID: PMC3181216.
3. Kern H, Carraro U, Adami N, Biral D, Hofer C, Forstner C, Mödlin M, Vogelauer M, Pond A, Boncompagni S, Paolini C, Mayr W, Protasi F, Zampieri S. Home-based functional electrical stimulation rescues permanently denervated muscles in paraplegic patients with complete lower motor neuron lesion. Neurorehabil Neural Repair. 2010 Oct;24(8):709-21. doi: 10.1177/1545968310366129. Epub 2010 May 11. PMID: 20460493.
4. Carraro U, Kern H, Gava P, Hofer C, Loefler S, Gargiulo P, Mosole S, Zampieri S, Gobbo V, Ravara B, Piccione F, Marcante A, Baba A, Schils S, Pond A, Gava F. Biology of Muscle Atrophy and of its Recovery by FES in Aging and Mobility Impairments: Roots and By-Products. Eur J Transl Myol. 2015 Aug 25;25(4):221-30. doi: 10.4081/ejtm.2015.5272. PMID: 26913160; PMCID: PMC4748978.
5. Kern H, Hofer C, Loefler S, Zampieri S, Gargiulo P, Baba A, Marcante A, Piccione F, Pond A, Carraro U. Atrophy, ultra-structural disorders, severe atrophy and degeneration of denervated human muscle in SCI and Aging. Implications for their recovery by Functional Electrical Stimulation, updated 2017. Neurol Res. 2017 Jul;39(7):660-666. doi: 10.1080/01616412.2017.1314906. Epub 2017 Apr 13. PMID: 28403681.
6. Ravara B, Hofer C, Kern H, Guidolin D, Porzionato A, De Caro R, Albertin G. Dermal papillae flattening of thigh skin in Conus Cauda Syndrome. Eur J Transl Myol. 2018 Dec 13;28(4):7914. doi: 10.4081/ejtm.2018.7914. PMID: 30662702; PMCID: PMC6317141.
7. Kern H, Carraro U. Home-Based Functional Electrical Stimulation of Human Permanent Denervated Muscles: A Narrative Review on Diagnostics, Managements, Results and Byproducts Revisited 2020. Diagnostics (Basel). 2020 Jul 29;10(8):529. doi: 10.3390/diagnostics10080529. PMID: 32751308 Free PMC article. Review.

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40 years of basic and applied myology for hbDDM FES in 20 slides

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I will begin by describing my research activities in 1979 and the serendipitous events of my dedication to denervation-reinnervation of muscles and their electrical stimulation in animal models,[1-4] and years later in patients.[5-11] After many years of basic research, I found myself conducting human studies to apply our findings to human mobility disorders, including those of aging. My contributions have been light and ultrastructural microscopy and molecular approaches, in particular on isomyosins and other muscle-type markers, but above all I have had the good fortune to attract brilliant young collaborators,[7] and to propose them to apply to skeletal muscle approaches that had proven to be effective in clinical cardiology.[9] Along the way, a few scientists and clinicians (particularly physical medicine and rehabilitation specialists) with similar interests approached me.[5-11] Some collaborations yielded exciting results,[4-11] most frustrations. However, this is the normal ratio in translational studies from basic science to medicine: many exciting preliminary results end in failure, especially the most original and promising ones. Fortunately, after so many years in which we were the only research team to publish good results in the field of

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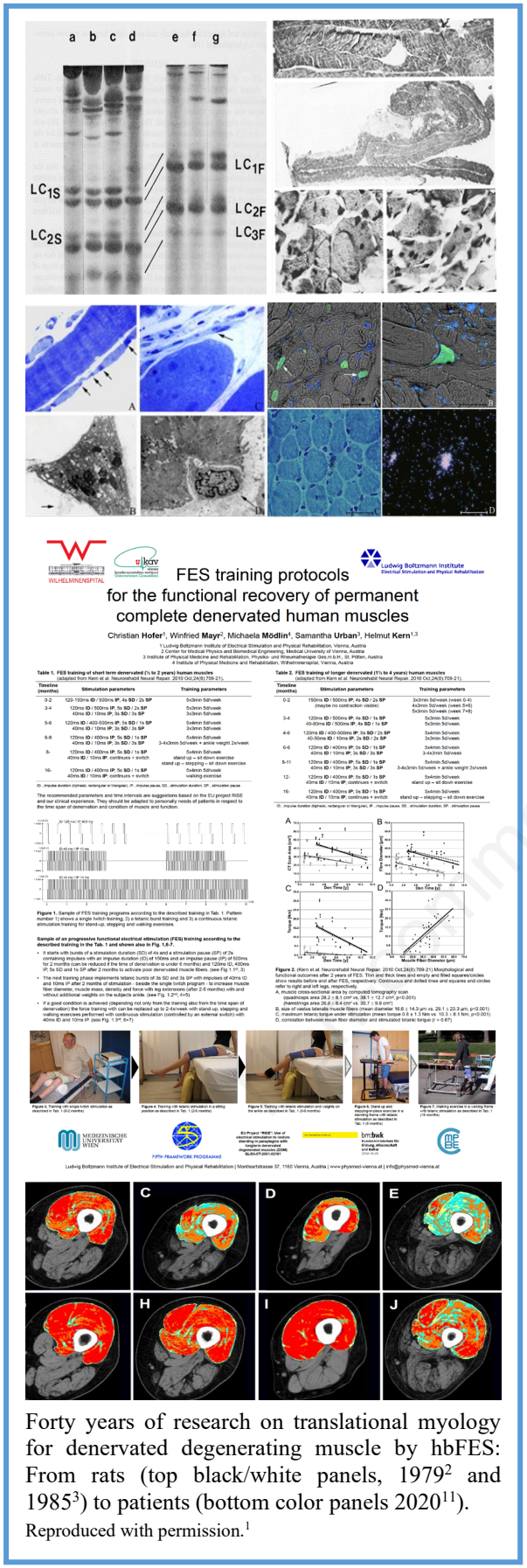

Forty years of research on translational myology for denervated degenerating muscle by hbFES: From rats (top black/white panels, 1979[2] and 1985[3]) to patients (bottom color panels 2020[11]).
Reproduced with permission.[1]

electrical stimulation of chronically denervated muscles, independent groups are following our lead, obtaining promising results.[12,13] I have to admit that most of my projects have ended in disappointments, but I still think it's more than enough to have dreams and the great luck to test them with rigorous scientific approaches, sharing emotions and frustrations with brilliant young collaborators.

Key words: Permanent muscle denervation; electrical stimulation; hbFES for DDM; countermeasures for aging and preliminary aging.

References

1. Carraro U. Translational mobility medicine: Dreams, hopes, frustrations. CLEUP, Padua, Italy. ISBN 978 88 5495 609 4.
2. Carraro U, Catani C, Biral D. Selective maintenance of neurotrophically regulated proteins in denervated rat diaphragm. Exp Neurol. 1979 Mar;63(3):468-75. doi: 10.1016/0014-4886(79)90165-1. PMID: 155010.
3. Carraro U, Morale D, Mussini I, Lucke S, Cantini M, Betto R, Catani C, Dalla Libera L, Danieli Betto D, Noventa D. Chronic denervation of rat hemidiaphragm: maintenance of fiber heterogeneity with associated increasing uniformity of myosin isoforms. J Cell Biol. 1985 Jan;100(1):161-74. doi: 10.1083/jcb.100.1.161. PMID: 3965469 Free PMC article.
4. Carraro U, Catani C, Belluco S, Cantini M, Marchioro L. Slow-like electrostimulation switches on slow myosin in denervated fast muscle. Exp Neurol. 1986 Dec;94(3):537-53. doi: 10.1016/0014-4886(86)90236-0. PMID: 3780906.
5. Kern H, Boncompagni S, Rossini K, Mayr W, Fanò G, Zanin ME, Podhorska-Okolow M, Protasi F, Carraro U. Long-term denervation in humans causes degeneration of both contractile and excitation-contraction coupling apparatus, which is reversible by functional electrical stimulation (FES): a role for myofiber regeneration? J Neuropathol Exp Neurol. 2004 Sep;63(9):919-31. doi: 10.1093/jnen/63.9.919. PMID: 15453091.
6. Boncompagni S. Severe muscle atrophy due to spinal cord injury can be reversed in complete absence of peripheral nerves. Eur J Transl Myol 2012;22:161–200. 10.4081/bam.2012.4.161 – DOI
7. Squecco R, Carraro U, Kern H, Pond A, Adami N, Biral D, Vindigni V, Boncompagni S, Pietrangelo T, Bosco G, Fanò G, Marini M, Abruzzo PM, Germinario E, Danieli-Betto D, Protasi F, Francini F, Zampieri S. A subpopulation of rat muscle fibers maintains an assessable excitation-contraction coupling mechanism after long-standing denervation despite lost contractility. J Neuropathol Exp Neurol. 2009 Dec;68(12):1256-68. doi: 10.1097/NEN.0b013e3181c18416. PMID: 19915489.

8. Kern H, Carraro U, Adami N, Biral D, Hofer C, Forstner C, Mödlin M, Vogelauer M, Pond A, Boncompagni S, Paolini C, Mayr W, Protasi F, Zampieri S. Home-based functional electrical stimulation rescues permanently denervated muscles in paraplegic patients with complete lower motor neuron lesion. Neurorehabil Neural Repair. 2010 Oct;24(8):709-21. doi: 10.1177/1545968310366129. Epub 2010 May 11. PMID: 20460493.
9. Gargiulo P, Reynisson PJ, Helgason B, Kern H, Mayr W, Ingvarsson P, Helgason T, Carraro U. Muscle, tendons, and bone: structural changes during denervation and FES treatment. Neurol Res. 2011 Sep;33(7):750-8. doi: 10.1179/1743132811Y.0000000007. PMID: 21756556.
10. Kern H, Carraro U. Home-Based Functional Electrical Stimulation of Human Permanent Denervated Muscles: A Narrative Review on Diagnostics, Managements, Results and Byproducts Revisited 2020. Diagnostics (Basel). 2020 Jul 29;10(8):529. doi: 10.3390/diagnostics10080529. PMID: 32751308 Free PMC article. Review.
11. Albertin G, Ravara B, Kern H, Zampieri S, Loefler S, Hofer C, Guidolin D, Messina F, De Caro R, Alaibac M, Carraro U. Trauma of Peripheral Innervation Impairs Content of Epidermal Langerhans Cells. Diagnostics (Basel). 2022 Feb 23;12(3):567. doi: 10.3390/diagnostics12030567. PMID: 35328120 Free PMC article.
12. Bersch I, Fridén J. Electrical stimulation alters muscle morphological properties in denervated upper limb muscles. EBioMedicine. 2021 Dec;74:103737. doi: 10.1016/j.ebiom.2021.103737. Epub 2021 Dec 9.
13. Gorgey AS, Khalil RE, Alrubaye M, Gill R, Rivers J, Goetz LL, Cifu DX, Castillo T, Caruso D, Lavis TD, Lesnefsky EJ, Cardozo CC, Adler RA. Testosterone and long pulse width stimulation (TLPS) for denervated muscles after spinal cord injury: a study protocol of randomised clinical trial. BMJ Open. 2022 Oct 5;12(10):e064748. doi: 10.1136/bmjopen-2022-064748. PMID: 36198461 Free PMC article.

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THURSDAY March 30, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

SESSION Va: Genetic muscle diseases

Elisabeth R. Barton, H. Lee Sweeney, Chairs

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2023Pdm3 March 29 - Abstract 27

LECTURE

Improving upon AAV.micro-dystrophin gene therapy for DMD

H. Lee Sweeney, *University of Florida, FL, USA*

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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Proteomic profiling of reactive myofibrosis in the aged and dystrophic diaphragm

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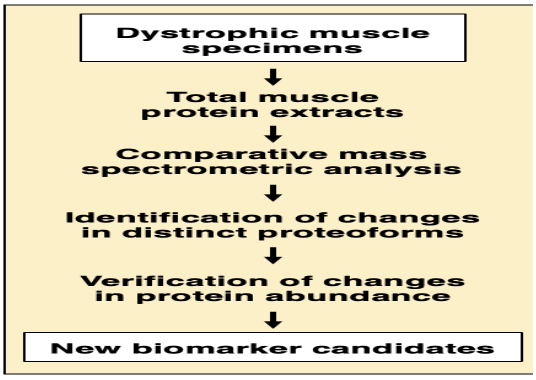
The membrane cytoskeletal protein dystrophin and its associated sarcolemmal protein complex are involved in contractile fibre stability, lateral force transmission and cellular signaling mechanisms in skeletal muscle tissues. Primary abnormalities in the DMD gene result in the almost complete loss of the Dp427-M isoform of dystrophin and cause progressive skeletal muscle wasting in association with fat substitution and chronic inflammation. A striking pathophysiological hallmark of X-linked muscular dystrophy is reactive myofibrosis that results in fibre scarring and the loss of muscle elasticity during excitation-contraction relaxation cycles. In order to study changes in the extracellular matrix in association with Duchenne muscular dystrophy, our laboratories have carried out mass spectrometry-based proteomic surveys of the dystrophic and aged diaphragm muscle from the mdx-4cv model of dystrophinopathy. A drastic increase in components of the matrisome, including various collagens, proteoglycans, fibronectin and the matricellular protein periostin, were identified. Changes in protein abundance related to the extracellular matrix were confirmed by comparative immunoblotting and immunofluorescence microscopy. We are currently evaluating the suitability of fibrotic markers to characterize patient biopsy specimens. Novel proteomic



Mass spectrometry-based proteomic analysis pipeline for the identification of dystrophinopathy-associated changes in the matrisome.

markers can now be tested for their suitability to improve diagnostic procedures, prognosis, and therapeutic monitoring, as well as for being used for the identification of new therapeutic targets.

Key Words: Duchenne muscular dystrophy; dystrophin; dystrophinopathy; fibrosis; matrisome.

References

1. Ohlendieck K, Swandulla D. Complexity of skeletal muscle degeneration: multi-systems pathophysiology and organ crosstalk in dystrophinopathy. Pflugers Arch. 2021 Dec;473(12):1813-1839. doi: 10.1007/s00424-021-02623-1. Epub 2021 Sep 22. PMID: 34553265; PMCID: PMC8599371.
2. Dowling P, Gargan S, Murphy S, Zweyer M, Sabir H, Swandulla D, Ohlendieck K. The Dystrophin Node as Integrator of Cytoskeletal Organization, Lateral Force Transmission, Fiber Stability and Cellular Signaling in Skeletal Muscle. Proteomes. 2021 Feb 2;9(1):9. doi: 10.3390/proteomes9010009. PMID: 33540575; PMCID: PMC7931087.
3. Zweyer M, Sabir H, Dowling P, Gargan S, Murphy S, Swandulla D, Ohlendieck K. Histopathology of Duchenne muscular dystrophy in correlation with changes in proteomic biomarkers. Histol Histopathol. 2022 Feb;37(2):101-116. doi: 10.14670/HH-18-403. Epub 2021 Dec 7. PMID: 34873679.
4. Dowling P, Gargan S, Swandulla D, Ohlendieck K. Proteomic profiling of impaired excitation-contraction coupling and abnormal calcium handling in muscular dystrophy. Proteomics. 2022 Dec;22(23-24):e2200003. doi: 10.1002/pmic.202200003. Epub 2022 Aug 8. PMID: 35902360.
5. Gargan S, Dowling P, Zweyer M, Henry M, Meleady P, Swandulla D, Ohlendieck K. Proteomic Identification of Markers of Membrane Repair, Regeneration and Fibrosis in the Aged and Dystrophic Diaphragm. Life (Basel). 2022 Oct 22;12(11):1679. doi: 10.3390/life12111679. PMID: 36362832; PMCID: PMC9696191.
6. Dowling P, Gargan S, Zweyer M, Sabir H, Henry M, Meleady P, Swandulla D, Ohlendieck K. Proteomic profiling of the interface between the stomach wall and the pancreas in dystrophinopathy. Eur J Transl Myol. 2021 Mar 26;31(1):9627. doi: 10.4081/ejtm.2021.9627. PMID: 33709651; PMCID: PMC8056161.

Pdm3 March 29 - April 1, 2023

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2023Pdm3 March 29 - Abstract 29

To unravel immune response in Duchenne Muscular Dystrophy

Marina Bouchè
DAHFM, Sapienza University of Rome, Italy:

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

Pdm3 March 29 - April 1, 2023

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2023Pdm3 March 29 - Abstract 30

Postural control impairments in Fabry disease

Philippe Perrin (1-3), Roland Jaussaud (1,4), Laetitia Peultier-Celli (1,2), Joëlle Deibener-Kaminsky (4), François Feillet (5), Pierre Kaminsky (1,4)

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Fabry disease (FD) is a rare inherited lysosomal storage disorder caused by the deficiency of the enzyme alpha-galactosidase A. This deficiency leads to an accumulation of glycosphingolipids leading to progressive and multisystemic disease, including renal, cardiac, and neurological damages. Neuro-otological and visual impairments can generate postural control impairments, inner ear, and vision being involved in this function (1-4). Fourteen adult patients (8 men/6 women, mean age = 37.6 ± 11.4 years) and two children (mean age = 11 years) with FD, and 19 healthy adults (12 men/7 women, mean age = 36.5 ± 16.9 years) and two healthy children (mean age = 10.5 years) took part in this study

Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

Computerized Dynamic Posturography (Equitest, NeuroCom, Clackhamas, OR) - Sensory organization test.

to assess the impact of FD on postural control. The sensory organization test (SOT) (EquiTest, NeuroCom, Clackamas, OR, USA) was used to assess overall balance and the use of specific sensory inputs to maintain postural control. An environmental conflict (visual and/or somatosensory) was created combining three visual situations (eyes open, eyes closed, and sway referenced visual surround motion) with two platform situations (stable platform and sway referenced platform motion), aiming to calculate a composite equilibrium score (CES), a high score being representative of good postural control. Somatosensory (RSOM), visual (RVIS), and vestibular (RVEST) contributions to postural control were calculated, a low score reflecting a poor use of the indicated sensory input. The CES ($p < 0.001$), RVIS ($p = 0.001$) and RVEST ($p = 0.003$) were lower in adult patients with FD compared with the healthy subjects, whereas no difference in RSOM was observed. Inner ear and visual pathologies associated with the central nervous system impairments are factors of postural control impairments. Understanding the specific balance control deficits in FD, determining the appropriate modalities of visuo-vestibular rehabilitation and quantifiably assessing its effect on improving postural stability and quality of life, could help to provide better balance-oriented programs (5). Physical activities, which can also be rehabilitative, by maintaining or increasing the weight of proprioception, may help diminish dependency on altered sensorial inputs, with the particular attempt of preventing falls.

Key words: Fabry disease; postural control; posturography; rehabilitation; cochleo-vestibular disorders.

References

1. Peultier-Celli L, Jaussaud R, Kaminsky P, Deibener-Kaminsky J, Feillet F, Perrin P. Balance control impairments in Fabry disease. Front Neurol. 2022 Sep 30;13:856946. doi: 10.3389/fneur.2022.856946.
2. Germain DP. Fabry disease. Orphanet J Rare Dis. 2010 Nov 22;5:30. doi: 10.1186/1750-1172-5-30.
3. Lidove O, Kaminsky P, Hachulla E, Leguy-Seguin V, Lavigne C, Marie I et al.; FIMeD investigators. Fabry disease 'The New Great Imposter': results of the French Observatoire in Internal Medicine Departments (FIMeD). Clin Genet. 2012 Jun;81(6):571-7. doi: 10.1111/j.1399-0004.2011.01718.x
4. Cammarata G, Fatuzzo P, Rodolico MS, Colomba P, Sicurella L, Iemolo F, Zizzo C, Alessandro R, Bartolotta C, Duro G, Monte I. High variability of Fabry disease manifestations in an extended Italian family. Biomed Res Int. 2015;2015:504784. doi: 10.1155/2015/504784.
5. Buatois S, Gauchard GC, Aubry C, Benetos A, Perrin P. Current physical activity improves balance control during sensory conflicting conditions in older adults. Int J Sports Med. 2007 Jan;28(1):53-8. doi: 10.1055/s-2006-924054.

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THURSDAY March 30, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

SESSION Vb: Genetic muscle diseases

Capucine Trollet, H. Lee Sweeney, Chairs

2023Pdm3 March 30 - Abstract 31

Novel role of store operated $Ca2^{+}$ entry in Limb-Girdle Muscular Dystrophy 2A

Katelyn Villani, Renjia Zhong, Zachary Brandt, C. Spencer Henley-Beasley, Lan Wei-LaPierre, Elisabeth Barton

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Limb-Girdle Muscular Dystrophy 2A (LGMD2A) is an autosomal recessive muscle disease characterized by progressive weakness of pelvic and scapular muscles. LGMD2A results from loss-of-function mutations in Calpain-3 (CAPN3), a calcium-dependent, non-lysosomal protease strictly expressed in skeletal muscle (1). Although LGMD2A is the most prevalent of the LGMDs, the the exact contribution of CAPN3 loss to the

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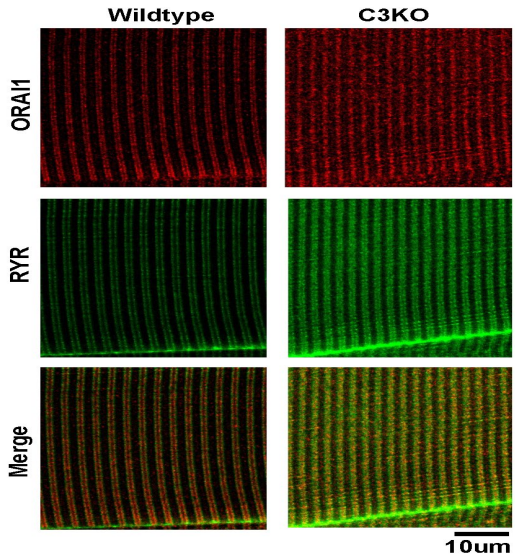

Immunostaining of ORAI1 and RYR show absence of Orai1 doublet in resting C3KO muscle.

variable pathology remains unclear. Initially, CAPN3 was found to maintain sarcomere integrity by regulating sarcomere remodeling through its localization on Titin (2). However, recent evidence suggests CAPN3 is also localized at the triad and may contribute to Ca^{2+} regulation and signaling during excitation-contraction coupling. In particular, the main SR Ca2+ pump, sarco/endo-plasmic reticulum Ca2+ ATPase (SERCA) activity is significantly reduced in calpain-3 knockout (C3KO) mice, which may lead to SR store depletion and the activation of store operated Ca2+ entry to replensish the SR Ca2+ store (3). SOCE activity was assessed at baseline then subsequently evoked with a treadmill running protocol in C57BL/6J (C57) and Calpain-3 knockout (C3KO) mice at pre-symptomatic (8 weeks old) and symptomatic (6-months old) ages (4). Muscle bundles from Extensor Digitorum Longus (EDL) muscles, selected due to their high SOCE activity, were analyzed using immunohistochemistry for proteins in the triad associated with SOCE activity. SOCE activity was measured in Flexor Digitorum Brevis fibers via Indo-1 Ca^{2+} measurements. Surprisingly, muscles from C3KO mice showed evidence of SOCE activity at rest, which persisted following treadmill running. This was in distinct contrast to muscles from C57 mice, where no SOCE occurred at rest, but was apparent after treadmill running. Thus, constitutively active SOCE in C3KO muscles is a newly identified mechanism underlying LGMD2A pathology of LGMD2A and supports a role of CAPN3 in Ca^{2+} homeostasis and handling

Key Words: Orai1; Stim 1; SOCE.

References:

1. Sorimachi H, Kimura S, Kinbara K, Kazama J, Takahashi M, Yajima H, Ishiura S, Sasagawa N, Nonaka I, Sugita H, Maruyama K, Suzuki K. Structure and physiological functions of ubiquitous and tissue-specific calpain species. Muscle-specific calpain, p94, interacts with connectin/titin. Adv Biophys. 1996;33:101-22. doi: 10.1016/s0065-227x(96)90026-x. PMID: 8922106.
2. Kramerova I, Kudryashova E, Tidball JG, Spencer MJ. Null mutation of calpain 3 (p94) in mice causes abnormal sarcomere formation in vivo and in vitro. Hum Mol Genet. 2004 Jul 1;13(13):1373-88. doi: 10.1093/hmg/ddh153. Epub 2004 May 11. PMID: 15138196.
3. Lyfenko AD, Dirksen RT. Differential dependence of store-operated and excitation-coupled Ca2+ entry in skeletal muscle on STIM1 and Orai1. J Physiol. 2008 Oct 15;586(20):4815-24. doi: 10.1113/jphysiol.2008.160481. Epub 2008 Sep 4. PMID: 18772199; PMCID: PMC2614059.
4. Boncompagni S, Michelucci A, Pietrangelo L, Dirksen RT, Protasi F. Exercise-dependent formation of new junctions that promote STIM1-Orai1 assembly in skeletal muscle. Sci Rep. 2017 Oct 27;7(1):14286. doi: 10.1038/s41598-017-14134-0. Erratum in: Sci Rep. 2018 Nov 27;8(1):17463. PMID: 29079778; PMCID: PMC5660245.
5. Michelucci A, Boncompagni S, Pietrangelo L, García-Castañeda M, Takano T, Malik S, Dirksen RT, Protasi F. Transverse tubule remodeling enhances Orai1-dependent Ca^{2+} entry in skeletal muscle. Elife. 2019 Oct 28;8:e47576. doi: 10.7554/eLife.47576. PMID: 31657717; PMCID: PMC6837846.

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2023Pdm3 March 30 - Abstract 32

Cell and molecular actors of fibrosis in muscle diseases

Capucine Trollet (1), Mona Bensalah (1), Laura Muraine (1), Alexis Boulinguiez (1), Paul Dowling (2), Jean Lacau-St Guily (1,3), Sophie Perie (4), Kay Ohlendieck (2), Vincent Mouly (1), Gillian Butler-Browne (1), Anne Bigot (1), Elisa Negroni (1)

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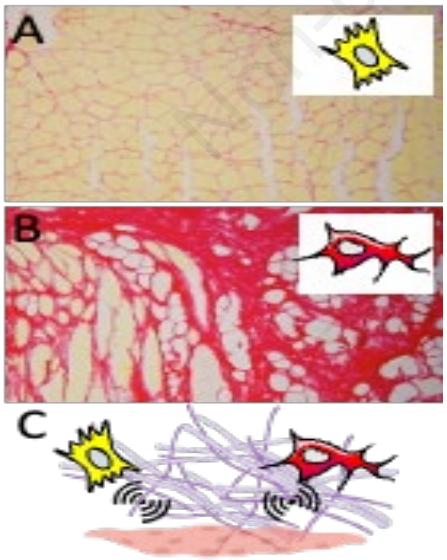
Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

Fibrosis is described in many organs as an excessive accumulation of extracellular matrix (ECM) proteins that replace tissue and alter its function. In skeletal muscle, fibrosis is a pathological feature common to many myopathies, such as Duchenne muscular dystrophy (DMD), oculopharyngeal muscular dystrophy (OPMD) or inclusion body myositis (IBM). Excessive accumulation of ECM alters the muscular function and the potential innovative therapeutic strategies. Several cellular actors are known to be implicated in the establishment and the maintenance of the fibrosis: macrophages, fibroadipogenic progenitors (FAPS) as well as satellite cells. The ECM, apart from its essential role as an architectural scaffold, has also a pivotal role in this process influencing muscle-resident cells through biochemical and biomechanical signals. Combining mass cytometry, transcriptome profiling, secretome analysis, in vitro co-culture experiments and in vivo transplantation in immunodeficient mice, we first investigated the role and nature of FAPs from human fibrotic muscles and compared them to FAPs from healthy muscle. Our results show that human FAPs from fibrotic muscles display a strikingly different profile than FAPs from non fibrotic muscles; fibrotic FAPs show an exacerbated proliferation and ECM secretion, and when activated, have a detrimental effect on muscle differentiation. In pharyngeal muscles, we also demonstrated the role of endothelin, a new targetable regulator involved in this process. Then using mass spectrometry, we characterized the ECM composition of DMD, OPMD and IBM human skeletal muscle biopsies. We identified a few shared ECM protein components as well as many specific ones for each pathology, highlighting differences in the amount and nature of ECM components. This work on human muscle biopsies provides a better understanding (a) of the key role of FAPs and their cross-talk with muscle cells through a paracrine signaling pathway and (b) of the ECM proteome of the muscle in pathological conditions. Altogether these data will lead the way to the identification of key components and targetable pathways for anti-fibrosis therapies.



FAPs from (A) healthy or (B) fibrotic human skeletal muscle. (C) cross-talk with muscle cells.

Key Words: Skeletal muscle; fibrosis; FAPs; cell-cell communication; ECM; myopathies.

References

1. Muscle fibro-adipogenic progenitors from a single-cell perspective: Focus on their "virtual" secretome. Negroni E, Kondili M, Muraine L, Bensalah M, Butler-Browne GS, Mouly V, Bigot A, Trollet C. Front Cell Dev Biol. 2022 Sep 19;10:952041. doi: 10.3389/fcell.2022.952041.
2. A negative feedback loop between fibroadipogenic progenitors and muscle fibres involving endothelin promotes human muscle fibrosis. Bensalah M, Muraine L, Boulinguiez A, Giordani L, Albert V, Ythier V, Dhiab J, Oliver A, Hanique V, Gidaro T, Perie S, Lacau St-Guily J, Corneau A, Butler- Browne G, Bigot A, Mouly V, Negroni E, Trollet C. J Cachexia Sarcopenia Muscle. 2022 Jun;13(3):1771-1784. doi: 10.1002/jcsm.12974.
3. Combined methods to evaluate human cells in muscle xenografts. Bensalah M, Klein P, Riederer I, Chaouch S, Muraine L, Savino W, Butler- Browne GS, Trollet C, Mouly V, Bigot A, Negroni E. PLoS One. 2019 May 2;14(5):e0211522. doi: 10.1371/journal.pone.0211522.
4. Update on anti-fibrotic pharmacotherapies in skeletal muscle disease. Muraine L, Bensalah M, Butler-Browne G, Bigot A, Trollet C, Mouly V, Negroni E. Curr Opin Pharmacol. 2022 Dec 23;68:102332. doi: 10.1016/j.coph.2022.102332.

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2023Pdm3 March 29 - Abstract 33

Investigating pathogenic mechanisms in FSHD myogenesis

Massimo Ganassi, Peter S. Zammit

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Muscle strength is essential for efficient movement and muscle weakness affects function to rapidly impinge on the quality of life. Facioscapulohumeral muscular dystrophy (FSHD) is usually characterized by weakness and wasting of specific muscle groups and disease can progress and compromise self-sufficiency. FSHD pathogenesis is associated with epigenetic derepression

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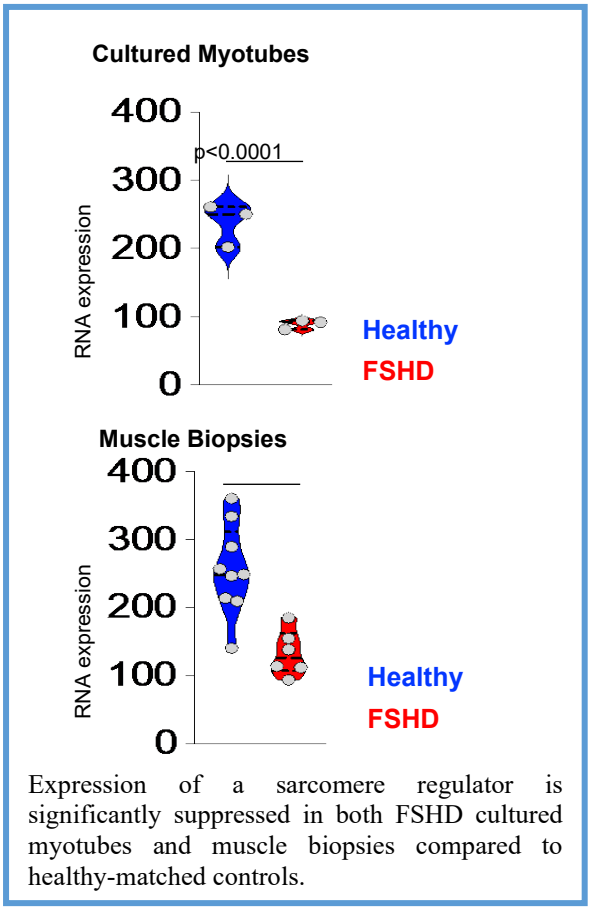

Expression of a sarcomere regulator is significantly suppressed in both FSHD cultured myotubes and muscle biopsies compared to healthy-matched controls.

at chromosome 4q35, unleashing expression of the transcription factor DUX4, whose accumulation hampers myogenesis and induces cell-death. Why FSHD muscle progressively weakens is still unclear, and is likely not solely caused by DUX4. Efficient muscle function is usually maintained by a specialized group of proteins that remove and replace worn components of the sarcomere, the force-generating apparatus, to assure its working integrity throughout life. Little is known on muscle integrity in FSHD, but sarcomeric dysfunction contributes to muscle weakness and reduced growth (1), suggesting that suppression of factors involved in sarcomere homeostasis may participate to FSHD pathogenesis. Our transcriptomic analysis (2) revealed suppression of genes involved in sarcomere homeostasis in FSHD muscles. Specifically, we found severely reduced level of a factor involved in sarcomere maintenance and regulating crucial myogenic signals during myogenesis. Here we show how manipulation of this factor in muscle cells affects FSHD myogenesis and modulate DUX4-induced signals (3) indicating its contribution FSHD muscle dysfunction. Ongoing epigenomics analysis will clarify upstream regulation of sarcomere integrity and expand understanding of FSHD pathogenesis. MG is supported by Amis FSH (20210627-1) and SOLVE-FSHD.

Key Words: FSHD; DUX4; sarcomere; myotubes; muscular dystrophy.

References

1. Lassche S, Stienen GJ, Irving TC, van der Maarel SM, Voermans NC, Padberg GW, Granzier H, van Engelen BG, Ottenheijm CA. Sarcomeric dysfunction contributes to muscle weakness in facioscapulohumeral muscular dystrophy. Neurology. 2013 Feb 19;80(8):733-7. doi: 10.1212/WNL.0b013e318282513b. Epub 2013 Jan 30. PMID: 23365058; PMCID: PMC3589299.
2. Banerji CRS, Panamarova M, Pruller J, Figeac N, Hebaishi H, Fidanis E, Saxena A, Contet J, Sacconi S, Severini S, Zammit PS. Dynamic transcriptomic analysis reveals suppression of PGC1α/ERRα drives perturbed myogenesis in facioscapulohumeral muscular dystrophy. Hum Mol Genet. 2019 Apr 15;28(8):1244-1259. doi: 10.1093/hmg/ddy405.
3. Ganassi M, Figeac N, Reynaud M, Ortuste Quiroga HP, Zammit PS. Antagonism Between DUX4 and DUX4c Highlights a Pathomechanism Operating Through β-Catenin in Facioscapulohumeral Muscular Dystrophy. Front Cell Dev Biol. 2022 Sep 7;10:802573. doi: 10.3389/fcell.2022.802573.
4. Ganassi M, Zammit PS. Involvement of muscle satellite cell dysfunction in neuromuscular disorders: Expanding the portfolio of satellite cell-opathies. Eur J Transl Myol. 2022 Mar 18;32(1):10064. doi: 10.4081/ejtm.2022.10064.

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THURSDAY March 30, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

02:00 PM - SESSION VI: Twenty Years of AIM

Daniela Tavian, Corrado Angelini, Chairs

2023Pdm3 March 30 - Abstract 34

***Gabriele Siciliano**, University of Pisa, Italy: Phenotype variabilities of laminopathies*

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

2023Pdm3 March 30 - Abstract 35

Pharmacological profile of the most promising CFTR corrector for sarcoglycanopathy treatment

Alberto Benetollo (1), Martina Scano (1), Sofia Parrasia (2), Lucia Biasutto (1,3), Francesco Dalla Barba (1), Paola Caccin (1), Marcello Carotti (1), Nogara Leonardo (1), Bert Blaauw (1), Dorianna Sandonà (1)

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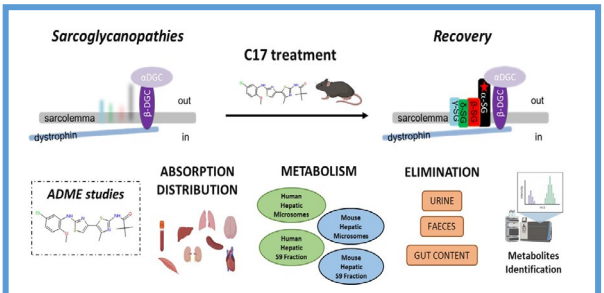
E-mail: alberto.benetollo@phd.unipd.it

Sarcoglycanopathies (LGMDR3-6) are the most severe forms of autosomal recessive limb-girdle muscular dystrophies. Sarcoglycanopathies, due to mutations in sarcoglycan (SG) genes, are characterized by progressive weakness of the shoulder and pelvic muscles. Most of these genetic defects, accounting for about the 65%, are missense mutations. They lead to a non-properly folded, even though potentially functional protein that is removed from the cellular context through the quality control (QC) system. Treatments with a small molecule called C17, belonging to the CFTR modulator family, resulted in the effective rescue of the mutant R98H-alpha-SG in vivo in a mouse model characterized by "humanized hind-limbs" expressing the mutated-SG. In particular, this compound produced a general amelioration of the pathological phenotype, and, most importantly, the recovery of the muscle force. These very promosing results moved us toward an in-depth investigation of the pharmacological properties of this compound, performing preliminary ADME (adsorption, distribution, metabolism and elimination) studies. We assessed the concentration-time (C-T) kinetic relationship, the biodistribution, the formation of drug metabolites in vitro and in vivo, and the elimination from the body. The in vitro drug biotransformation studies resulted in no formation of C17 derivatives using both human and mouse hepatic fractions (microsomes and S9 fraction). On the other hand, the analysis of urine and faeces of C17-treated mice evealed the presence of 2 metabolites in urine and 5 metabolites in faeces. These results could suggest that C17 is not metabolized at the level of liver, but rather through the activity of intestinal drug metabolizing enzymes. The analysis of gut content of C17-treated mice is ongoing. The concentration-time kinetic relationship revealed that C17 reaches the maximum concentration in the plasma after 2 hours from the administration and it is well distributed in all the mouse body compartments. Through the C17 steady-state study, we observed that C17 achieves the pharmacological plateau after 3 days. It was interesting to observe that at the level of the brain, heart and particularly skeletal muscle, our target-tissue, the pattern



Summary panel of ADME studies performed with the CFTR corrector C17.

is compatible with the way of administration and the concentration-time kinetic of the plasma. After 48 hours from the injection, the C17 corrector is still detectable in skeletal muscles, and this information allowed us to perform a new chronic treatment with a lengthened regimen of administration that resulted, as in Scano et al. (2022), in an effective recovery of the tibialis anterior force as the rescue of the sarcoglycans mutant and the sarcoglycan complex at the sarcolemma.
Key Words: Sarcoglycanopathies; CFTR correctors; pharmacokinetics; in vitro drug biotransformation.

References

1. Mariz Vainzof, Lucas S. Souza, Juliana Gurgel-Giannetti, Mayana Zatz, Sarcoglycanopathies: an update, Neuromuscular Disorders, Volume 31, Issue 10, 2021, Pages 1021-1027, ISSN 0960-8966.
2. Martina Scano, Alberto Benetollo, Leonardo Nogara, Michela Bondì, Francesco Dalla Barba, Michela Soardi, Sandra Furlan, Eylem Emek Akyurek, Paola Caccin, Marcello Carotti, Roberta Sacchetto, Bert Blaauw, Dorianna Sandonà, CFTR corrector C17 is effective in muscular dystrophy, in vivo proof of concept in LGMDR3, Human Molecular Genetics, Volume 31, Issue 4, 15 February 2022, Pages 499–509.
3. M. Schrag, K. Regal, Chapter 4 - Pharmacokinetics and Toxicokinetics, Editor(s): Ali Said Faqi, A Comprehensive Guide to Toxicology in Nonclinical Drug Development (Second Edition), Academic Press, 2013, Pages 69-106, ISBN 9780128036204.
4. J. Vrbanac, R. Slauter, Chapter 3 - ADME in Drug Discovery, Editor(s): Ali Said Faqi, A Comprehensive Guide to Toxicology in Nonclinical Drug Development (Second Edition), Academic Press, 2017, Pages 39-67, ISBN 9780128036204.
5. Lu, F.C., 1996. Biotransformation of toxicants, in: Basic Toxicology: Fundamentals, Target Organs and Risk Assessment, third ed., Taylor and Francis: Washington, DC, pp. 27–39.

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Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

2023Pdm3 March 30 - Abstract 36

Zebrafish and sarcoglycanopathies: characterization of models suitable for phenotype-based screening of drugs

Francesco Dalla Barba (1), Marcello Carotti (1), Alberto Benetollo (1), Martina Scano (1), Paola Caccin (1), Francesco Argenton (2), Dorianna Sandonà (1)

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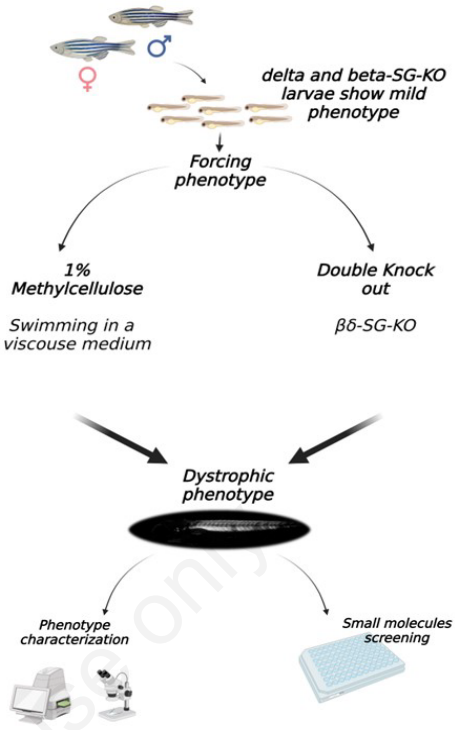
Sarcoglycanopathies (LGMDR3-6) are four severe autosomal recessive limb-girdle muscular dystrophies caused by mutations in the SGCA, SGCB, SGCG and SGCD genes, resulting in the strong reduction of alpha, beta, gamma and delta-sarcoglycan (SG) proteins. The consequence is the disruption of a key complex protecting striated muscle membrane (sarcolemma) from contraction stress. The typical clinical phenotype is characterized by early onset and includes progressive weakness of the proximal pelvic girdle and shoulder muscles, with variable cardiac and respiratory involvement (1). For the in vivo modelling of sarcoglycanopathies, different KI and KO mouse lines have been generated so far, while in zebrafish only morpholino KD models have been produced. Several are the advantages of using zebrafish as animal model, especially considering the similarity of the skeletal muscle structure and function with those of mammals. In addition, the conservation of several components of the DGC and sarcoglycan proteins (particularly beta- and delta- SG) prompted us to focus on zebrafish for modelling LGMDR4 and LGMDR5 (2).
We exploited the CRISPR/Cas9 technology to generate two KO zebrafish mutants, the beta-SG-KO and delta-SG-KO lines (3). Despite the absence of a sarcoglycan subunit, the characterization of the two single KO mutants during the first 6dpf revealed a mild phenotype. We observed a small reduction in the embryo dimension, as well as a slight alteration in the organization of the skeletal muscle fibers (4). At resting conditions, KO embryos performed like wild type zebrafish and only if subjected to stressful conditions, it was possible to highlight a slight reduction in the swimming performance.
The advantage of using zebrafish, especially for drug screening, lies in the possibility of performing experiments during the early stages of the fish's life. Therefore, in order to accelerate the onset of the disease traits, we decided to use two approaches:

- Induce the manifestation of the dystrophic features by growing from 2 to 5dpf delta-SG-KO and wild type zebrafish in a viscous medium (fish water added with 1% methyl cellulose)(5). By swimming in a high-density water since from hatching, muscles experiment a greater than normal effort. If the sarcolemma of delta-SG-KO zebrafish is more fragile than the wild type one, the expected outcome is the appearance of muscle damage.
- Production of a double knock out zebrafish (bd-SG-DKO), by breeding beta-SG-KO with delta-SG-KO. In this case, a reduced dimension of the body length was clear evident as early as 3dpf, as well as the presence of larvae with altered phenotype. The swimming ability was severely impaired as expected by the presence of damaged skeletal muscle fibers.



Both delta- and beta-SG-KO zebrafish present a mild myopathic phenotype at the larval stage.

Two strategies were adopted to accelerate the onset of the disease traits early during development:

- growing the larvae in viscous medium
- generating a double KO line for delta- and beta-sarcoglycan.

In both cases, zebrafish larvae presented damaged sarcomeres.

In both cases the phenotype of the larvae closely resembles the characteristics observed in sarcoglycanopathies, suggesting them as useful tools for the study of the disease and for development of in vivo phenotype-based screening of new drugs.

Key Words: Sarcoglycanophaties, CRISPR/Cas9, zebrafish model, drug screening.

References:

1. Vainzof M, Souza LS, Gurgel-Giannetti J, Zatz M. Sarcoglycanopathies: an update. Neuromuscul Disord. 2021 Oct;31(10):1021-1027. doi:

10.1016/j.nmd.2021.07.014. Epub 2021 Jul 28. PMID: 34404573.
2. Cheng L, Guo XF, Yang XY, Chong M, Cheng J, Li G, Gui YH, Lu DR. Delta-sarcoglycan is necessary for early heart and muscle development in zebrafish. Biochem Biophys Res Commun. 2006 Jun 16;344(4):1290-9. doi: 10.1016/j.bbrc.2006.03.234. Epub 2006 Apr 19. PMID: 16650823.
3. Andrew P.W. Gonzales, Jing-Ruey Joanna Yeh, Chapter Eighteen - Cas9-Based Genome Editing in Zebrafish, Editor(s): Jennifer A. Doudna, Erik J. Sontheimer, Methods in Enzymology, Academic Press, Volume 546, 2014, Pages 377-413, ISSN 0076-6879, ISBN 9780128011850, https://doi.org/10.1016/B978-0-12-801185-0.00018-0.
4. Smith, L. L., Beggs, A. H., Gupta, V. A. Analysis of Skeletal Muscle Defects in Larval Zebrafish by Birefringence and Touch-evoke Escape Response Assays. J. Vis. Exp. (82), e50925, doi:10.3791/50925 (2013).
5. Ruparelia AA, Oorschot V, Vaz R, Ramm G, Bryson-Richardson RJ. Zebrafish models of BAG3 myofibrillar myopathy suggest a toxic gain of function leading to BAG3 insufficiency. Acta Neuropathol. 2014 Dec;128(6):821-33. doi: 10.1007/s00401-014-1344-5. Epub 2014 Oct 2. PMID: 25273835

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2023Pdm3 March 29 - Abstract 37

Sara Missaglia, Elena Pennisi, Daniela Tavian, *et al., Milan, Italy:* **Exploring triheptanoin as treatment for neutral lipid storage disease with myopathy**

On-site presentation of unpublished results. The authors denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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2023Pdm3 March 30 - Abstract 38

Giulia Ricci, Gabriele Siciliano, *et al., University of Pisa, Italy:* **New avenues for treatment of facioscapulohumeral MD (FSHD)**

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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2023Pdm3 March 30 - Abstract 39

Two plasma circulating-miRs for the diagnosis of idiopathic inflammatory myopathies

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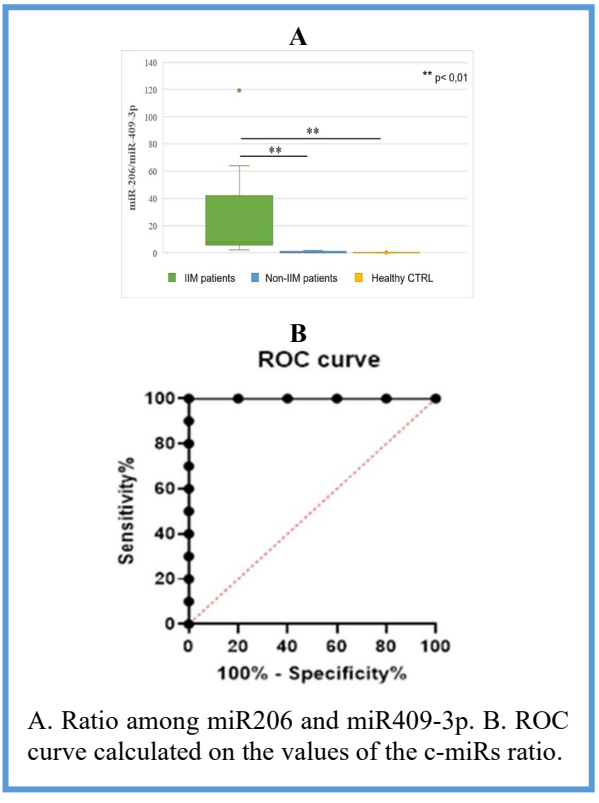
Idiopathic inflammatory myopathies (IIMs) are a group of rare diseases characterized by muscle pain and weakness associated with lymphocyte infiltration in the muscle tissue. Etiopathogenesis is not yet fully understood and the diagnosis is long-lasting and costly, often leading to a delay in the therapy. The diagnosis requires several steps, including an accurate clinical and laboratory investigation, EMG and muscle biopsy. The latter permits to define the diagnosis, distinguishing between IIM and hereditary myopathies, but it is an invasive procedure. The identification of new biomarkers



A. Ratio among miR206 and miR409-3p. B. ROC curve calculated on the values of the c-miRs ratio.

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able to differentiate patients with myositis by simple, low cost and non-invasive tests could improve the diagnostic efficiency, reducing the time to diagnosis/handling patients, and the costs generated by wrongly or untreated patients. MicroRNAs (miRs) are post transcriptional regulators of gene expression and the circulating ones are appealing non-invasive potential biomarkers. We have analyzed the expression of plasma circulating-miRs (c-miRs) in patients with or without IIM, compared with healthy subjects, and we have identified an index, based on the ratio between two c-miRs, which is able to distinguish with high specificity and sensitivity among patients with IIM or with other neuromuscular disorders with clinical signs similar to myositis. The study has been conducted in blind and confirmed by standard diagnostic tools. The index, based on a simple and rapid method of analysis, is patent protected and has a great potential as non-invasive diagnostic biomarkers for IIMs. Current experiments are focused on the identification of molecular mechanisms underpinning the alteration of the two identified c-miRs.

Key Words: Idiopathic inflammatory myopathies; microRNA; biomarkers.

References

1. Lundberg IE, Tjärnlund A, Bottai M, et al. 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. Ann Rheum Dis. 2017;76(12):1955-1964. doi:10.1136/annrheumdis-2017-211468.
2. Leclair V, Lundberg IE. New Myositis Classification Criteria-What We Have Learned Since Bohan and Peter. Curr Rheumatol Rep. 2018 Mar 17;20(4):18. doi: 10.1007/s11926-018-0726-4.
3. Olivieri F, Rippo MR, Monsurrò V, Salvioli S, Capri M, Procopio AD, Franceschi C. MicroRNAs linking inflamm-aging, cellular senescence and cancer. Ageing Res Rev. 2013 Sep;12(4):1056-68.doi: 10.1016/j.arr.2013.05.001.
4. Georgantas RW, Streicher K, Greenberg SA, Greenlees L, Zhu W, Brohawn P, Higgs BW, Czapiga M, Morehouse C, Amato A, Richman L, Jallal B, Yao Y, Ranade K. Inhibition of myogenic MicroRNAs-1, 133, and 206 by inflammatory cytokines links inflammation and muscle degeneration in adult inflammatory myopathies. Arthritis Rheumatol. 2014 Apr;66(4):1022-33. doi: 10.1002/art.38292.

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Morpho-functional characterization of Transportin3 in myogenic differentiation of a cell model of LGMD D2

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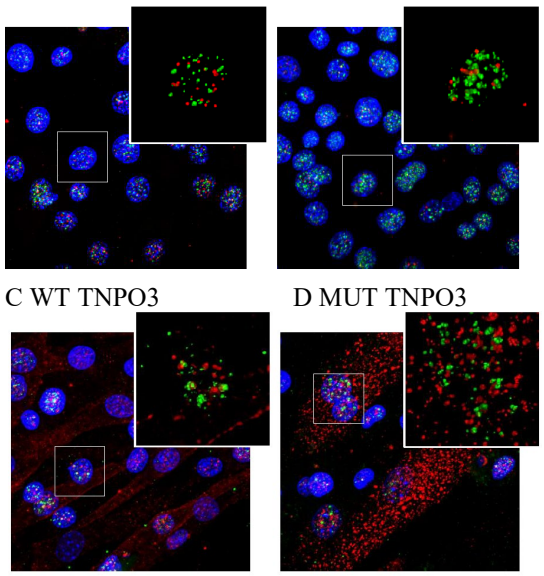
Limb Girdle Muscular Dystrophy D2 (LGMD D2) is caused by a heterozygous mutation in the termination codon of the TNPO3 gene. This mutation gives a protein which is 15-aminoacids longer in its C-terminal domain. TNPO3 gene encodes for TNPO3, which normally mediates the translocation to the nucleus of SR proteins, a family of splicing factors and other proteins related to RNA metabolism. Recently a relationship among TNPO3 mutation and alteration in myogenic pathways has been suggested. The goal of this work was to investigate the pathogenetic mechanism of LGMD D2 creating a cell model of disease in which would be



If staining for TNPO3 (red) and SRSF1 (green) during myogenesis after cell transfection with WT TNPO3 or MUT TNPO3.
A and B undifferentiated cells, C and D cells at middle differentiation.

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possible to study the role of TNPO3 in the myogenic process and in possible muscle-specific molecular pathways. Murine C2C12 myoblasts were transfected with a plasmid carring respectively the wild type (WT) or the mutated (MUT) sequence of TNPO3. We monitored the gene and protein expression profiles of TNPO3, of myogenic regulatory factors (MRFs), myomiRNA and muscle-specific proteins. Preliminary data suggest morphological and expression changes of genes and proteins involved in myogenic differentiation in comparison to the C2C12 control line. The approach used is a first step to understand the role of TNPO3 in muscle physiology and in the pathogenetic mechanism underlying LGMD D2 which is still unknown.

Key Words: LGMD D2; TNPO3; myogenesis; myogenic regulatory factors: myomiRNA.

References

1. Torella A, Fanin M, Mutarelli M, et al. Next-generation sequencing identifies transportin 3 as the causative gene for LGMD1F. PLoS One. 2013;8(5):e63536. Published 2013 May 7. doi:10.1371/journal.pone.0063536.
2. Costa R, Rodia MT, Vianello S, et al. Transportin 3 (TNPO3) and related proteins in limb girdle muscular dystrophy D2 muscle biopsies: A morphological study and pathogenetic hypothesis. Neuromuscul Disord. 2020;30(8):685-692. doi:10.1016/j.nmd.2020.05.006.
3. Costa R, Rodia MT, Zini N, et al. Morphological study of TNPO3 and SRSF1 interaction during myogenesis by combining confocal, structured illumination and electron microscopy analysis [published online ahead of print, 2021 Jan 15]. Mol Cell Biochem. 2021;10.1007/s11010-020-04023-y. doi:10.1007/s11010-020-04023-y.
4. Costa R, Rodia MT, Pacilio S, Angelini C, Cenacchi G. LGMD D2 TNPO3-Related: From Clinical Spectrum to Pathogenetic Mechanism. Front Neurol. 2022 Mar 4;13:840683. doi: 10.3389/fneur.2022.840683.
5. Pegoraro V, Angelini C. Circulating miR-206 as a Biomarker for Patients Affected by Severe Limb Girdle Muscle Dystrophies. Genes (Basel). 2021 Jan 12;12(1):85. doi: 10.3390/genes12010085.

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N-glycosylation inhibition impairs C2C12 and L6 myoblast differentiation and IGF-1 signalling

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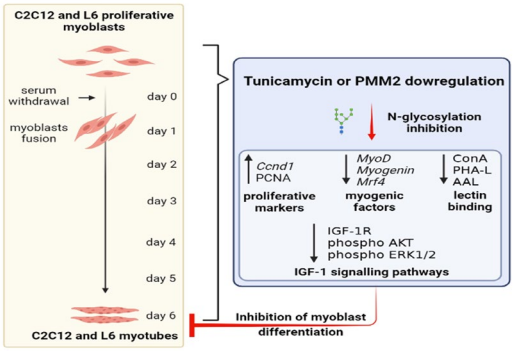
Several muscular diseases are associated with aberrant protein glycosylation, suggesting essential glycan-mediated functions in myogenesis and muscle development (1). However, the role played by protein N-glycosylation in the process of muscle differentiation remains poorly characterized. Here, we used C2C12 and L6 muscle cell cultures to investigate the effects of pharmacological inhibition of N-glycosylation by Tunicamycin (TUN) on myoblast differentiation.

Non-toxic doses of TUN (0.01µg/ml) inhibited C2C12 and L6 myoblast fusion and disrupted the coordinated temporal expression of myogenic regulator genes Ccnd1, MyoD, Myogenin and Mrf4. C2C12 control myotubes also showed an increase lectin binding (ConA; PHA-L and AAL) compared to myoblasts, while lectin reactivities decreased in TUN-treated myotubes indicating a N-glycosylation deficiency. Intrestingly, similar resulst were obtained by genetic knockdown of phosphomannomutase 2 (PMM2) gene in C2C12 cells, which encode an enzyme essential for catalysing an early step of the N-glycosylation pathway (2). Finally, TUN treatment decreased the IGF-1R level and markedly attenuated the IGF-1-induced ERK-1/2 and Akt phosphorylation (3). These results suggest that impaired myoblast differentiation could be a key factor in the pathophysiology of muscle-related manifestations commonly found in congenital disorders of N-



The pharmacological inhibition of N-glycosylation by Tunicamycin or by genetic knockdown of PMM2 gene inhibited C2C12 and L6 myoblast differentiation, disrupted the coordinated temporal expression of myogenic regulatory genes, decreased lectin binding, IGF-1R expression and signalling pathway.

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glycosylation. Our data form a valuable resource to further understand the glycobiology of myogenesis and will aid to explain the association between abnormal N-glycosylation and defects in muscle development and regeneration commonly found in individuals with Congenital disorders of glycosylation (CDG), such as PMM2-CDG, and other disease associated with protein hypo-Nglycosylation.

Acronyms

PMM2, Phosphomannomutase 2; Ccnd1, Cyclin D1; PCNA, Proliferating Cell Nuclear Antigen; MyoD, Myogenic differentiation 1; Mrf4, Myogenic Factor 6; Con A, Concanavalin A; PHA-L, Phaseolus vulgaris leucoagglutinin; AAL, Aleuria Aurantia (AAL); IGF-1R, Insulin-like growth factor-1 receptor; AKT, Serine/threonine protein kinase B; ERK1/2 Extracellular signal-regulated kinase 1/2.

Key Words: Myoblast differentiation; N-glycosylation; IGF-1 pathway; PMM2; Congenital Disorders of Glycosylation.

References

1. Blazev R, Ashwood C, Abrahams JL, Chung LH, Francis D, Yang P, Watt KI, Qian H, Quaife-Ryan GA, Hudson JE, Gregorevic P, Thaysen-Andersen M, Parker BL. Integrated Glycoproteomics Identifies a Role of N-Glycosylation and Galectin-1 on Myogenesis and Muscle Development. Mol Cell Proteomics. 2021;20:100030. doi: 10.1074/mcp.RA120.002166. Epub 2020 Dec 19. PMID: 33583770; PMCID: PMC8724610.
2. Freeze HH, Jaeken J, Matthijs G. CDG or not CDG. J Inherit Metab Dis. 2022 May;45(3):383-385. doi: 10.1002/jimd.12498. Epub 2022 Apr 1. PMID: 35338706; PMCID: PMC9121739.
3. Di Patria L, Annibalini G, Morrone A, Ferri L, Saltarelli R, Galluzzi L, Diotallevi A, Bocconcelli M, Donati MA, Barone R, Guerrini R, Jaeken J, Stocchi V, Barbieri E. Defective IGF-1 prohormone N-glycosylation and reduced IGF-1 receptor signaling activation in congenital disorders of glycosylation. Cell Mol Life Sci. 2022 Feb 24;79(3):150. doi: 10.1007/s00018-022-04180-x. PMID: 35211808; PMCID: PMC8873121.

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Clinical and genetic characterization of Neutral lipid storage disease with myopathy (NLSDM)

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Neutral lipid storage disease with myopathy (NLSD-M) is an autosomal recessive muscle disorder characterized by triglyceride-containing cytoplasmic droplets in leukocytes and muscle tissue. It presents with adult onset slowly progressive proximal muscle weakness often associated with hypertrophic cardiomyopathy. Here, we report a 42-year-old patient who presented progressive proximal upper limb weakness since age 38. Clinical examination showed asymmetrical (right> left) proximal upper limb weakness and muscle hypotrophy, mild weakness of both orbicularis oculi muscles and difficulty in walking on heels. Diffuse accumulation of lipid droplets in muscle cells was detected on muscle biopsy and Jordan anomaly, a well-known NLSD marker, was revealed by peripheral blood smear. Genetic analysis displayed a novel homozygote deletion in the PNPLA2 gene (exon2: c [45_47de]) causing the in frame p.[Gly16Del]. Both unaffected parents harbored the heterozygote deletion. Upper-limb muscle MRI showed atrophy of the supraspinatus and infraspinatus muscles, especially on the right side. Cardiac focal inferolateral intramural fibrosis was noted by MRI as a possible manifestation of lipid accumulation. However, no cardiac involvement was clinically detected. Our study confirms that 1) distal muscle involvement can be a feature of NLSD-M, 2) in Italian patients cardiac involvement is usually mild, differently from Far East subjects in which it is frequent and often leads to heart transplantation, 3) infraspinatus muscle is one of the most radiologically affected muscles and 4) Italian families usually harbor private mutations. Moreover, our patient presents with orbicularis oculi muscle weakness, therefore indicating that facial muscles can also be involved and confirming clinical heterogeneity of this disease.

Key Words: Skeletal muscle weakness; lipid storage myopathy; NLSD-M.

References

1. Pennisi EM, Arca M, Bertini E, Bruno C, Cassandrini D, D'amico A, Garibaldi M, Gragnani F, Maggi L, Massa R, Missaglia S, Morandi L, Musumeci O, Pegoraro E, Rastelli E, Santorelli FM, Tasca E, Tavian D, Toscano A, Angelini C; Italian NLSD Group. Neutral Lipid Storage Diseases: clinical/genetic features and natural history in a large cohort of Italian patients. Orphanet J Rare Dis. 2017 May 12;12(1):90. doi: 10.1186/s13023-017-0646-9. PMID: 28499397; PMCID: PMC5427600.

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Estrogens recover muscle regeneration impaired by the pathogenic gene, DUX4, in orthotopic human xenograft

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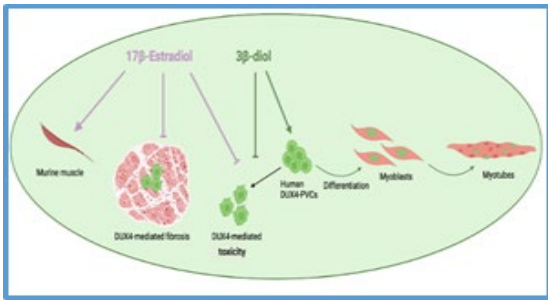
Facioscapulohumeral dystrophy (FSHD) is an autosomal dominant muscular dystrophy and one of the more frequent hereditary myopathy. The pathology shows a wide range of clinical signs, with modifying factors contributing to this variability. Among these factors, the beneficial activity of estrogen hormones is still controversial. We investigated the effect of the estrogens 17β-estradiol (E2) and the 5α-dihydrotestosterone-derived 3β-androstenediol (3β-diol) on muscle regeneration. To recapitulate human cell hormone sensitivity, we exploited a humanized heterokaryon FSHD mouse model, constituted by engrafting of human primary muscle mesenchymal stroma cells with perivascular cells (PVCs)-like phenotype in surgery-treated murine muscle. Lentiviral expression of the pathogenic FSHD gene, DUX4, in these cells impaired muscle structural and functional recovery. Notably, both hormones counteracted DUX4 activity and rescued structural and functional muscle performance impaired by DUX4 expression. Interestingly, E2 and 3β-diol act differently on muscle recovery by reducing muscle fibrosis and improving muscle differentiation, respectively. These results demonstrate that estrogens recover murine muscle regeneration reduced by DUX4 expression and support the hypothesis of their beneficial activity on human FSHD muscle.



Model of E2 and 3β-diol activity on murine muscle implanted with human DUX4-expressing PVCs

Key Words: DUX4/ Estrogen/ FSHD/ Muscle regeneration/ muscle mesenchymal stroma cells (MMSC)

References:

1. Teveroni E, Pellegrino M, Saccon S, Calandra P, Cascino I, Farioli-Vecchioli S, Puma A, Garibaldi M, Morosetti R, Tasca G, Ricci E, Trevisan CP, Galluzzi G, Pontecorvi A, Crescenzi M, Deidda G, Moretti F. Estrogens enhance myoblast differentiation in facioscapulohumeral muscular dystrophy by antagonizing DUX4 activity. J. Clin. Invest. 2017; 127:1531-1545, doi: 10.1172/JCI89401, PMID: 28263188.
2. Mul K, Horlings CGC, Voermans NC, Schreuder THA, van Engelen BGM. Lifetime endogenous estrogen exposure and disease severity in female patients with facioscapulohumeral muscular dystrophy. Neuromuscul Disord. 2018 Jun;28(6):508-511. doi: 10.1016/j.nmd.2018.02.012. Epub 2018 Mar 8. PMID: 29655530.
3. Zatz M, Marie SK, Cerqueira A, Vainzof M, Pavanello RC, Passos-Bueno MR. The facioscapulohumeral muscular dystrophy (FSHD1) gene affects males more severely and more frequently than females. Am J Med Genet. 1998 May 1;77(2):155-61. PMID: 9605290.
4. Ricci E, Galluzzi G, Deidda G, Cacurri S, Colantoni L, Merico B, Piazzo N, Servidei S, Vigneti E, Pasceri V, Silvestri G, Mirabella M, Mangiola F, Tonali P, Felicetti L. Progress in the molecular diagnosis of facioscapulohumeral muscular dystrophy and correlation between the number of KpnI repeats at the 4q35 locus and clinical phenotype. Ann Neurol. 1999 Jun;45(6):751-7. doi: 10.1002/1531-8249(199906)45:6<751::aid-ana9>3.0.co;2-m. PMID: 10360767.

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Perturbations of cholesterol metabolism in the dystrophic muscle in DMD

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Duchenne muscular dystrophy (DMD), an X-linked progressive muscular dystrophy, is characterized by muscle wasting, fibrosis, fat accumulation, loss of motor functions and cardio-respiratory failure. DMD is caused by an absent or a dysfunctional dystrophin. Dystrophin is thought to stabilize the sarcolemma, with suggestions for additional biochemical functions. Incomplete understanding of dystrophin's functions is a barrier for the development of improved therapeutic approaches. Previously, we profiled miRNA in the plasma of DMD patients and found high level of miRNA dysregulation (Amor et al. 2021), which predicted mitochondrial dysfunction (Sanson et al. 2020; Vu Hong et al. 2022) and perturbations of cholesterol metabolism (Amor et al. 2021; Israeli et al. 2022).

The goal of the present study is the characterization of lipid metabolism perturbations in the dystrophic muscle, with the prospect of development of improved therapy (Bourg et al. 2022). Our preliminary data show that cholesterol accumulates in the endolysosomal system in the dystrophic muscle of the mdx mouse. This accumulation may affect intracellular trafficking. We are also developing an in vitro screening system for the identification of compounds to accelerate cholesterol removal from the endolysosomal system. A progress in the understanding of the partipation of the endolysosomal system in DMD pathophysiology may offer new therapeutic perspective in muscular dystrophy.

Key Words: Duchenne Muscular Dystrophy; cholesterol; lysosome; combined therapy; miRNA.

References

1. Amor F, Vu Hong A, Corre G, Sanson M, Suel L, Blaie S, Servais L, Voit T, Richard I, Israeli D, et al. 2021. Cholesterol metabolism is a potential therapeutic target in Duchenne muscular dystrophy. J Cachexia Sarcopenia Muscle 12: 677–693. https://onlinelibrary.wiley.com/doi/10.1002/jcsm.12708.
2. Bourg N, Hong AV, Lostal W, Jaber A, Guerchet N, Tanniou G, Bordier F, Bertil-Froidevaux E, Georger C, Daniele N, et al. 2022. Co-Administration of Simvastatin Does Not Potentiate the Benefit of Gene Therapy in the mdx Mouse Model for Duchenne Muscular Dystrophy. Int J Mol Sci 2022, Vol 23, Page 2016 23: 2016. https://www.mdpi.com/1422-0067/23/4/2016..
3. Israeli D, Vu Hong A, Corre G, Miagoux Q, Richard I. 2022. Deciphering the Molecular Mechanism of Incurable Muscle Disease by a Novel Method for the Interpretation of miRNA Dysregulation. Non-coding RNA 8: 48. https://pubmed-ncbi-nlm-nih-gov.proxy.insermbiblio.inist.fr/35893231/
4. Sanson M, Hog Vu A, Massourides E, Bourg N, Suel L, Amor F, Corre G, Bénit P, Barthelemy I, Blot S, et al. 2020. miR-379 links glucocorticoid treatment with mitochondrial response in Duchenne muscular dystrophy. Sci Rep 10: 9139. http://www.nature.com/articles/s41598-020-66016-7.
5. Vu Hong A, Bourg N, Sanatine P, Poupiot J, Charton K, Gicquel E, Massourides E, Spinazzi M, Richard I, Israeli D. 2022. Dlk1-Dio3 cluster miRNAs regulate mitochondrial functions in the dystrophic muscle in Duchenne muscular dystrophy. Life Sci alliance 6: e202201506. https://pubmed.ncbi.nlm.nih.gov/36265896/

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Modulation of vesicles' secretion by EPS in an in vitro muscle model

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Skeletal muscle (SkM) has emerged as an important secretory organ releasing myokines and, as demonstrated in recent literature, also extracellular vesicles (EVs) during aerobic exercise, which contributes mainly to exercise adaptations in an autocrine, paracrine or endocrine manner.[1] There is a substantial interest in how acute and chronic exercise can promote EV release and its role in mediating the systemic effects of skeletal muscle activity. Nevertheless, most previous studies about EV secretion in acute and chronic exercise have focused on circulating EVs, which comprise a mixture of vesicles derived from circulating cells and other secretory tissues besides skeletal muscle. For these reasons,[2] the present study aims to clarify if a prolonged acute session of electric pulse stimulation (EPS) in differentiated C2C12 myocytes, reproducing a high-intensity exercise bout, can promote the secretion of both large and small extracellular vesicles. Subsequently, large and small EVs from contracting myocytes have been defined in particle concentration and vesicle marker content. To compare the impact of different muscle stress levels on EV secretion, we performed EPS sessions using two pulse width conditions, simulating non-damaging (1 ms) and damaging (10 ms) contraction conditions, respectively. Finally, the influence of stimulated muscle-derived EVs on SkM microenvironment has been investigated. Notably, we found that 10-ms EVs stimulated the expression of higher levels of IL-1beta mRNA than 1-ms EVs in RAW-264.7 macrophages. Altogether, these data suggest that EVs could have a role in regulating physical adaptations to high-intensity exercise.

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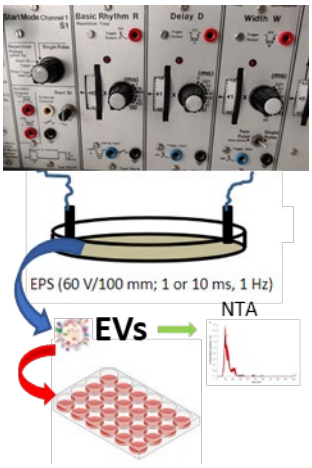

Schematic representation of the study workflow: electric pulse stimulation of C2C12 myotubes, EV isolation from conditioned medium, quantification of the secreted EVs, and study of biological activity of the EPS-induced EVs.

Key words: Extracellular vesicles; electric pulse stimulation (EPS); myokines; inflammation.

References:

1. Joshua P Nederveen, Geoffrey Warnier, Alessia Di Carlo, Mats I Nilsson, Mark A Tarnopolsky Extracellular Vesicles and Exosomes: Insights From Exercise Science. Front Physiol . 2021 Feb 1;11:604274. doi: 10.3389/fphys.2020.604274
2. Martin Whitham, Benjamin L Parker, Martin Friedrichsen, Janne R Hingst, Marit Hjorth, William E Hughes, Casey L Egan, Lena Cron, Kevin I Watt, Rhiannon P Kuchel, Navind Jayasooriah, Emma Estevez, Tim Petzold, Catherine M Suter, Paul Gregorevic, Bente Kiens, Erik A Richter, David E James, Jørgen F P Wojtaszewski, Mark A Febbraio. Extracellular Vesicles Provide a Means for Tissue Crosstalk during Exercise. Cell Metab 2018 Jan 9;27(1):237-251.e4. doi: 10.1016/j.cmet.2017.12.001.

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2023Pdm3 March30 - Abstract 46

Activation of muscle-specific Akt1 reverts cancer-dependent muscle wasting and reduces tumor mass

Alessia Geremia et al., University of Padua, Italy

On-site presentation of unpublished results. The authors denied also Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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FRIDAY March 31, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:00 AM SESSION VII:

Senescence&Rejuvenation

Nathan K. LeBrasseur, Christiaan Leeuwenburgh, Chairs

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2023Pdm3 March 30 - Abstract 47

LECTURE

Skeletal muscle electron microscopy, still a mandatory approach in muscle rejuvenation research

Simona Boncompagni, *University of Chieti, Italy*

On-site presentation of unpublished results. The authors denied also Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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2023Pdm3 March 31 - Abstract 48

Cellular senescence as a driver of skeletal muscle aging

Nathan K. LeBrasseur

Professor, Department of Physical Medicine and Rehabilitation; Director, Robert and Arlene Kogod Center on Aging, Mayo Clinic, Rochester, MN, USA
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Senescence is a cell fate in response to various stressors that has been implicated in the pathogenesis of multiple aging-related conditions. Despite profound age-associated changes in skeletal muscle, the extent to which senescence may impact its constituent cells has not been methodically examined. This lecture will highlight our recent work (Zhang, Nature Aging, 2022) using single cell and bulk RNA-sequencing and complementary imaging methods on skeletal muscle of young and old mice that demonstrated that a subpopulation of old fibroadipogenic progenitors (FAPs) highly expresses p16Ink4a in concert with multiple senescence-related genes and, in parallel, exhibits DNA damage and chromatin reorganization. It will also review our analysis of isolated myofibers, as we observed a senescence phenotype within a subset of old cells, governed instead by p21cip1. New unpublished and published (e.g., Englund, Molecular Metabolism, 2023) insights into the contributions of senescent FAPs and p21-expressing myofibers to skeletal muscle aging will be shared, as will our efforts to discover senotherapeutic interventions to target these specific cell populations. Collectively, this

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lecture will provide compelling evidence for cellular senescence as a hallmark and potentially tractable mediator of skeletal muscle aging.

Key words: Cellular senescence; skeletal muscle; aging.

References

1. Zhang X, Habiballa L, Aversa Z, Ng YE, Sakamoto AE, Englund DA, Pearsall VM, White TA, Robinson MM, Rivas DA, Dasari S, Hruby AJ, Lagnado AB, Jachim SK, Granic A, Sayer AA, Jurk D, Lanza IR, Khosla S, Fielding RA, Nair KS, Schafer MJ, Passos JF, LeBrasseur NK. Characterization of cellular senescence in aging skeletal muscle. Nat Aging. 2022 Jul;2(7):601-615. doi: 10.1038/s43587-022-00250-8. Epub 2022 Jul 15. PubMed PMID: 36147777; PubMed Central PMCID: PMC9491365.
2. Englund DA, Jolliffe A, Aversa Z, Zhang X, Sturmlechner I, Sakamoto AE, Zeidler JD, Warner GM, McNinch C, White TA, Chini EN, Baker DJ, van Deursen JM, LeBrasseur NK. p21 induces a senescence program and skeletal muscle dysfunction. Mol Metab. 2023 Jan;67:101652. doi: 10.1016/j.molmet.2022.101652. Epub 2022 Dec 9. PMID: 36509362; PMCID: PMC9800630.
3. Fielding RA, Atkinson EJ, Aversa Z, White TA, Heeren AA, Achenbach SJ, Mielke MM, Cummings SR, Pahor M, Leeuwenburgh C, LeBrasseur NK. Associations between biomarkers of cellular senescence and physical function in humans: observations from the lifestyle interventions for elders (LIFE) study. Geroscience. 2022 Dec;44(6):2757-2770. doi: 10.1007/s11357-022-00685-2. Epub 2022 Nov 11. PMID: 36367600; PMCID: PMC9768064

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2023Pdm3 March 31 - Abstract 49

Impact of age and sex on lysosomes and mitophagy during muscle use and disuse

David A. Hood

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Mitochondria are dynamic organelles that are constantly being synthesized (biogenesis) and recycled. This "turnover" promotes the maintenance of an optimally functioning pool of mitochondria.[1] While considerable work has documented the processes of organelle biogenesis, less is understood about the recycling of mitochondria, termed mitophagy. In particular, mitochondrial content is diminished with age, suggesting that biogenesis could be impaired, and/or that mitophagy is accelerated.[2] Our work has shown that mitophagy is accelerated up to the point of the lysosome, the organelle responsible for the terminal degradation of mitochondria. However, evidence exists for lysosomal dysfunction in aging muscle. In addition, there has been very little reported on possible biological sex differences in lysosomal content or function in muscle. Our recent research illustrates that lysosomal content is elevated in muscle of female mice, and that this persists and is exaggerated with age, suggesting that females have an enhanced capacity to clear dysfunctional organelles.[3,4] This is evidenced by a higher mitophagy flux in female muscle. Remarkably, this is unaffected by the loss of the transcription factor TFE3, which is purported to be an important regulator of lysosomal gene expression.[4] However, when the expression of both TFE3 and its family member TFEB is reduced, mitophagy flux is attenuated and lysosomal function is impaired.[5] This seminar 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 behavioural therapeutic modality to reverse impairments in the mitophagy pathway that arise with age and muscle disuse.

Key Words: Mitochondria; muscle adaptations; biological sex differences; lysosomal biogenesis; aging.

References

1. Hood DA, Memme JM, Oliveira AN, Triolo M. Maintenance of Skeletal Muscle Mitochondria in Health, Exercise, and Aging. Annu Rev Physiol. 2019 Feb 10;81:19-41. doi: 10.1146/annurev-physiol-020518-114310. Epub 2018 Sep 14. PMID: 30216742.
2. Carter HN, Chen CC, Hood DA. Mitochondria, muscle health, and exercise with advancing age. Physiology (Bethesda). 2015 May;30(3):208-23. doi: 10.1152/physiol.00039.2014. PMID: 25933821.
3. Triolo M, Oliveira AN, Kumari R, Hood DA. The influence of age, sex, and exercise on autophagy, mitophagy, and lysosome biogenesis in skeletal muscle. Skelet Muscle. 2022 Jun 11;12(1):13. doi: 10.1186/s13395-022-00296-7. PMID: 35690879; PMCID: PMC9188089.
4. Oliveira A.N., J.M. Memme, J. Wong, D.A. Hood. Dimorphic effect of TFE3 in determining mitochondrial and lysosomal content in muscle following denervation. J. Cachexia, Sarcopenia Muscle (in revision, 2023).
5. Oliveira A.N., Y. Tamura, J.M. Memme, D.A. Hood. Role of TFEB and TFE3 in mediating lysosomal and mitochondrial adaptations to contractile activity in muscle cells. Autophagy Reports (in revision, 2023).

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2023Pdm3 March 31 - Abstract 50

Inflammation, mitochondrial dysfunction senescense in skeletal muscle with aging and in peripheral artery disease

Sunil K Saini (1) and Christiaan Leeuwenburgh (2)

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Aging and diseases such as cancer, peripheral artery disease (PAD) are associated with skeletal muscle inflammation, oxidative stress, increased senescense, altered muscle metabolism; and mitochondrial dysfunction [1-3]. Many of the biological changes in calf skeletal muscle have been associated with functional impairment and mobility loss [2]. We will discuss several recent studies which show that specific genes, miRNA, and biological pathways in skeletal muscle are tightly associated with functional performance in aging and clinical progression of PAD [3-6]. We found damage in the genes encoding polypeptides for the electron transport chain (ETC) in skeletal muscle was associated with walking performance in people with and without PAD [5]. We also found marked changes in cellular pathways in subjects with peripheral artery disease progression in specific genes and pathways involve in cellular senescense, inflammation and muscle contraction. Identifying what biological pathways are specifically associated with impaired skeletal muscle function may lead to new effective strategies that can reverse muscle dysfunction and in turn, can improve mobility.
Key Words: Aging; peripheral artery disease; inflammation; senescense; muscle; miRNA; mitochondria.

References

1. Zhang D et al, Analysis of Biological Aging and Risks of All-Cause and Cardiovascular Disease-Specific Death in Cancer Survivors. JAMA Netw Open. 2022. PMID: 35731518
2. McDermott, M.M., et al., Skeletal Muscle Pathology in Peripheral Artery Disease: A Brief Review. Arterioscler Thromb Vasc Biol, 2020. 40(11): p. 2577-2585.
3. Picca A et al. Altered Expression of Mitoferrin and Frataxin, Larger Labile Iron Pool and Greater Mitochondrial DNA Damage in the Skeletal Muscle of Older Adults. 2022, Cells. PMID: 33276460
4. Saini SK et al. Dysregulated Genes, MicroRNAs, Biological Pathways, and Gastrocnemius Muscle Fiber Types Associated With Progression of Peripheral Artery Disease: A Preliminary Analysis. 2022, JAHA.PMID: 36300658
5. Saini SK et al, Mitochondrial DNA damage in calf skeletal muscle and walking performance in people with peripheral artery disease. Free Radic Biol Med. 2020, PMID: 32911084
6. Saini SK Time-Restricted Eating Regimen Differentially Affects Circulatory miRNA Expression in Older Overweight Adults. Nutrients. 2022 PMID: 35565812.

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2023Pdm3 March 31 - Abstract 51

Nitrate supplementation promotes an anabolic response and attenuates neuromuscular alterations in 24-months old male mice

Maira Rossi (1), Lucrezia Zuccarelli (2), Lorenza Brocca (1), Cristiana Sazzi (1), Simone Porcelli (1), Bruno Grassi (2), Roberto Bottinelli (1,3,4), Maria Antonietta Pellegrino (1,3)

(1) Department of Molecular Medicine, University of Pavia; (2) Department of Medicine, University of Udine; (3) Interdepartmental Centre for Biology and Sport Medicine, University of Pavia; (4) National Neurological Institute C. Mondino Foundation, Pavia.
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Aging is associated with a progressive loss of muscle mass and strength, defined as sarcopenia. Neuromuscular junction (NMJ) deterioration plays a key role in age-related musculoskeletal impairment. Moreover, loss of nitric oxide synthase in skeletal muscle is associated with defects at NMJ,[1] and, together with a reduced age-related nitric oxide bioavailability,[2] is causative of muscle wasting[3] and harmed mitochondria.[4] Here we investigated the ability of chronic nitrate

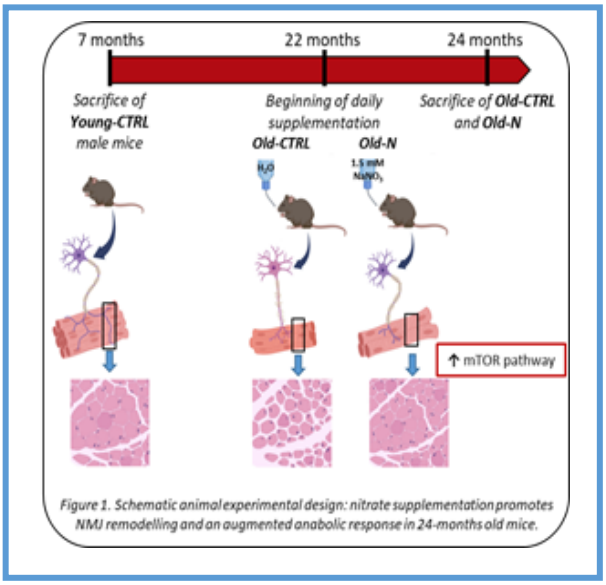

Figure 1. Schematic animal experimental design: nitrate supplementation promotes NMJ remodelling and an augmented anabolic response in 24-months old mice.

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supplementation to counteract neuromuscular alterations during aging. 22-months-old C57BL/6 male mice were assigned as follows: old controls (Old-CTRL) and old supplemented with 1.5 mM inorganic nitrate in drinking water for two months (Old-N). All mice were sacrificed at 24 months and skeletal muscles dissected for ex-vivo determinations. A cohort of young male mice (7 months) was also evaluated to quantify age-related changes.Compared to Old-CTRL, treated mice showed a positive remodelling of the NMJ morphology (evaluated through the confocal microscopy) and an improvement of fibers innervation status supported by a decreased postsynaptic fragmentation and a reduced number of NCAM-positive fibers, respectively. Moreover, Old-N mice showed an improvement in mitochondrial respiratory function (assessed through the High-Resolution Respirometry), despite no change in mitochondrial dynamics. Furthermore, nitrate treatment induced an anabolic response through higher activation of factors involved in protein synthesis (P70S6K and S6), consistent with higher Gastrocnemius fibers cross-sectional area found in treated animals in comparison to Old-CTRL. The present data indicate that nitrate supplementation has the potential to counteract age-related neuromuscular deterioration.

Key Words: Neuromuscular junction; aging; nitrate supplementation; muscle wasting.

References

1. Adams ME, Anderson KN, Froehner SC. The alpha-syntrophin PH and PDZ domains scaffold acetylcholine receptors, utrophin, and neuronal nitric oxide synthase at the neuromuscular junction. J Neurosci. 2010 Aug 18;30(33):11004-10. doi: 10.1523/JNEUROSCI.1930-10.2010
2. Di Massimo C, Scarpelli P, Di Lorenzo N, Caimi G, di Orio F, Ciancarelli MG. Impaired plasma nitric oxide availability and extracellular superoxide dismutase activity in healthy humans with advancing age. Life Sci. 2006 Feb 9;78(11):1163-7. doi: 10.1016/j.lfs.2005.06.037. Epub 2005 Oct 7
3. Samengo G, Avik A, Fedor B, Whittaker D, Myung KH, Wehling-Henricks M, Tidball JG. Age-related loss of nitric oxide synthase in skeletal muscle causes reductions in calpain S-nitrosylation that increase myofibril degradation and sarcopenia. Aging Cell. 2012 Dec;11(6):1036-45. doi: 10.1111/acel.12003. Epub 2012 Oct 4
4. Nisoli E, Clementi E, Paolucci C, Cozzi V, Tonello C, Sciorati C, Bracale R, Valerio A, Francolini M, Moncada S, Carruba MO. Mitochondrial biogenesis in mammals: the role of endogenous nitric oxide. Science. 2003 Feb 7;299(5608):896-9. doi: 10.1126/science.1079368

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Insulin resistance modification during bed rest: relationship with circulating and muscular MMP and TIMPs

Nicola Fiotti (1), Filippo Giorgio di Girolamo (1), Emiliana Giacomello (1), Rado Pisot (2), Gianni Biolo (1)

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Physical inactivity or bed rest increase insulin resistance and predispose to diabetes. Matrix MetalloProteinases (MMPs), a class of extra and intracellular endoproteases, and their inhibitors, Tissue Inhibitors of MmPs (TIMPs) play a role in muscle remodeling but limited evidence exists on their relationship with metabolic changes following muscular inactivity.[1-3] We looked for an association between modifications of muscle and plasma MMPs and TIMPs with changes in glucose tolerance during experimental microgravity. In ten young healthy males (18-33 yr) undergoing 10 days of horizontal bed rest, muscle expression and plasma levels of MMP-1, -2, -8, -9 and -13 and of their inhibitors TIMP-1 and TIMP-2 have been compared with changes in fasting glucose, insulin and HOMA index. At baseline, cytoplasmic and pericellular MMP13 positively correlated with circulating glucose, while MMP-8 and -9 plasma levels positively correlate with Homa index and insulin levels (P<.008). These MMP13 and MMP8 correlations with the glucose tolerance test were lost by day 5 and that of MMP9 by the end (day 10) of bed rest. During bed rest, changes (i.e. final/initial) in cytoplasm TIMP1 expression negatively correlated with those of HOMA

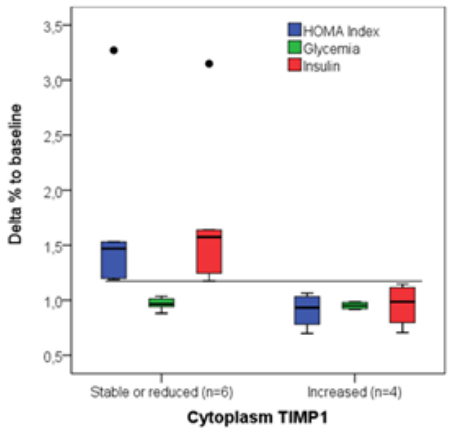

Figure. Changes in insulin resistance indicators (expressed as ratio final/baseline) according to muscle cytoplasm TIMP1 pattern.

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index (-.721, P=0.019) and insulin (-.697, P= 0.025). In detail, Homa index and insulin increased substantially (>15% from baseline) in 6 subjects and remained stable in 4 (insulin: +57 Vs -1.5 and HOMA-IR: + 47% Vs -7%, respectively, P=0.01). The six subjects with worsening of glucose tolerance also had a stable or reduced cytoplasm TIMP1 (-27 %, range -80-0%) during bed rest, while it remained increased in the other 4 (+37% range 7-78%), as in Figure. Homa index and Insulin reached and AUC of 1.0 (p=.011) on ROC curve when compared according to TIMP1 pattern (stabe or reduced Vs increased). In conclusions, short term glucose levels regulation seems associated with cellular and pericellular MMP-13, and MMP-8 and -9 at baseline. Worsening of glucose tolerance during bed rest is observed in subjects with lowering of TIMP-1 cytoplasm muscle content during physical inactivity.

Key Words: Insulin resistance; bed rest; TIMP-1, immunofluorescence, Physical inactivity.

References:

1. Kologrivova IV et al. System of matrix metalloproteinases and cytokine secretion in type 2 diabetes mellitus and impaired carbohydrate tolerance associated with arterial hypertension. Bull Exp Biol Med. 2014 Mar;156(5):635-8.
2. Kadoglou NP et al. Exercise ameliorates serum MMP-9 and TIMP-2 levels in patients with type 2 diabetes. Diabetes Metab. 2010 Apr;36(2):144-51.
3. Hopps E et al. Gelatinases and their tissue inhibitors in a group of subjects with metabolic syndrome. J Investig Med. 2013 Aug;61(6):978-83.

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FRIDAY March 31, 2023

ROOM B, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:30 AM Practical Course on functional analysis of the stomatognathic system

Claudia Dellavia, Riccardo Rosati, Chairs

For dentists who want to expand the analyses of the stomatognathic system developed at the Laboratory of Functional Anatomy of the Stomatognathic Apparatus (LAFAS) of the University of Milan, Italy

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2023Pdm3 March 31 - Abstract 53

Instrumental evaluations of the stomatognathic apparatus: static and dynamic tests.

Claudia Dellavia, Riccardo Rosati

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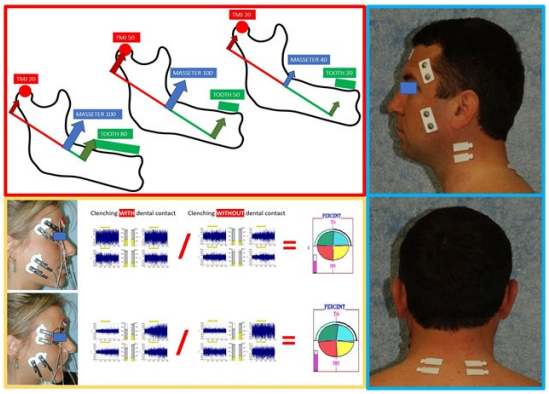

Biomechanical models of the jaw, combined with standardized sEMG procedures, help dentists understand oral and neck muscle physiology.

The stomatognathic apparatus constantly performs complex activities, such as deglutition, mastication, speech, suction. The muscles that move mandibula, tongue, hyoid, soft palate and lips generate mechanical forces dissipated by 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 non-invasive low-cost method usable in research and in dental clinical practice for the quantitative and qualitative analysis of head and neck muscles. sEMG does not directly assess the muscular fibers then, to remove (or reduce) technical and biological artefacts, a well-standardized protocol should be used. In addition, the crosstalk from different muscles, the instrumental noise, the thickness of the hypodermis, the position of the electrodes relative to the muscle fibers and other factors can influence the sEMG signal. Taking into consideration these technical features, a correct sEMG assessment should be performed only with a reproducible protocol, and with standardized⁄normalized potentials to remove most of biological and technical noises. sEMG analysis based on standardized indexes computation, allow to evaluate, in a reliable way, occlusal-induced proprioceptive mediated muscular recruitment. Combining sEMG standardized indexes with biomechanical concepts, occlusal devices and prosthesis adapting procedures could be clinically performed in order to re-establish the physiological muscular coordination or to reduce the muscular adaption to the new occlusal conditions.

Key Words: sEMG masticatory muscle; dental occlusion; dental rehabilitation; swallowing, neck muscles.

References

1. Dong Y, Wang XM, Wang MQ, Widmalm SE. Asymmetric muscle function in patients with developmental mandibular asymmetry. J Oral Rehabil. 2008;35(1):27-36.
2. Ferrario VF, Tartaglia GM, Luraghi FE, Sforza C. The use of surface electromyography as a tool in

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differentiating temporomandibular disorders from neck disorders. Man Ther. 2007;12(4):372-379.
3. Armijo–Olivo S, Magee DJ. Electromyographic activity of the masticatory and cervical muscles during resisted jaw opening movement. J Oral Rehabil. 2007;34(3):184-194.
4. Botelho AL, Gentil FH, Sforza C, da Silva MA. Standardization of the electromyographic signal through the maximum isometric voluntary contraction. Cranio. 2011;29(1):23-31.
5. Ferrario VF, Sforza C. Biomechanical model of the human mandible in unilateral clench: distribution of temporomandibular joint reaction forces between working and balancing sides. J Prosthet Dent. 1994;72(2):169-176.

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FRIDAY March 31, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

10:30 AM SESSION VIII: Muscle Fascia, biology and pathology

Carla Stecco, Alessandro Martini, Chairs

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2023Pdm3 March 31 - Abstract 54

Fascia and aging

Carla Stecco, Chenglei Fan, Carmelo Pirri, Caterina Fede, De Caro Raffaele

Department of Neuroscience, University of Padua, Italy
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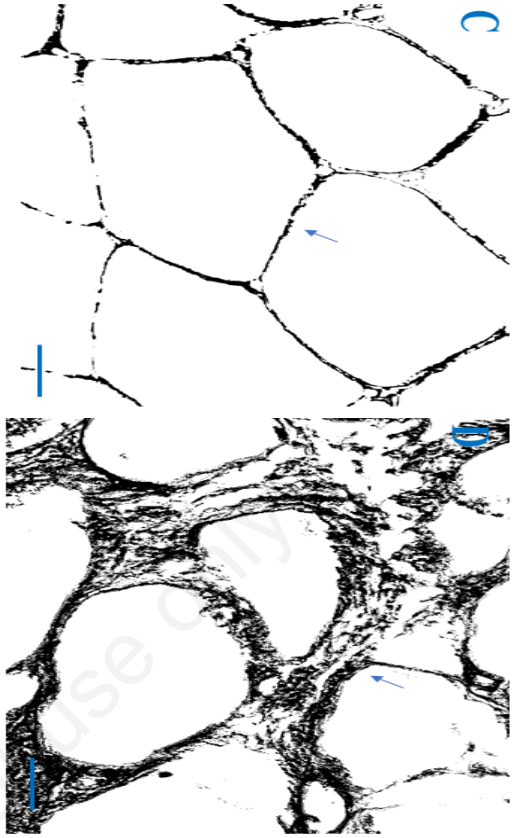
Extracellular matrix (ECM) of intramuscular connective tissue (IMCT) play critical role not only in maintaining integrity of muscle, but also in providing mechanical properties and local signals to modulate muscle cell fusion and regeneration. The aim of this study was to investigate whether the contents of ECM of IMCT change with aging. Age-related changes of ECM in human quadriceps femoris were compared in 10 young men (37.5±9.0y), 12 elderly men (79.0±12.4y) patients with traumatic fracture (Studio 3027P/AO/13). Age-related ECM alterations in mice hindlimb were compared in 6-weeks puberty (group A); 8-months middle age (group B) and 2-years old (group C) C57BL/6J male mice. Hematoxylin Eosin, Picrosirius-red, the collagen type I (COLI), III (COLIII) antibody, and biotinylated hyaluronan binding protein (HABP) immunohistochemistry staining were used to evaluate the morphology, collagen content, COLI, COLIII and HA both in human and mice muscle cross-section. Alcian Blue, Weigert Van Gieson staining were used to evaluate the glycosaminoglycans and elastic fiber components in human male specimens. Age-related alterations of HA concentrations were evaluated both in human and mice specimens using Purple-Jelley HA assay. The collagen contents in IMCT were also significantly increased in mice with aging, above all due to an increase in COLI both in the human (P =0.001) and mice specimens, while there were no significantly differences in COLIII. In addition, the area percentage of elastic fibers in perimysium was significantly lower (P<0.01) in the elderly men group. The HA content was significantly decreased in the elderly men compare to the young men (P=0.04). In addition, the amount of HA in mouse hindlimb muscle was also significantly decreased with health aging. The accumulation of collagen content and decreased HA in ECM of IMCT, the decreased relative elastic fibers in perimysium may cause the IMCT stiffer and reduce its' adaptability, changing gliding of the IMCT and influence the function of muscle fibers. These alterations of ECM in IMCT properly can partly explain the peripheral mechanisms of the decline of age-related locomotor ability



Amount of collagen fibers in the endomysium of a young (top) and old (bottom) man.

Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

Key Words: Aging; intramuscular connective tissue; collagen; hyaluronan.
References

1. Fede C, Fan C, Pirri C, Petrelli L, Biz C, Porzionato A, Macchi V, De Caro R, Stecco C. The Effects of Aging on the Intramuscular Connective Tissue. Int J Mol Sci. 2022 Sep 21;23(19):11061. doi: 10.3390/ijms231911061.
2. Fan C, Pirri C, Fede C, Guidolin D, Biz C, Petrelli L, Porzionato A, Macchi V, De Caro R, Stecco C. Age-Related Alterations of Hyaluronan and Collagen in Extracellular Matrix of the Muscle Spindles. J Clin Med. 2021 Dec 24;11(1):86. doi: 10.3390/jcm11010086.
3. Gaudreault N, Benoît-Piau J, van Wingerden JP, Stecco C, Daigle F, Léonard G. An Investigation of the Association between Transversus Abdominis Myofascial Structure and Activation with Age in Healthy Adults using Ultrasound Imaging. Int J Sports Phys Ther. 2021 Aug 1;16(4):1093-1103. doi: 10.26603/001c.25168.
4. Pavan P, Monti E, Bondí M, Fan C, Stecco C, Narici M, Reggiani C, Marcucci L. Alterations of Extracellular Matrix Mechanical Properties Contribute to Age-Related Functional Impairment of Human Skeletal Muscles. Int J Mol Sci. 2020 Jun 2;21(11):3992. doi: 10.3390/ijms21113992.
5. Wilke J, Macchi V, De Caro R, Stecco C. Fascia thickness, aging and flexibility: is there an association? J Anat. 2019 Jan;234(1):43-49. doi: 10.1111/joa.12902. Epub 2018 Nov 11.

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2023Pdm3 March 31 - Abstract 55

***Alessandro Martini**, et al. University of Padua, Italy:*
Tensor Tympani and Stapedius: two unknown muscles

On-site presentation of unpublished results. The authors denied also Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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2023Pdm3 March 31 - Abstract 56

Ultrasound imaging and fasciae

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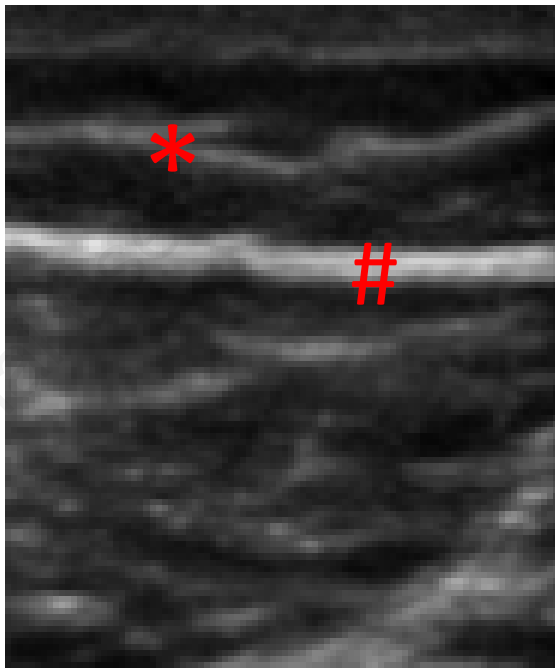
Ultrasound (US) imaging has assumed an important role in the soft tissue assessments. The fascia is actually one of those interesting structures, and its pathologic characteristics are worth discussing with regard to our daily practice. Fasciae are extensive connective tissues that envelope our muscles, nerves, organs, and viscera. Actually, many histologic and macroscopic studies have described the same fascial organization in all regions of the body, with few regional specializations. The knowledge about these fasciae can help the sonographer easily recognize them throughout the whole body—for a better orientation as well as prompt diagnosis. On US imaging the superficial fascia is a thin hyperchoic layer



Examples of US imaging of fasciae. *: superficial fascia; #: deep fascia.

in the subcutaneous tissue, whereas the deep/muscular fascia is a thick hyperchoic layer in closed relationship with the muscles. Some studies investigated the value of US examination of fasciae in different topographical regions. Varoius US parameters were evaluated in the last years, such as thickness and echogenicity. The latter two, in particular the thickness, showed a variability among the various topographical regions. Moreover, the reliability of US imaging for measuring these structures has also been assessed in various other studies, showing a good/optimal intra- and inter-rater reliability. US imaging is a reliable tool for assessing the fasciae, providing an excellent anatomical definition that accurately corresponds to histological findings.
Key Words: Ultrasound imaging; deep fascia; superficial fascia; thickness; echogenicity; reliability.

Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

References
1. Özçakar L, Kara M, Chang KV, Çarl AB, Akkaya N, Tok F, Chen WS, Wang TG, Tekin L, Ulaşl AM, Chen CP, Çapkn E, De Muynck M. Nineteen reasons why physiatrists should do musculoskeletal ultrasound: EURO-MUSCULUS/USPRM recommendations. Am J Phys Med Rehabil. 2015 Jun;94(6):e45-9. doi: 10.1097/PHM.0000000000000223.
2. Stecco C, Macchi V, Porzionato A, Duparc F, De Caro R. The fascia: the forgotten structure. Ital J Anat Embryol. 2011;116(3):127-38.
3. Pirri C, Stecco C, Fede C, Macchi V, Özçakar L. Ultrasound Imaging of the Fascial Layers: You See (Only) What You Know. J Ultrasound Med. 2020 Apr;39(4):827-828. doi: 10.1002/jum.15148. Epub 2019 Oct 23.
4. Pirri C, Guidolin D, Fede C, Macchi V, De Caro R, Stecco C. Ultrasound Imaging of Brachial and Antebrachial Fasciae. Diagnostics (Basel). 2021 Dec 2;11(12):2261. doi: 10.3390/diagnostics11122261.
5. Pirri C, Pirri N, Porzionato A, Boscolo-Berto R, De Caro R, Stecco C. Inter- and Intra-Rater Reliability of Ultrasound Measurements of Superficial and Deep Fasciae Thickness in Upper Limb. Diagnostics (Basel). 2022 Sep 9;12(9):2195. doi: 10.3390/diagnostics12092195.

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How sex hormones can affect the fasciae

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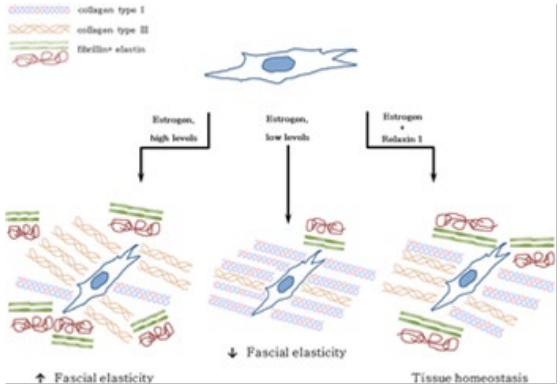
It is well established that the prevalence rate of musculoskeletal pain is significantly higher in women with respect to males, with an even greater onset of chronic conditions (Ceccarelli et al., 2021). It is recently reported that fascia can be a possible source of pain: if the connective tissue is altered, the behaviour of the fascial tissue and the underlying muscle may become compromised causing myofascial pain. Sex hormone disorders can dysregulate the fascial tissue: the comprehension of this mechanism is an important step for understanding gender differences in myofascial pain, helping clinicians to diagnose and treat patients (Fede et al., 2022). Sex hormone receptors are expressed by fascial fibroblasts, with a lower expression with the decrease in hormone levels in post-menopausal women (Fede et al., 2016). The cells of the fascia can moreover modulate the synthesis of extracellular matrix components depending on hormone levels: when β-estradiol levels are low, fascial tissue becomes enriched in collagen-I (from 5.2% of control sample to 8.4%), with a parallel decrease in collagen-III (from 2.4% to 1.5%) and elastic fibres (from 0.5% to 0.2%) (Fede et al., 2019). Consequently, the tissue becomes less elastic and more rigid, something that normally occurs during menopause. Conversely, when hormone levels are high, as they normally are during the ovulatory peak or during pregnancy, the opposite takes place: collagen-III rises to 6.8% during ovulation and 6.7% during pregnancy as does Fibrillin-1 (from 0.2% in menopause to 3.6% during pregnancy) while collagen-I falls to 1.9% (Fede et al., 2019). The result is softer, more elastic tissue. These results highlight how hormonal disorders in women can dysregulate the extracellular matrix synthesis (Figure), modifying the properties of tissue and evoking the sensitization of fascial nociceptors. Further studies on multifactorial effects of sex hormones on fasciae and pain mechanisms will permit to correlate any dysfunctions in hormonal levels linked to pathologies, ageing and period of the cycle, to the onset of myofascial pain, thus making it possible to find out a targeted gender therapy.



Scheme of fascial cell response and extracellular matrix rearrangement at different hormone levels (estrogen and relaxin-1) (from Fede et al., PLoS One. 2019;14(9):e0223195).

Key Words: Fascia; women chronic pain; sex hormones, β-estradiol.

References
1. Ceccarelli I, Bioletti L, Peparini S, Solomita E, Ricci C, Casini I, Miceli E, Aloisi AM. Estrogens and phytoestrogens in body functions. Neurosci Biobehav Rev. 2022;132:648-663. doi: 10.1016/j.neubiorev.2021.12.007.
2. Fede C, Pirri C, De Caro R, Stecco C. Myofascial pain in females and personalized care: The key role played by sex hormones. Eur J Pain. 2022;26(4):939-940. doi: 10.1002/ejp.1920.
3. Fede C, Albertin G, Petrelli L, Sfriso MM, Biz C, De Caro R, Stecco C. Hormone receptor expression in

human fascial tissue. Eur J Histochem. 2016;60(4):2710. doi: 10.4081/ejh.2016.2710.
4. Fede C, Pirri C, Fan C, Albertin G, Porzionato A, Macchi V, De Caro R, Stecco C. Sensitivity of the fasciae to sex hormone levels: Modulation of collagen-I, collagen-III and fibrillin production. PLoS One. 2019;14(9):e0223195

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Lymphatic vessels detection in subcutis and superficial fascia

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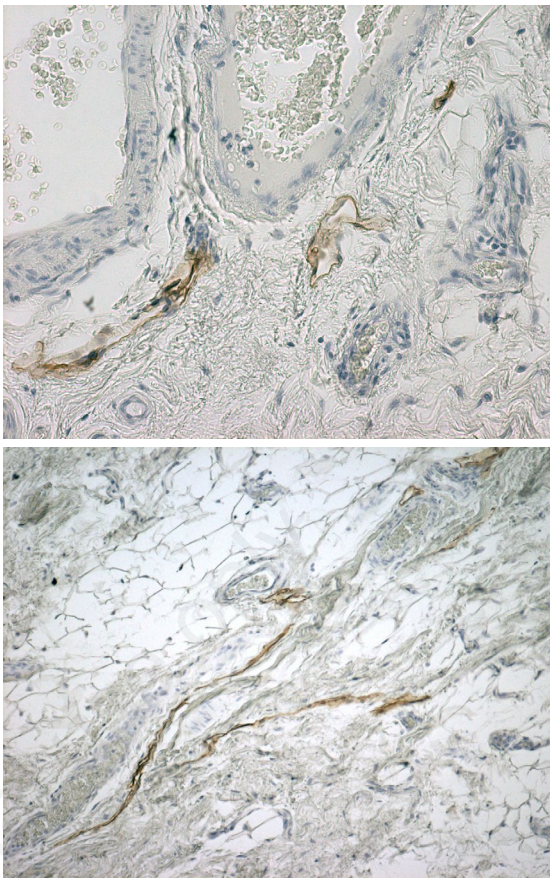
Lymphedema, defined as the abnormal accumulation of protein-rich fluid in soft tissues, results from the dysfunction of lymphatic system, an imbalance between lymph formation and its absorption into the initial lymphatics. The chronic accumulation of interstitial fluid leads adipose deposition, fibrosis, or persistent inflammation on subcutis (1). Today, lymphedema's therapies require a detailed understanding of the anatomy of subcutaneous lymphatic system (2), moreover, the exact localization of the collectors and their relationships with fascial layers have not been defined yet. The aim of this study was to investigate the distribution, density and organization of lymphatic vessels (LV) with reference to the layered conformation of the subcutaneous tissue, that consist in the superficial adipose tissue (SAT), deep adipose tissue (DAT) and superficial fascia (SF) (3, 4). With this purpose, the subcutaneous tissue of three adult voluntary patients was harvested during abdominoplastic surgery and stained with a specific marker for the endothelial cells of lymphatic vessels, the monoclonal antibody D2-40 (5). LV, present massively on the papillary dermis, run parallel to the skin surface and are incorporated in the loose connective tissue to form a lymphatic plexus. On SAT, only thin LV, with a mean diameter of 11.6±7.71 µm, were visible close to the fibrous septa (retinacula cutis that connects the dermis to the deeper layers). In the DAT, the LV follow above all the blood vessel, they are thicker with a mean diameter of 22.5±12.77 µm. The SF exhibits the highest density of



Immunohistochemistry with D2-40 antibody on superficial fascia.

LV, with a mean diameter of 19.5±5.77 µm, they show a path parallel to the surface, where intertwining each other form a characteristic plexus. This study has shown the different distribution of the lymphatic vessels in the various subcutaneous layers and the existence of a new lymphatic plexus within the superficial fascia, adding new information on the alterations involving the subcutaneous tissues and consequently opening up new perspectives for surgery and manual treatments.

Key Words: Lymphedema; fascial tissue; lymphatic vessels.

References

1. Mehrara BJ, Greene AK. Lymphedema and obesity: is there a link? Plast Reconstr Surg. 2014 Jul;134(1)154e-160e.
2. Savetsky IL, Torrisi JS, Cuzzone DA, Ghanta S, Albano NJ, Gardenier JC, Joseph WJ, Mehrara BJ. Obesity increases inflammation and impairs lymphatic function in a mouse model of lymphedema. Am J Physiol Heart Circ Physiol. 2014 Jul 15;307(2):H165-72.
3. Lancerotto L, Stecco C, Macchi V, Porzionato A, Stecco A, De Caro R. Layers of the abdominal wall: anatomical investigation of subcutaneous tissue and

Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

superficial fascia. Surg Radiol Anat. 2011 Dec;33(10):835-42
4. Fede C, Pirri C, Fan C, et al. A Closer Look at the Cellular and Molecular Components of the Deep/Muscular Fasciae. Int J Mol Sci. 2021 Jan 30;22(3):1411.
5. Fukunaga M. Expression of D2-40 in lymphatic endothelium of normal tissues and in vascular tumours. Histopathology. 2005 Apr;46(4):396-402.

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The superficial fascia: Anatomy, innervation and vascularization

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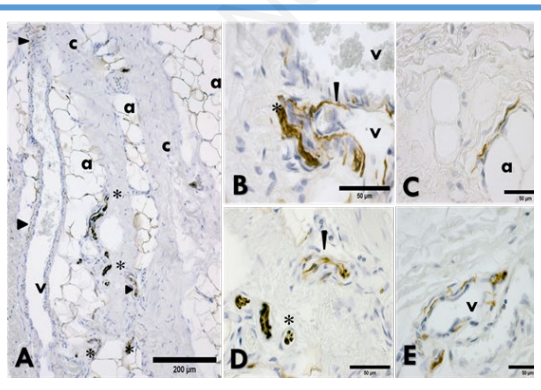
The superficial fascia has only recently been recognized as a specific anatomical structure in its own right anatomical entity, being first considered as included in the hypodermis. Furthermore, whereas it is actually recognized that the innervation of the deep/muscular fascia plays a key role in proprioception and nociception,[1] and there are studies highlighting the cell populations and the extracellular matrix characterization of the deep fascia,[2] there are very few studies that have analyzed these characteristics in the superficial fascia.
The superficial fascia is the second most highly innervated tissue after the skin, with a density of 33.0 ± 2.5/cm2, and a mean nerve sizes of 19.1 ± 7.2 µm.[3] Free nerve endings innervate the tissue, and autonomic nerve fibers are present in the blood vessels, in the areas of vascularization and near adipocytes and in the connective tissue itself (Figure).
A rich vascular pattern forming a fine, dense meshwork with an area percentage of 6.20% ± 2.10% von Willebrand factor stained vessels was noted in all the specimens of the fascia examined; the area percentage of the αSMA-stained vessels was 2.93% ± 1.80% . The diameters of the vessels fell between the 13 and 65 µm range; the network was composed of arteries, veins, capillaries and lymphatic segments.[4] Fibroblasts, myofibroblasts, mast cells are evident in the tissue. Finally, the elastic fibers are more abundant in the superficial fascia than the deep fascia, demonstrating that the superficial fasciae are more adaptable.[5] In the light of these findings is evident that the superficial fasciae have a clear and distinct anatomical entity, and that they should be considered according to their characteristics, innervation and vascularization to better understand their role in thermoregulation, exteroception and pain perception. The knowledge of the superficial fascia may improve grading and developing of different manual approach for treatments of fascial dysfunctions.



Distribution of the innervation in superficial fascia: immunohistochemistry by S100 antibody. A = Adipocyte, v = vassel, c = Connective Tissue, * = Nerve, Arrows = Nerve fiber.
Reprinted with permission from Fede et al. 2022.[3]

Key Words: Superficial fascia; innervation; vascularization; autonomic innervation; arteries.

References

1. Fede C, Petrelli L, Guidolin D, Porzionato A, Pirri C, Fan C, De Caro R, Stecco C. Evidence of a new hidden neural network into deep fasciae. Sci Rep, 11: 12623, 2021. doi: 10.1038/s41598-021-92194-z.
2. Fede C, Pirri C, Fan C, Petrelli L, Guidolin D, De Caro R, Stecco C. A Closer Look at the Cellular and Molecular Components of the Deep/Muscular Fasciae. Int J Mol Sci, 22: 1411, 2021.
3. Fede C, Petrelli L, Pirri C, Neuhuber W, Tiengo C, Biz C, De Caro R, Schleip R, Stecco C. Innervation of human superficial fascia. Front Neuroanat. 2022 Aug 29;16:981426. doi: 10.3389/fnana.2022.981426
4. Pirri C, Petrelli L, Fede C, Guidolin D, Tiengo C, De Caro R, Stecco C. Blood supply to the superficial fascia of the abdomen: An anatomical study. Clin Anat. 2022 Dec 28. doi: 10.1002/ca.23993
5. Pirri C, Fede C, Petrelli L, Guidolin D, Fan C, De Caro R, Stecco C. Elastic Fibres in the subcutaneous tissue: Is there a difference between superficial and muscular fascia? A cadaver study. Skin Res Technol, 28: 21-27, 2022. doi: 10.1111/srt.13084

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Biomechanical properties of the fascial system

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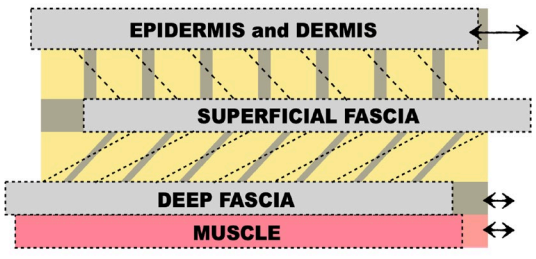
The "fascial system" has been defined as a fascial network involved in functional aspects such as force transmission.[1] The fascial system comprises the superficial and deep fasciae which are connected through skin ligaments, also known as retinacula, providing a continuity from the skin to the muscular plane (See Figure).[2] Indeed, superficial and deep fascia roles in clinical disorders have been shown to reflect their structures.[3] Specifically, the superficial fascia has been described anatomically as an irregular multilamellar structure of interconnected substrates with islets of fat cells. Meanwhile, for example, the deep aponeurotic fascia consists of multilayered structures of dense and loose connective tissues, where collagen fibers follow specific directions.[4] Since the properties of superficial and deep fasciae mimic their structural organization, the biomechanical characterization of these tissues is key to understanding how they influence each other. Despite the clinical impact of these arguments, to date, the literature is still poor in data comparing different substrates of the fascial system through mechanical tests. Therefore, the aim of this work is to investigate this open topic by presenting the biomechanical properties of both superficial and deep fasciae.[5,6] The study highlights how these tissues have different biomechanical properties in relation to their specific structures and functions. These results have a direct impact in the medical field such as in the surgical treatment of soft tissue repair or reconstruction, as well as in rehabilitation intervention (e.g., manual treatment).



The fascial system.

Key Words: Connective tissue; musculoskeletal system; fascial system; superficial fascia; deep fascia; biomechanical characterization.

References:

1. Stecco C, Schleip R. A fascia and the fascial system. J Bodyw Mov Ther. 2016;20(1):139-140. doi:10.1016/j.jbmt.2015.11.012
2. Stecco C, Macchi V, Porzionato A, Duparc F, De Caro R. The fascia: the forgotten structure. Ital J Anat Embryol. 2011;116(3):127-138.
3. Stecco A, Stern R, Fantoni I, De Caro R, Stecco C. Fascial Disorders: Implications for Treatment. PM R. 2016;8(2):161-168. doi:10.1016/j.pmrj.2015.06.006
4. Stecco C. Functional Atlas of the human fascial system. Churchill Livingstone. 2015.
5. Bonaldi L, Berardo A, Stecco C, Fontanella CG. Biomechanical characterization of human superficial fascia from abdomen: A case study. XI meeting: Italian Chapter of the ESB, 6-7 October 2022, Massa.
6. Bonaldi L, Fontanella CG, Stecco C, Berardo A. Uniaxial Tensile Tests On Human Fascia Lata: Stress Relaxation And Failure Phenomena From Frozen Cadavers. 27th Congress of the ESB, 26-29 June 2022, Porto.

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Fascia Lata alterations in hip osteoarthritis: An observational cross-sectional study

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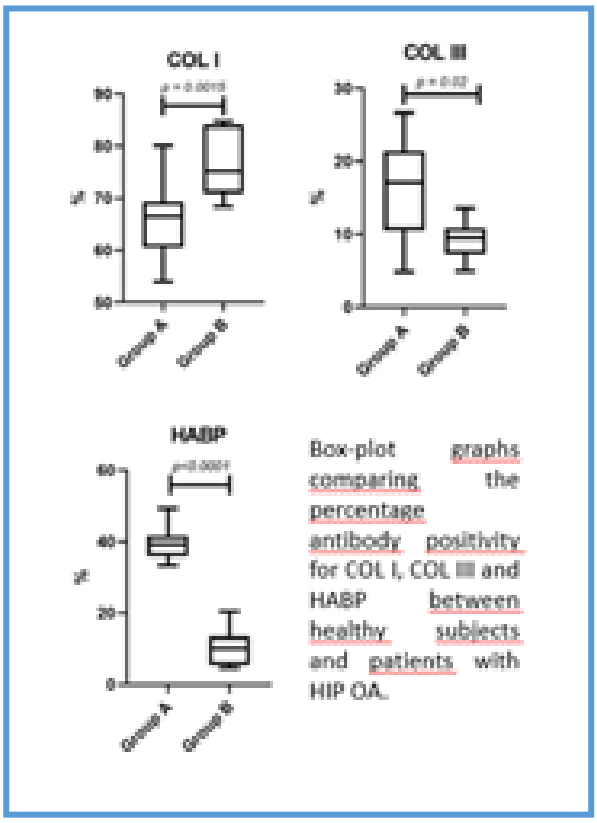
The present study compares the structure and composition of fascia lata in healthy subjects and in patients with hip osteoarthritis (OA), to evaluate any differences in the amount of Collagen type I, Collagen type III, and Hyaluronan. Fascia lata samples from voluntary healthy subjects and patients with OA were harvested during surgery. Collagen type I (COL I), III (COL III) antibody, and biotinylated hyaluronan binding protein (HABP) immunohistochemistry stainings were used to evaluate fascial morphology and COL I, COL III, and Hyaluronan (HA) content in both groups. Ten samples from healthy subjects (group A) and 11 samples



from OA patients (group B) were collected. COL I was significantly more abundant in the OA group ($p = 0.0015$), with a median percentage positivity of 75.2 (IQR 13.11)%, while representing only 67 (IQR: 8.71)% in control cases. COL III, with median values of 9.5 (IQR 3.63)% (OA group) and 17.10 (IQR 11)% (control cases), respectively, showed significant reduction in OA patients ($p = 0.002$). HA showed a median value of 10.01 (IQR 8.11)% in OA patients, denoting significant decrease ($p < 0.0001$) with respect to the control group median 39.31 (IQR 5.62)%. The observed differences suggest a relationship between fascial pathology and hip OA. The observed increase in COL I in OA patients, along with the reduction of COL III and HA, could lead to fascial stiffening, which could alter fascial mechanics and be linked to the development and symptoms of OA.

Key Words: Fascia; hip osteoarthritis; hyaluronan; collagen; stiffness; myofascial pain.

References

1. Fede C, Angelini A, Stern R, Macchi V, Porzionato A, Ruggieri P, De Caro R, Stecco C. Quantification of hyaluronan in human fasciae: variations with function and anatomical site. J Anat. 2018 Oct;233(4):552-556. doi: 10.1111/joa.12866. Epub 2018 Jul 24. PMID: 30040133; PMCID: PMC6131966.
2. Stecco C, Stern R, Porzionato A, Macchi V, Masiero S, Stecco A, De Caro R. Hyaluronan within fascia in the etiology of myofascial pain. Surg Radiol Anat. 2011 Dec;33(10):891-6. doi: 10.1007/s00276-011-0876-9. Epub 2011 Oct 2. PMID: 21964857.
3. Pratt RL. Hyaluronan and the Fascial Frontier. Int J Mol Sci. 2021 Jun 25;22(13):6845. doi: 10.3390/ijms22136845. PMID: 34202183; PMCID: PMC8269293.
4. Rees HW. Management of Osteoarthritis of the Hip. J Am Acad Orthop Surg. 2020 Apr 1;28(7):e288-e291. doi: 10.5435/JAAOS-D-19-00416. PMID: 31800436.
5. Grässel S, Muschter D. Recent advances in the treatment of osteoarthritis. F1000Res. 2020 May 4;9:F1000 Faculty Rev-325. doi: 10.12688/f1000research.22115.1. PMID: 32419923; PMCID: PMC7199286.

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FRIDAY March 31, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

02:00 PM SESSION IX:

Non-invasive Assessments in Myology

Paolo Gargiulo, Ugo Carraro, Chairs

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LECTURE

3D Quantitative Muscle Color Computed Tomography (3D-QMCCT)

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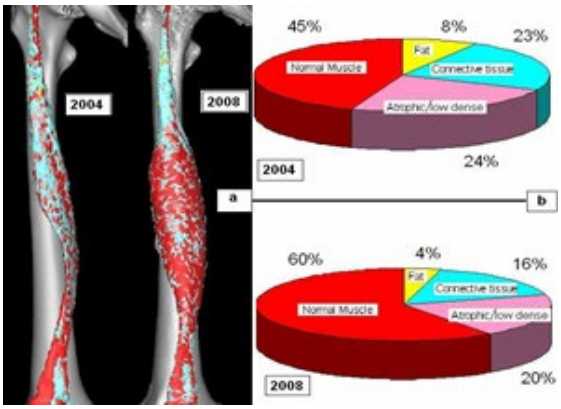
In 2009 Ugo Carraro and Paolo Gargiulo introduced the term 3D Quantitative Muscle Color Computed Tomography (3D-QMCCT) as the process which, starting from computed tomography images, analyzes the distribution in Hounsfield Units (HU), that is the densitometry of a specific anatomical region, assigning a color (essentially derived from the colors of histologically labeled muscle biopsies) based on its density or morphology.[1,2] 3D-QMCCT has been a key tool primarily to assess, quantify, and monitor muscle atrophy in denervated tissue,[3] but also to advance bone mineral density assessment and support surgical planning.[4] 3D-QMCCT provided the best evidence of the effectiveness of home-based Functional Electrical Stimulation of denervated muscles (hbFES) during validation by the Europenan project RISE.[5] A development of 3D-QMCCT is the numerical muscle



3D models of rectus femoris (a) at beginning and after 4 years of electrical stimulation treatment; (b) chart pies showing the muscle composition in 2004 and 2008.

Reproduced with permission from Basic Applied Myology 19 (4): 157-161, 2009.[1]

profile called Nonlinear Trimodal Regression Analysis (NTRA), which numerically summarizes the connective tissue, fat and muscle content from a CT cross section. NTRAs have significantly contributed to demonstrating the interactions between muscle tissue quality and comorbidities such as cholesterol disease and diabetes and correlations with lifestyle and mobility in the aging population.[6,7] Today, with the improvement of medical imaging, human anatomy can be studied non-invasively with micrometre resolution. As the dose of X-rays has been drastically reduced in recent years, the use of CT for research purposes is now much more feasible. In conclusion, new frontiers and applications, such as virtual cardiac histology, can be explored using 3D-QMCCT and NTRA methods.

Key words: 3D Quantitative Muscle Color Computed Tomography (3D-QMCCT); Nonlinear Trimodal Regression Analysis (NTRA); skeletal muscle atrophy and degeneration; home-based Functional Electrical Stimulation of denervated muscles (hbFES).

1. Gargiulo P, Vatnsdal B, Ingvarsson P, Knútsdóttir S, Gudmundsdóttir V, Yngvason S, Kern H, Carraro U, Helgason T. Computational methods to analyze tissue composition and structural changes in denervated muscle undergoing therapeutic electrical stimulation. Basic Applied Myology 19 (4): 157-161, 2009.
2. Gargiulo P, Kern H, Carraro U, Ingvarsson P, Knútsdóttir S, Gudmundsdóttir V, Yngvason S, Vatnsdal B, Helgason T. Quantitative color three-dimensional computer tomography imaging of human long-term denervated muscle. Neurol Res. 2010 Feb;32(1):13-9. doi: 10.1179/016164109X12536042424171. PMID: 20092691.
3. Gargiulo P, Reynisson PJ, Helgason B, Kern H, Mayr W, Ingvarsson P, Helgason T, Carraro U. Muscle, tendons, and bone: structural changes during denervation and FES treatment. Neurol Res. 2011 Sep;33(7):750-8. doi: 10.1179/1743132811Y.0000000007. PMID: 21756556.
4. Esposito L, Bifulco P, Gargiulo P, Gíslason MK, Cesarelli M, Iuppariello L, Jónsson H, Cutolo A, Fraldi M. Towards a patient-specific estimation of intra-operative femoral fracture risk. Comput Methods Biomech Biomed Engin. 2018 Sep;21(12):663-672. doi: 10.1080/10255842.2018.1508570. Epub 2018 Oct 27. PMID: 30370789.
5. Kern H, Carraro U, Adami N, Biral D, Hofer C, Forstner C, Mödlin M, Vogelauer M, Pond A, Boncompagni S, Paolini C, Mayr W, Protasi F, Zampieri S. Home-based functional electrical stimulation rescues permanently denervated muscles in paraplegic patients with complete lower motor neuron lesion. Neurorehabil Neural Repair. 2010 Oct;24(8):709-21. doi: 10.1177/1545968310366129. Epub 2010 May 11. PMID: 20460493.
6. Recenti M, Ricciardi C, Edmunds K, Jacob D, Gambacorta M, Gargiulo P. Testing soft tissue radiodensity parameters interplay with age and self-reported physical activity. Eur J Transl Myol. 2021 Jul 12;31(3):9929. doi: 10.4081/ejtm.2021.9929. PMID: 34251162; PMCID: PMC8495362.
7. Edmunds K, Gíslason M, Sigurðsson S, Guðnason V, Harris T, Carraro U, Gargiulo P. Advanced quantitative methods in correlating sarcopenic muscle degeneration with lower extremity function biometrics and comorbidities. PLoS One. 2018 Mar 7;13(3):e0193241. doi: 10.1371/journal.pone.0193241. PMID: 29513690; PMCID: PMC5841751

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Virtual cardiac histology: a densitometric characterisation of left ventricular tissue

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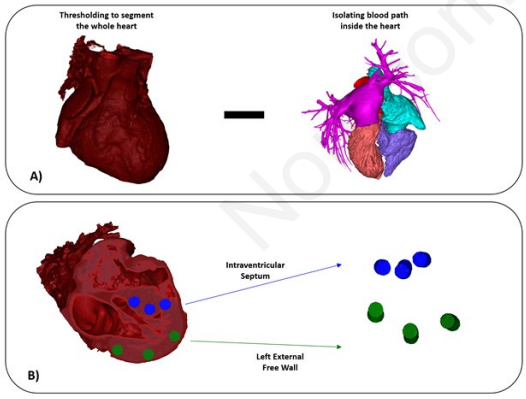
Understanding the mechanisms behind changes in cardiac tissue has always been a topic of great interest. In recent years, biochemical, molecular, and genetic aspects have been studied. In this work, we investigated tissue properties from Computed Tomography images. We designed a densitometric profile and assessed its relations with age, gender, and pathological conditions such as ventricular septal defect/rupture and hypertrophic cardiomyopathy. We developed a novel workflow to segment cardiac tissue to extract 3D samples from regions of clinical interest on the left ventricle. The densitometric profile evaluates the average density, variability, and complexity of the Hounsfield distribution. To assess these relationships, we implemented a linear mixed model, taking into account the non-independence of the data due to repeated measurements of the same subjects within different regions. The results showed that gender is a discriminating factor in average cardiac tissue density, while there is no real relationship between age and absorption. The study, including the diseases, showed that the mean free wall density of the left ventricle changes in the presence of hypertrophic cardiomyopathy. At the same time, there were no statistically significant changes between healthy subjects and patients with post-infarction septal rupture. Moreover, we employed machine learning technology to evaluate the densitometric profile's predictive power, finding peak amplitude and peak position as the most promising features. Finally, this work shows a novel methodology to study cardiac tissue non-invasive, potentially becoming a valid clinical assessment to support an early-stage diagnosis.



3D samples segmentation graphical workflow: A) the first step consists in creating a mask of the whole heart. Pixels' values in the [−200; 1600] HU range are included in the mask. Simultaneously a mask of the blood path is created and then excluded from the whole heart through boolean subtraction. B) Cylindrical holes are created, as negative, in a copy of the resulting mask, and the 3D samples are isolated with boolean subtraction. Each volume is stored separately

Key Words: Virtual histology; cardiac tissue composition; densitometric profile; hypertrophic cardiomyopathy, ventricular septal rupture.

References

1. Mazonakis M, Damilakis J. Computed tomography: What and how does it measure? Eur J Radiol. 2016 Aug;85(8):1499-504. doi: 10.1016/j.ejrad.2016.03.002. Epub 2016 Mar 10. PMID: 26995675.
2. Maron BJ, Maron MS. Hypertrophic cardiomyopathy. Lancet. 2013 Jan 19;381(9862):242-55. doi: 10.1016/S0140-6736(12)60397-3. Epub 2012 Aug 6. PMID: 22874472.
3. Olivetti G, Melissari M, Capasso JM, Anversa P. Cardiomyopathy of the aging human heart. Myocyte loss and reactive cellular hypertrophy. Circ Res. 1991 Jun;68(6):1560-8. doi: 10.1161/01.res.68.6.1560. PMID: 2036710.
4. Recenti M, Ricciardi C, Edmunds KJ, Gislason MK, Sigurdsson S, Carraro U, Gargiulo P. Healthy Aging Within an Image: Using Muscle Radiodensitometry and Lifestyle Factors to Predict Diabetes and Hypertension. IEEE J Biomed Health Inform. 2021 Jun;25(6):2103-2112. doi: 10.1109/JBHI.2020.3044158. Epub 2021 Jun 3. PMID: 33306475.
5. Bates D, Mächler M, Bolker B, Walker S. Fitting linear mixed-effects models using lme4. arXiv preprint 2014; arXiv:1406.5823.
6. Recenti M, Ricciardi C, Edmunds K, Jacob D, Gambacorta M, Gargiulo P. Testing soft tissue radiodensity parameters interplay with age and self-reported physical activity. Eur J Transl Myol. 2021 Jul 12;31(3):9929. doi: 10.4081/ejtm.2021.9929. PMID: 34251162; PMCID: PMC8495362.

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Assessing early-stage Parkinson's Disease using a moving platform (BioVRSea)

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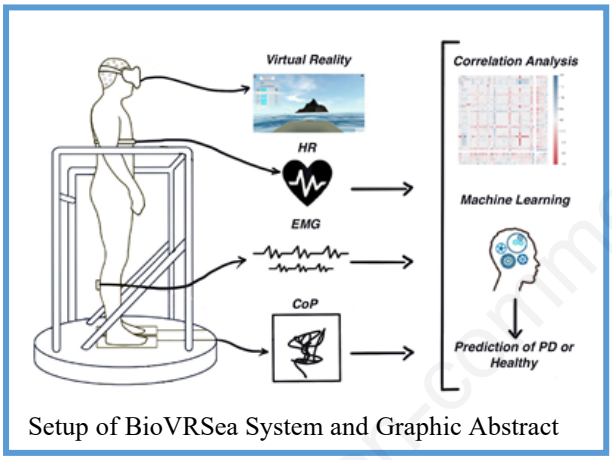
Parkinson's Disease is among the most prevalent neurological diseases in the world today. Typically characterised by impairments in motor function, there remains no known cure for the disease. Treatments generally take the form of medication and/or surgical intervention in combination with physical therapy. Deficits in postural control are commonly seen in Parkinson's sufferers. Our work using the unique BioVRSea setup aims to assess early-stage Parkinson's using a combination of neurphysiological (Electromyography and Heart Rate) and centre of pressure (or sway) measurements. 11 early-stage Parkinson's subjects and 46 healthy over-50s took part in the experiment. Significant differences were found between the two groups in electromyographic and centre of pressure measurements. Correlation analysis indicated opposite correlations in skewness in the right soleus muscle. Finally, machine learning was able to predict with a maximum of 94.6% accuracy whether a subject belonged to the healthy or Parkinson's group based on their measurements from the experiment. Our results are a first step in a prototype of the quantitative evaluation of early-stage Parkinson's.



Setup of BioVRSea System and Graphic Abstract

Key Words: Parkinson's Disease; biomarkers; BioVRSea; electromyography; centre of pressure; postural control.

References

1. Doná F, Aquino CC, Gazzola JM, Borges V, Silva SM, Ganança FF, Caovilla HH, Ferraz HB. Changes in postural control in patients with Parkinson's disease: a posturographic study. Physiotherapy. 2016 Sep;102(3):272-9. doi: 10.1016/j.physio.2015.08.009. Epub 2015 Oct 3. PMID: 26582134
2. Recenti M, Ricciardi C, Aubonnet R, Picone I, Jacob D, Svansson HÁR, Agnarsdóttir S, Karlsson GH, Baeringsdóttir V, Petersen H, Gargiulo P. Toward Predicting Motion Sickness Using Virtual Reality and a Moving Platform Assessing Brain, Muscles, and Heart Signals. Front Bioeng Biotechnol. 2021 Apr 1;9:635661. doi: 10.3389/fbioe.2021.635661. PMID: 33869153; PMCID: PMC8047066..
3. Jacob D, Unnsteinsdóttir Kristensen IS, Aubonnet R, Recenti M, Donisi L, Ricciardi C, Svansson HÁR, Agnarsdóttir S, Colacino A, Jónsdóttir MK, Kristjánsdóttir H, Sigurjónsdóttir HÁ, Cesarelli M, Eggertsdóttir Claessen LÓ, Hassan M, Petersen H, Gargiulo P. Towards defining biomarkers to evaluate concussions using virtual reality and a moving platform (BioVRSea). Sci Rep. 2022 May 30;12(1):8996. doi: 10.1038/s41598-022-12822-0. PMID: 35637235; PMCID: PMC9151646.
4. Busa MA, van Emmerik REA. Multiscale entropy: A tool for understanding the complexity of postural control. J Sport Health Sci. 2016 Mar;5(1):44-51. doi: 10.1016/j.jshs.2016.01.018. Epub 2016 Jan 21. PMID: 30356502; PMCID: PMC6188573.
5. Fadil R, Huether A, Brunnemer R, Blaber AP, Lou JS, Tavakolian K. Early Detection of Parkinson's Disease Using Center of Pressure Data and Machine Learning. Annu Int Conf IEEE Eng Med Biol Soc. 2021 Nov;2021:2433-2436. doi: 10.1109/EMBC46164.2021.9630451. PMID: 34891772.
6. Recenti M, Ricciardi C, Edmunds K, Jacob D, Gambacorta M, Gargiulo P. Testing soft tissue radiodensity parameters interplay with age and self-reported physical activity. Eur J Transl Myol. 2021 Jul 12;31(3):9929. doi: 10.4081/ejtm.2021.9929. PMID: 34251162; PMCID: PMC8495362.

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An in silico 3d approach to evaluate bone remodelling after total hip arthroplasty: a six years longitudinal study

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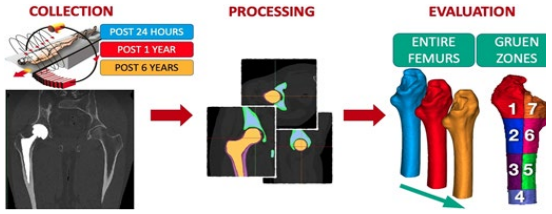
Nowadays, research on bone remodelling after a total hip arthroplasty (THA) is mainly performed using DXA-scans, which gives a quantitative assessment but it can lose some pivotal features of how bone remodels since it is a 3d mechanism. The aim of this work was to enhance the understanding of the volumetric bone mineral density (vBMD) evolution after THA by developing a protocol to (i) three-dimensionally localise the changes in the



Study workflow. The CT scans were collected and processed to obtain the 3d models of the proximal femur for the vBMD evaluation.

proximal femur, and (ii) assess such changes in the long term. Twelve patients that underwent unilateral THA (with cemented/uncemented prostheses) were recruited. Three calibrated CT scans of the proximal femur were collected at different time points: 24 hours, 1 year and 6 years after surgery. The 3D models of the proximal femur were extracted, and an algorithm was developed to split them into the Gruen zones. The bone density gain and loss for both the whole proximal femur and those specific regions was calculated by comparing density values between the three sets of scans. Results showed lower amount of trabecular bone observed in the cemented cohort compared to the uncemented group, and some differences in terms of vBMD evolution were noticed in the whole femur and specifically in some Gruen zones. A high inter-patient variability was observed, ranging from some cases that showed a physiological bone remodelling, to some pathological conditions in which an unexpected increase/decrease of vBMD (e.g. +340% after one year) was noticed. In conclusion, the presented analysis is an useful tool (i) to understand the vBMD evolution in THA patients in the long-term, and (ii) for the follow-up of patients where a failure of the implant is to be expected.

Key Words: Bone remodeling; total hip arthroplasty; Gruen zones; longitudinal study.

References

1. Gislason MK, Lupidio F, Jónsson H Jr, Cristofolini L, Esposito L, Bifulco P, Fraldi M, Gargiulo P. Three dimensional bone mineral density changes in the femur over 1 year in primary total hip arthroplasty patients. Clin Biomech (Bristol, Avon). 2020 Aug;78:105092. doi: 10.1016/j.clinbiomech.2020.105092. Epub 2020 Jun 11. PMID: 32590143.
2. Gargiulo P, Edmunds KJ, Gíslason MK, Latour C, Hermannsson Þ, Esposito L, Bifulco P, Cesarelli M, Fraldi M, Cristofolini L, Jónsson H Jr. Patient-specific mobility assessment to monitor recovery after total hip arthroplasty. Proc Inst Mech Eng H. 2018 Oct;232(10):1048-1059. doi: 10.1177/0954411918797971. Epub 2018 Sep 7. PMID: 30191747.
3. Pitto RP, Bhargava A, Pandit S, Walker C, Munro JT. Quantitative CT-assisted osteodensitometry of femoral adaptive bone remodelling after uncemented total hip arthroplasty. Int Orthop. 2008 Oct;32(5):589-95. doi: 10.1007/s00264-007-0389-7. Epub 2007 Jun 20. PMID: 17579860; PMCID: PMC2551722.
4. Recenti M, Ricciardi C, Edmunds K, Jacob D, Gambacorta M, Gargiulo P. Testing soft tissue radiodensity parameters interplay with age and self-reported physical activity. Eur J Transl Myol. 2021 Jul 12;31(3):9929. doi: 10.4081/ejtm.2021.9929. PMID: 34251162; PMCID: PMC8495362.

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Novel strategies for cartilage assessment, interplay between bone and muscles

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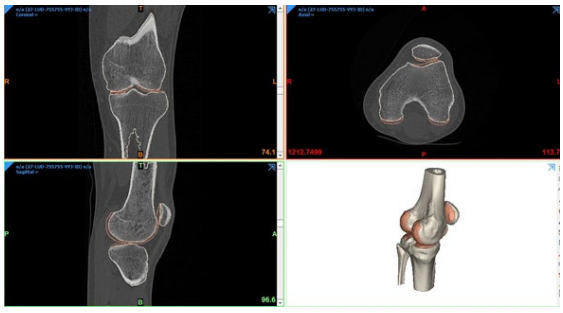
Assessment of human joint cartilage is a crucial tool to detect and diagnose pathological conditions. This exploratory study develop a workflow for 3D modeling of cartilage, muscle and bone based on multimodal imaging. We present a novel methodology to evaluate knee condition using features extracted from magnetic resonance imaging (MRI) and computed tomography (CT) data. New evaluation metrics were created and a unique set of data was gathered from healthy control subjects and patients with clinically evaluated degeneration or trauma. We developed patient specific 3D models of the tibial, femoral, and patellar bones and cartilages. We compare the sensitivity of different



Segmented bones and cartilages and 3D model

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metrics to classify the cartilage condition and evaluate degeneration based on bones and muscle densitometry. The present work demonstrates the potential for improving sensitivity in cartilage assessment.

Key Words: Image segmentation; knee cartilage; classification; osteoarthritis; 3D models.

References

1. Zhang Y, Jordan JM. Epidemiology of osteoarthritis. Clin Geriatr Med. 2010 Aug;26(3):355-69. doi: 10.1016/j.cger.2010.03.001. Erratum in: Clin Geriatr Med. 2013 May;29(2):ix. PMID: 20699159; PMCID: PMC2920533.
2. Roemer FW, Demehri S, Omoumi P, Link TM, Kijowski R, Saarakkala S, Crema MD, Guermazi A. State of the Art: Imaging of Osteoarthritis-Revisited 2020. Radiology. 2020 Jul;296(1):5-21. doi: 10.1148/radiol.2020192498. Epub 2020 May 19. PMID: 32427556.
3. Ciliberti FK, Guerrini L, Gunnarsson AE, Recenti M, Jacob D, Cangiano V, Tesfahunegn YA, Islind AS, Tortorella F, Tsirilaki M, Jónsson H Jr, Gargiulo P, Aubonnet R. CT- and MRI-Based 3D Reconstruction of Knee Joint to Assess Cartilage and Bone. Diagnostics (Basel). 2022 Jan 22;12(2):279. doi: 10.3390/diagnostics12020279. PMID: 35204370; PMCID: PMC8870751
4. Baker JF, Von Feldt J, Mostoufi-Moab S, Noaiseh G, Taratuta E, Kim W, Leonard MB. Deficits in muscle mass, muscle density, and modified associations with fat in rheumatoid arthritis. Arthritis Care Res (Hoboken). 2014 Nov;66(11):1612-8. doi: 10.1002/acr.22328. PMID: 24664868; PMCID: PMC4551488
5. Cai G, Otahal P, Cicuttini F, Wu F, Munugoda IP, Jones G, Aitken D. The association of subchondral and systemic bone mineral density with osteoarthritis-related joint replacements in older adults. Osteoarthritis Cartilage. 2020 Apr;28(4):438-445. doi: 10.1016/j.joca.2020.02.832. Epub 2020 Feb 28. PMID: 32119971.
6. Recenti M, Ricciardi C, Edmunds K, Jacob D, Gambacorta M, Gargiulo P. Testing soft tissue radiodensity parameters interplay with age and self-reported physical activity. Eur J Transl Myol. 2021 Jul 12;31(3):9929. doi: 10.4081/ejtm.2021.9929. PMID: 34251162; PMCID: PMC8495362.

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Interplay between the age and the asymmetry of NTRA in elderly people

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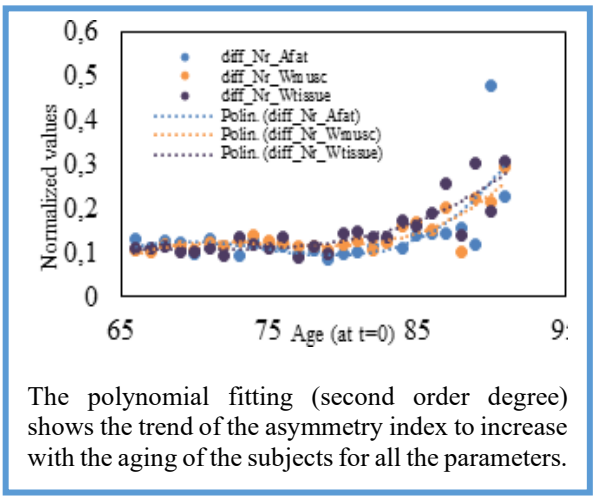
The 11 nonlinear trimodal regression analysis (NTRA) parameters represent the radiodensitometric distributions (RDD) of muscle, fat and connective tissues extracted from a CT scan of the mid-femur. Previous studies showed how these parameters are correlated with physiological variables (1) and can be used for building predictive models of cardiovascular diseases and for assessing the impact of lifestyle factors in aging subjects. The aim of this study is to assess the role of age in the asymmetry of the 11 NTRA parameters. The dataset consists of 3162 Icelandic subjects, aged between 65 and 95 years. A statistical approach was employed to investigate the interplay between the age and the NTRA asymmetry. A paired Student's t test was performed to compare right- and left-femur NTRA parameters. Then, 11 asymmetry indicators were calculated as the absolute difference between right- and left-femur values of each NTRA parameters. Finally, an analysis of variance (ANOVA) and a regression analysis were carried out to study the relationships between subjects' age and the degree of asymmetry. Results demonstrate a statistically significant difference between the RDDs of the right- and lef-femur for 7 out of 11 NTRA parameters. Then, the variation of the asymmetry indicators with respect to age is shown and the three most significant age-related asymmetry indicators were identified, namely the amplitude of the RDD of the fat (Nf), the width of the RDD of the muscle (σm), and the width of the RDD of the connective tissue (σt). It is finally observed that the age-related curves of the identified indicators follow a second-order polynomial law showing an increasing trend of the asymmetry indicators with age



The polynomial fitting (second order degree) shows the trend of the asymmetry index to increase with the aging of the subjects for all the parameters.

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(determination coefficients, R2, equal to 0.50 for Nf, 0.76 for σm, and 0.75 for σt). In conclusion, the work shows that the NTRA are sensitive to the asymmetry, the degree of asymmetry increases with age, and σm is among the most sensitive age-related asymmetry indicator.
Key Words: Aging; medical imaging; biomedical data analysis.
References

1. Edmunds K, Gíslason M, Sigurðsson S, Guðnason V, Harris T, Carraro U, Gargiulo P. Advanced quantitative methods in correlating sarcopenic muscle degeneration with lower extremity function biometrics and comorbidities. PLoS One. 2018 Mar 7;13(3):e0193241. doi: 10.1371/journal.pone.0193241. PMID: 29513690; PMCID: PMC5841751
2. Ricciardi C, Edmunds KJ, Recenti M, Sigurdsson S, Gudnason V, Carraro U, Gargiulo P. Assessing cardiovascular risks from a mid-thigh CT image: a tree-based machine learning approach using radiodensitometric distributions. Sci Rep. 2020 Feb 18;10(1):2863. doi: 10.1038/s41598-020-59873-9. PMID: 32071412; PMCID: PMC7029006.
3. Recenti M, Ricciardi C, Edmunds KJ, Gislason MK, Sigurdsson S, Carraro U, Gargiulo P. Healthy Aging Within an Image: Using Muscle Radiodensitometry and Lifestyle Factors to Predict Diabetes and Hypertension. IEEE J Biomed Health Inform. 2021 Jun;25(6):2103-2112. doi: 10.1109/JBHI.2020.3044158. Epub 2021 Jun 3. PMID: 33306475.
4. Recenti M, Ricciardi C, Edmunds K, Jacob D, Gambacorta M, Gargiulo P. Testing soft tissue radiodensity parameters interplay with age and self-reported physical activity. Eur J Transl Myol. 2021 Jul 12;31(3):9929. doi: 10.4081/ejtm.2021.9929. PMID: 34251162; PMCID: PMC8495362.

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Time shift of peak activation levels in quadriceps and hamstrings after ACL reconstruction during single leg jump

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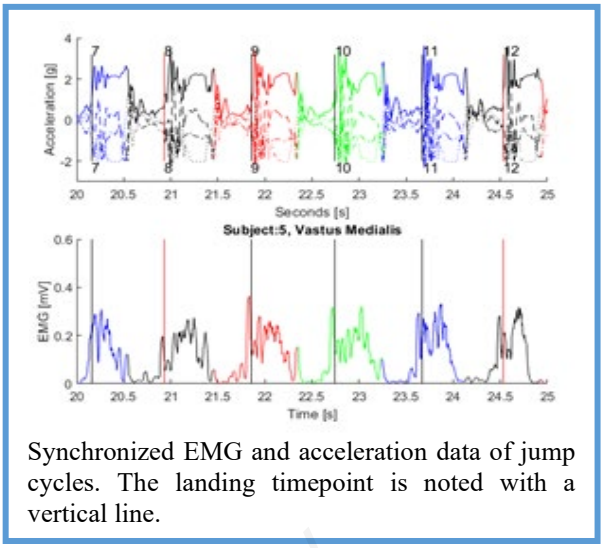
Recurrance of injuries are prevalent in athletes that have undergone ACL reconstruction which partly can be attributed to weakening and the reduction of neuromuscular control of the hamstrings and the quadriceps.[1,2] When using autograft for the ACL reconstruction, the tissue is mainly harvested either from the hamstring tendon or from the patellar tendon which can have an effect of the overall biomechanics and load transfer integrity of the knee joint. In the presented study a 30s continuous single leg jump was carried out by subjects from three cohorts: a healthy control, patients that were recovering after ACL reconstruction using both hamstring and patellar tendon autograft. EMG measurements were taken of six muscles during the jump sequence: 1) Vastus Lateralis, 2) Vastus Medialis, 3) Biceps Femoris 4) Tensor Fascia Latae, 5) Semitendinousus and 6) Gluteus Medius. An acceleorometer located at the inferior lumbar region was synchronized with the EMG measurements to capture the events of push off and landing. The jump cycle was normalized from push off to the next push off as can be seen in the figure and the EMG signals rectified and processed using a bandpass filter and RMS and finally fitted to each normalized jump cycle. The jump sequence was divided into three parts containing equal number of jumps. The average EMG values were analyzed between the first third and the final third of the jump sequence. The results demonstrated that there is a temporal shift in the peak activation levels of the quadriceps muscles. Significant shift in peak activation is seen in Control group for both quadriceps and hamstring, and in Injured HS group for quadriceps muscle and Healthy BTB for lateral hamstring muscle and lower peak activation levels of the vastus lateralis ($p<0.001$) and vastus medialis ($p<0.001$) and lateral hamstrings ($p<0.001$) in the injured compared to healthy legs.



Synchronized EMG and acceleration data of jump cycles. The landing timepoint is noted with a vertical line.

Key Words: ACL reconstruction; biomechanics; EMG; single leg jump .
References

1. Einarsson E, Thomson A, Sas B, Hansen C, Gislason M, Whiteley R. Lower medial hamstring activity after ACL reconstruction during running: a cross-sectional study. BMJ Open Sport Exerc Med. 2021 Mar

11;7(1):e000875. doi: 10.1136/bmjsem-2020-000875. PMID: 33782638; PMCID: PMC7957131.
2. Recenti M, Ricciardi C, Edmunds K, Jacob D, Gambacorta M, Gargiulo P. Testing soft tissue radiodensity parameters interplay with age and self-reported physical activity. Eur J Transl Myol. 2021 Jul 12;31(3):9929. doi: 10.4081/ejtm.2021.9929. PMID: 34251162; PMCID: PMC8495362.

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Exploring myofibril alignment in muscular tissues using circular statistics

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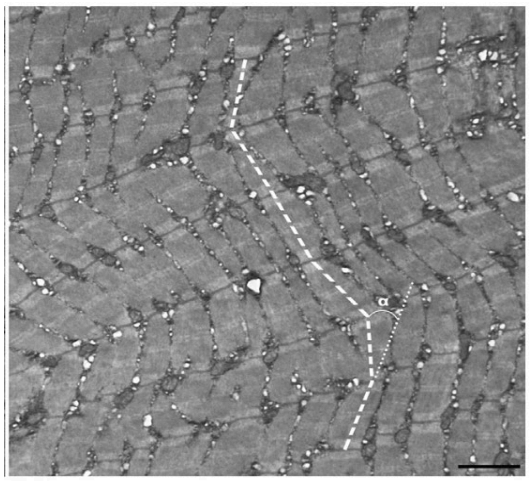
An interesting problem in analysing the image of muscle tissue is represented by the attempt to evaluate the linearity of myofibrillar structures and their possible deviation from a straight line. By indicating with αi the angles between two successive sarcomeres along the same myofibril, Cisterna et al. (2021) proposed an index that can be thought as the mean of the angles (taken in absolute value). In this contribution, we propose an alternative approach to the same problem. Our proposal, based on circular statistics, taking a cue from the same angular data αi proposed by Cisterna et al.; circular statistics has been used earlier to study muscle cell alignment. Ideally, for each angle αi, it is possible to construct a unit vector having the base at the centre of a goniometric circumference and the vertex on the circumference from which to calculate the resulting vector, which, divided by n (that is the number of angles or the number of sarcomeres minus 1), gives the resulting mean vector. From here, two parameters can be obtained: (a) the direction of the mean vector (if it is equal to 0, it means that the displacements to the right balance those to the left; or, as an extreme case, that the sarcomeres are perfectly aligned); b) the length of the mean vector r, that can range between 0 (representing perfect isotropy – or a circular uniform distribution – i.e., the maximum possible misalignment) and 1 (representing perfect anisotropy, i.e., the maximum possible alignment). It is also possible to perform a statistical test using the mean vector length r as test statistics: Rayleigh test is the best known in circular statistics; its null hypothesis is the uniform circular distribution of the angles, and the alternative hypothesis is a generic anisotropy. The method we propose, unlike the one indicated by Cisterna et al., uses circular analysis techniques instead of linear



Dotted line indicates the axis of each sarcomere composing a myofibril. Reported from Cisterna et al. (2021)

analysis methods, which makes it more elegant and gives greater substance to statistical analysis (but in contrast, it also has greater computational complexity).[2] In conclusion, our method has potential use in several sarcomere-related conditions by providing a quantitative definition of myofibril linearity in skeletal muscle.

Key Words: Circular statistics; myofibrillar structures; sarcomeres.

References

1. Cisterna B, Malatesta M, Zancanaro C, Boschi F. A computational approach to quantitatively define sarcomere dimensions and arrangement in skeletal muscle. Comput Methods Programs Biomed. 2021;211:106437. doi: 10.1016/j.cmpb.2021.106437.
2. Rocchi E, Peluso S, Amatori S, Sisti D. New indexes for myofibril linearity in muscle image analysis. Eur J Transl Myol. 2022 Oct 4;32(4):10736. doi: 10.4081/ejtm.2022.10736. PMID: 36193819; PMCID: PMC9830398.

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FRIDAY March 31, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

04:30 PM SESSION X: Muscle Rehabilitation in Dentistry and beyond

Riccardo Rosati, Elena P. Ivanova, Chairs

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Gaia Pellegrini, *University of Milan, Italy:* *Standardised protocols for sEMG of the masticatory muscles in oral rehabilitation*

On-site presentation of unpublished results. The author denied also Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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Innovative methods of full dental rehabilitation

Elena Ivanova (1), Frank Saxler (2), Andrey Lobanov (1), Sergey Andronov (1)

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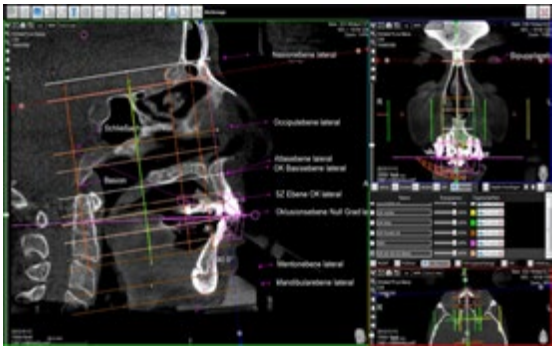

4D analysis of patient with cranio-mandibular disorders. CAD digital diagnosis

Dentistry in the twenty first century has been marked by multidisciplinary approach to diagnosis and treatment. Functional diagnosis, functional treatment, functional occlusion of patients with cranio-mandibular disorders depend on relation with functional diagnosis and treatment of full body. Innovative technologies of functional diagnosis and full dental rehabilitation calculating by 4D analysis developed on understanding dental and medical symptoms. Dental bruxism, abrasion shipping, parafunction, fracture of teeth, fracture of implant, fracture of prosthodontic, hyperemia of uninfected pulp of sensitive teeth, cranio-mandibular dysfunction CMD, TMJ Symptoms, structure loss with deflective contact, projection pain in teeth define function in cranio-mandibular system. Functional determinants of occlusion and individual tooth library include occlusion plane, vertical dimension, condyle inclination, mandibula position, inclination based on bones of the skull. So, we calculate complete digital concept of 4D Analysis connected with STL data, CAD device, 4D and Ray imaging of functional determinants, dynamic 4D moving of bone, patient adapting based to Fibonacci number, X-Ray and CAD with STL life on the screen. Digital way of examination and treatment options advantages changing occlusal plane, mandibular position, functional training device, resetting of bio processes and bone structure of the skull, directly changing of mobility of individual force, compliance of the patient mobility, rehabilitation functional determinants with new calculated functional occlusion after digital set up. Functional occlusion calculates with 4D Analysis service for prosthodontics, implantology and orthodontics. In every case we get the CNC file for high milling your functional occlusion and devices.

Key words: Functional diagnosis; functional treatment; functional occlusion; 4D analysis; cranio-mandibular disorders; multidisciplinary approach.

References

1. Baldini A, Nota A, Tripodi D, Longoni S, Cozza P. Evaluation of the correlation between dental occlusion and posture using a force platform. Clinics (Sao Paulo). 2013 Jan;68(1):45-9. doi: 10.6061/clinics/2013(01)oa07. PMID: 23420156; PMCID: PMC3552467..
2. Cuccia AM. Interrelationships between dental occlusion and plantar arch. J Bodyw Mov Ther. 2011;15(2):242–50. doi: 10.1016/j.jbmt.2010.10.007 PMID: 21419367
3. Saccucci M, Tettamanti L, Mummolo S, Polimeni A, Festa F, Tecco S. Scoliosis and dental occlusion: a review of the literature. Scoliosis. 2011 Jul 29;6:15. doi: 10.1186/1748-7161-6-15. PMID: 21801357; PMCID: PMC3162939.
4. Ohlendorf D, Seebach K, Hoerzer S, Nigg S, Kopp S. The effects of a temporarily manipulated dental occlusion on the position of the spine: a comparison during standing and walking. Spine J. 2014 Oct 1;14(10):2384-91. doi: 10.1016/j.spinee.2014.01.045. Epub 2014 Jan 31. PMID: 24486478.

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Electromyographic analysis of masticatory muscles before and after rapid palatal expansion

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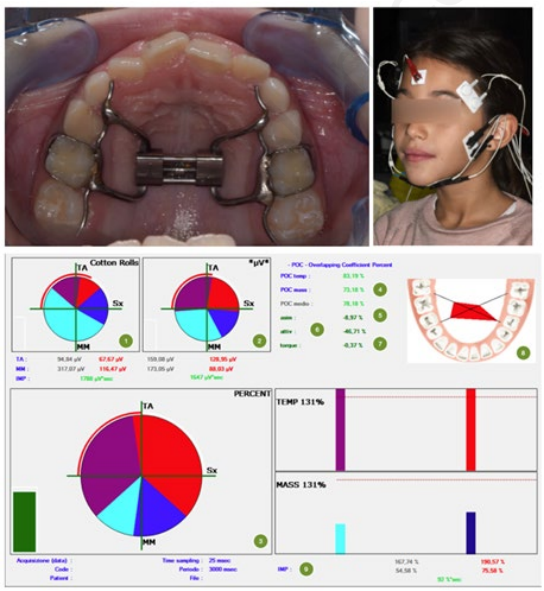
Maxillary contraction (MC) is one of the most pervasive disorders of the craniofacial region and Rapid Palatal Expansion (RPE) is an orthopedic procedure widely accepted and routinely used in growing patients to correct this condition, but its effects on the neuromuscular system are not clear yet. Surface electromyography (sEMG) is a valid non-invasive tool for assesing the activity of the main masticatory muscles. The present prospective clinical study aims to evaluate the sEMG activity of superficial masseters (MM) and anterior temporalis (TA) in patients with MC candidates to RPE, before treatment (t0), at the end of expansion (t1) and after 6 months (t2). sEMG activity were assessed bilaterally during maximum voluntary clenching (MCV). 21 patients were selected: 11 completed the protocol while 10 performed only the first two measurements. Preliminary results did not show statistically significant differences of the analyzed electromyographic indices, before and after RPE. Although there was no statistical significance, the main indices showed a reduction at t1, compared to t0. However, the ATTIV index at t1 is significantly different between patients with an initial Maxillary Transversal Diameter (MTD) shorter than 31 mm compared to those with an initial MTD longer than 31 mm. The first group showed a negative index value, contrary to the second group, which means a major TA recruitment. The greater involvement of TA during MCV, found in subjects with a more severe initial MC, could indicate a greater occlusal instability after the expansion. Therefore, the RPE appears not to affect neuromuscular activity significantly, but further studies are needed to either confirm or deny this hypothesis.

Key Words: Surface electromyography; rapid palatal expansion; masticatory muscles.



Patient with RPE who carries out sEMG analysis of masticatory muscles during clenching

References

1. McNamara JA. Maxillary transverse deficiency. Am J Orthod Dentofacial Orthop 2000 May;117(5):567-70. doi: 10.1016/s0889-5406(00)70202-2.
2. Ferrario et al. An electromyographic investigation of masticatory muscles symmetry in normo-occlusion subjects. Journal of Oral Rehabilitation 2000; 27:33–40. doi: 10.1046/j.1365-2842.2000.00490.x.
3. Botelho AL, et al. Standardization of the Electromyographic Signal Through the Maximum Isometric Voluntary Contraction, CRANIO 29:1, 23-31 2011. doi: 10.1179/crn.2011.005.
4. Di Palma E et al. Longitudinal effects of rapid maxillary expansion on masticatory muscles activity. J Clin Exp Dent 2017 May 1; 9(5):e635-40. doi: 10.4317/jced.53544.
5. Michelotti A et al. Evaluation of masticatory muscle activity in patients with unilateral posterior crossbite before and after rapid maxillary expansion. Eur J Orthod 2019 Jan 23; 41(1):46-53. doi: 10.1093/ejo/cjy019.

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2023Pdm3 March 31 - Abstract 73

Masticatory muscles pain management

Roberto Rongo, *University of Naples Federico II, Italy*
On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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Definite Orthodontic treatment for patients with Temporomandibular Joint problems and/or TMD

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The recent way of life and social stress can activate latent Temporomandibular Joint problems which is a severe physiological disease that affects and deteriorates the quality of life of many patients and has been increasing among our patients due to the different stressful situations. For more than half a century there has been controversy among general dentists, prosthodontists, orthognathic surgeons, and orthodontists on how to diagnose and treat TMD problems. This means that we have many different concepts in dentistry regarding how TMD problems must be diagnosed and approached. Some TMJ concepts and treatments are obsolete and only give a temporary solution to this very complex craniomandibular syndrome. Some invasive surgical treatments are performed, but many of them give a temporary or provisional solution to this complicated disease. An evidence-based “definite and non-invasive therapy” with orthodontic treatment has been performed for the last 15 years. A definitive treatment for the patients suffering from this severe disease is provided to avoid the long-term use of "an occlusal splint” as a lifelong therapy device”. The prolotherapy and infiltration of autogenous stem cells are used to regenerate the damaged tissues of the TMJ and avoid its continued degeneration.

Key words: Definite orthodontic treatment; patients with temporomandibular joint problems; TMD.

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Chewing hard food and its importance for general health

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Anthropological research has shown that the Japanese and the Mongolian populations share morphological and genetic similarities, although their dietary lives are not the same. The purpose of this study was to evaluate the relationship between environmental factors such as dietary life and stomatognathic function with a dynamic analysis of physiological tooth displacement. Ten clinically healthy subjects were recruited (mean age 24.8 +/- 1.0 years). The subjects were divided into two groups 1) Mongolian group: five Mongolians grown with a more or less natural texture diet and 2) Japanese group: five Japanese grown with a relatively soft diet. The displacement of the upper left first molar was measured during function using a three-dimensional tooth displacement transducer Type M-3 developed by Miura. The tooth displacement in the Japanese group occurred mostly in an apicopalatal direction but intruded basically parallel to the tooth axis in the Mongolian group. The stress-strain curve revealed that elastic socket deformation and viscous elements were more pronounced in the Japanese group. It was concluded that environmental factors such as dietary life could influence tooth displacement during function.

Key Words: Dentistry; chewing hard food; general health

References

1. Nishino M, Amarsaikhan B, Furumoto N, Hirao S, Bando H, Nakagawa A, Nomingerel S, Bolorchimeg B, Fujimoto M. Dental Caries in Children Under Five Years of Age in Mongolia. Int J Environ Res Public Health. 2020 Jul 1;17(13):4741. doi: 10.3390/ijerph17134741. PMID: 32630306; PMCID: PMC7370011.
2. Hasegawa Y, Batbayar N, Sukhbaatar N, Bazar A, Kageyama I. Relationship between index of orthodontic treatment need dental health component (IOTN-DHC) and caries prevalence in school-age children. Int J Dent Hyg. 2022 Dec 7. doi: 10.1111/idh.12647. Epub ahead of print. PMID: 36479593.

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Peculiarities of the chewing muscles electrophysiological activity in mouth breathing individuals

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Various factors, that play significant role in development of facial, bony structures, formation of normal growth and functionally correct dentition, have become the subject of increasing interest recently. According to the latest studies, neuromuscular balance is considered to be the main prerequisite for preventing relapse after orthodontic treatment and also the way to optimize its outcome. One of the main factors for normal growth of the jaws is not only masticatory muscles proper, coordinated work, but also its contractility (and therefore excitability) - physiological characteristics. It should be noted, that as a result of decreased muscle activity, significant changes in the location, size and growth of the jaws can develop, which can be manifested by the vertical growth of the face. The study was conducted on the group of 65 male and female volunteers. Several breathing tests were carried out to determine the

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breathing type. Cephalometric analysis was performed for all individuals to conclude the position, growth type and size of the jaws. In order to reduce the dentoalveolar proprioceptive signal, all subjects had been indicated to clench on the cotton rolls and the data was obtained during maximal voluntary contraction. In mouth breathing individuals, mean electromyographic activity of both masseter and temporalis muscles registered during maximal contraction, turned out to be inhomogeneous and asymmetric, occlusal anomalies had been noted, most often - skeletal second class.

Key Words: Electromyography; mouth breathing; skeletal growth; masticatory muscles; neuromuscular balance.

References

1. Ferrario VF, Alessandro miani, Chiarella Sforza, Antonio D'Addona. Electromyographic activityof human mastica- tory muscles in normal young people. Statistical evaluation of reference values for clinical application, J Oral Rehabil. 1993,May;20(3):271-80.
2. Souki BQ, Pimenta GB, Souki MQ, et al. Prevalence of malocclusion among mouth breathing children: do expectations meet reality? Int J Pediatr Otorhinolaryngol. 2009;73:767–773.
3. Valera FC, Travitzki LV, Mattar SE, et al. Muscular, functional and orthodontic changes in preschool children with enlarged adenoids and tonsils. J Pediatr Otorhinolaringol. 2003;67:761–770.
4. Vig KW. Nasal obstruction and facial growth: the strength of evidence for clinical assumptions. Am J Orthod Dentofacial Orthop. 1998;113:603–611.

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Improvement of gait, balance and coordination after application of Taopatch® device

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Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS) characterized by inflammation, demyelination, gliosis, and neuronal loss. Neurological symptoms vary, depending on lesion location - vertigo, gait imbalance, weakness, tremor, spasticity, fatigue, loss of sensation, paresthesias, dysesthesias. The most disabling symptoms are imbalance, muscle weakness and fatigue. Taopatch® is a patented wearable nanotechnology device that combines acupuncture with light therapy. It contains layers of nanocrystals, which capture body's heat and convert it into impulses of very weak light, and then emitted onto the specific points on the body. A recent study of Lomeo et al. in subjects with MS investigated the effect of Taopatch® and showed that the use of these devices can improve the proprioception, balance and movements of the affected limbs. The aim of the study was to evaluate properly the early effects of Taopatch® device on MS patients by applying clinical scales and tests for determining disability and the patient's subjective perspective of their condition severity. Twelve patients with MS were enrolled in the study – 4 males at average age of 38.3 ± 4.7 years and 8 females at average age of 44.5 ±10.5 years. The study protocol included Expanded Disability Status Scale (EDSS), Tandem gait - 10 m., Timed up and go, 9-Hole Peg Test (9-HPT test) at baseline and after the application of Taopatch® - one device on C7 and one on xyphoid process for 40 minutes. During Taopatch® wearing, every participant performed kinesitherapy and for proper hydration consumed 500 ml of water. The study showed no improvement in the EDSS score. There was a statistically significant reduction in tandem gait (from 40.6s. to 27.9s.) and in 9-HPT test in both dominant (from 39.5s. to 35.4s.) and non-dominant (from 37.6s. to 31.4s.) hands. We observed also improvement of coordination, stability and the quality of movements. Timed up and go test (TUG) was also reduced, but the change wasn't significant. In conclusion, the early effect (in 40 minutes) of Taopatch® device application showed immediate improvement of gate speed, stability and coordination with reduced tremor. Most probably the photons of light, which are very similar to the biophotons help the patients' cells to communicate with each other and give additional pathway of proprioception. It could allow the CNS to communicate with the rest of a body in a way faster and more efficient, bypassing the plaques of demyelination.

Key Words: multiple sclerosis, light therapy, tandem gait, 9-HPT test, Taopatch®.

References

1. Carbonari B, Balducci F, Cesaretti G et al. Performance, balance and posture variations with occlusal splint and Taopatch® devices. J Sport Med Phys Fitness, 2021; 61 (2):317-323.
2. Lomeo A, Cacciaguerra G, Garsia D, Scolaro A. Utilisation des dispositifs nanotechnologiques dans les pathologies degeneratives cerebrales. Etude prospective sur 28 patients de sclerose en plaques. Hegel. 2019:2:114
3. Messina G, Amato A, Alioto A, Stallone R, Rizzo F, Ragonese P, Fischetti F, Genua D, Francavilla V, Iovane A, Proia P. A new road to improve vitamin D and balance through Taopatch® and proprioceptive protocol in Multiple Sclerosis patients. Eur J Transl Myol. 2022 Sep 16;32(4):10774. doi:

10.4081/ejtm.2022.10774. PMID: 36112067; PMCID: PMC9830399.

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Intra-articular ultrasound-guided injection with Hyaluronic Acid and corticosteroid in retrodiscal tissue for TMD

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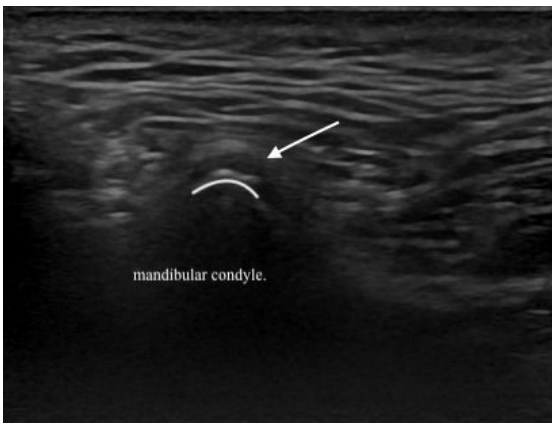
Temporomandibular disorders (TMD) are heterogeneous pathological conditions characterized by similar signs and symptoms. The main representative symptom is a dull pain near the ear that increase with the movement of jaw. Sometimes pain is associated with headache. In literature different methods of classification of TMD are described. The DC/TMD criteria are still fundamental for the diagnosis and classification of TMD.
28 patients (16 females and 10 males, with a mean age of 39± 8.9 years) undergone a specialist gnathological evaluation and MRI of the temporo-mandibular joint (TMJ) to value retrodiscal tissue of TMJ, were examined by Visual Analogical Scale (VAS) for ante-auricular pain and by the presence of other symptoms such as: tinnitus, vertigo, headache, joint click. Every evaluation were performed at basal time (T0) and at 7 (T1), 30 (T2) and 90 (T3) days from treatment. After a preliminary clinical and ultrasound evaluation, patients were undergone ultrasound-guided bilateral infiltration of low molecular weight (LMW) hyaluronic acid and corticosteroid (1 cc methylprednisolone aeacetate) (T0). An individualized interocclusal devices was used to perform ultrasound evaluation and ultrasound-guided infiltration; the device allows the mouth to be blocked in its maximum opening to facilitate the localization of the glenoid fossa, which is empty, as the condyle is moved towards the articular tubercle. 80% of the patients treated reported an immediately disappearance of joint click. Data analysis revealed a statistically significant ($p < 0.05$) reduction from baseline for all three subsequent measurements, but no significant change between measurements at 30, 60 and 90 days. Therefore it is evident that a plateau is reached after the 30th day. Clinical evaluations were accompanied by ultrasound exam which didn't show the presence of local complications. Ultrasound-guided infiltration seems a safe and efficacious treatment of TMD; the effects showed a rapid e significant reduction of pain. A longer follow-up and more cases are necessary to confirm the positive effects of this treatment.



US examination of temporo-mandibular joint

Key words: TMJ; hyaluronic acid; auricular pain; TMD.

References

1. Kapos FP, Exposto FG, Oyarzo JF, Durham J. Temporomandibular disorders: a review of current concepts in aetiology, diagnosis and management. Oral Surg. 2020 Nov;13(4):321-334.
2. Reiter S, Goldsmith C, Emodi-Perlman A, Friedman-Rubin P, Winocur E. Masticatory muscle disorders diagnostic criteria: the American Academy of Orofacial Pain versus the research diagnostic criteria/temporomandibular disorders (RDC/TMD). J Oral Rehabil. 2012 Dec;39(12):941-7.
3. Li DTS, Leung YY. Temporomandibular Disorders: Current Concepts and Controversies in Diagnosis and Management. Diagnostics (Basel). 2021 Mar 6;11(3):459.
4. De Nordenflycht D, Tesch RS. Advantages of ultrasound guidance for TMJ arthrocentesis and intra-articular injection: A narrative review. Dent Med Probl. 2022 Oct-Dec;59(4):647-656.
5. Tanaka, E., M. S. Detamore, and L. G. Mercuri. "Degenerative disorders of the temporomandibular joint: etiology, diagnosis, and treatment. Journal of dental research 87.4 (2008): 296-307.

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Effects of Platelet-Rich-Plasma injection in association with therapeutic exercise in the management of Medial Epicondylitis

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Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

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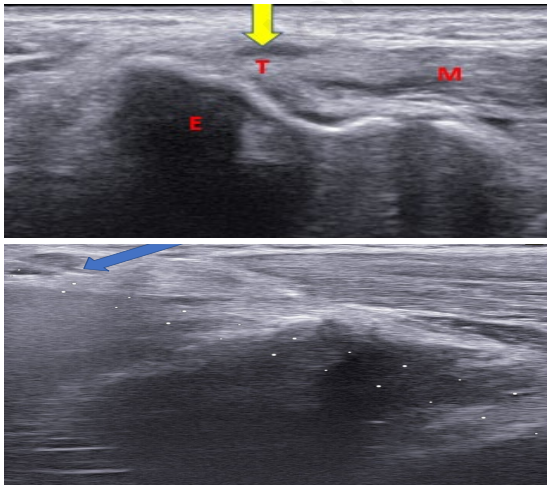
Medial epicondylitis (ME) is an inflammatory-degenerative tendinopathy that occurs typically in people playing sports like throwing sports, bowling, badminton, tennis and golf. Platelet-Rich-Plasma (PRP) is currently the most exploited strategy in the clinical practice to provide a regenerative stimulus for tendon healing. This paper values the effects of the ultrasound-guided injections with autologous PRP in association with a specific physiokinesitherapy program in the management of ME. We examined 18 patients (11 males and 7 females, with a mean age of 41 ± 8.4 years) with a diagnosis of ME, practicing sport activities. In according to imaging (US and MRI) we identified two groups: group A (n =12) included patients with ME without tendon lesion; group B (n=6) included ME with a focal tendon lesion. Both groups have undergone injection of PRP (T0). Patients were evaluated by the numeral rating score (NRS), hand grip strength (HGS), DASH and US examination at baseline, after 3 weeks (T1) and after 9 weeks from the treatment (T2). HGS wasn't performed at T1 to not overstress the tendon structures. At T1 patients started to receive a 3-week physiokinesitherapy treatment for 3 days a week. Both groups achieve significant improvements in NRS, DASH and HGST after 3 and 9 weeks from the infiltrative treatment. These improvements were similar in the two groups. Regarding the US evaluation at T1 it showed: the persistence of the typical signs of chronic tendinopathy, the reduction of the phenomena of neo-microangiogenesis, and in the group A the disappearance of the hypoechoic areas replaced by diffuse hyperechogenicity. At T2 the US exam showed the persistence of microangiogenesis phenomena in once patient out of 18. All patients resumed regular sporting activity. We recommend that autologous PRP injections should be considered in association with physiokinesitherapy for treating patients with newly diagnosed ME.



Top: US examination in flexor carpi radialis tendon lesion. Down: US-guided PRP injection in tendon lesion.

Key Words: Medial Epicondylitys; platelet-rich-plasma; ultrasound-guided; non-operative; injection.

References

1. Maffulli N, Longo UG, Loppini M, Denaro V. Current treatment options for tendinopathy. Expert Opin Pharmacother. 2010 Sep;11(13):2177-86. doi: 10.1517/14656566.2010.495715. PMID: 20569088.
2. Karjalainen TV, Silagy M, O'Bryan E, Johnston RV, Cyril S, Buchbinder R. Autologous blood and platelet-rich plasma injection therapy for lateral elbow pain. Cochrane Database Syst Rev. 2021 Sep 30;9(9):CD010951. doi: 10.1002/14651858.CD010951.pub2. PMID: 34590307; PMCID: PMC8481072.
3. Cavallo C, Roffi A, Grigolo B, Mariani E, Pratelli L, Merli G, Kon E, Marcacci M, Filardo G. Platelet-Rich Plasma: The Choice of Activation Method Affects the Release of Bioactive Molecules. Biomed Res Int. 2016;2016:6591717. doi: 10.1155/2016/6591717. Epub 2016 Sep 8. PMID: 27672658; PMCID: PMC5031826
4. la Fleur P, Argáez C. Platelet-Rich Plasma Injections for Wound Healing and Tissue Rejuvenation: A Review of Clinical Effectiveness, Cost-Effectiveness and Guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2017 Jun 13. PMID: 30188645.
5. Woodley BL, Newsham-West RJ, Baxter GD. Chronic tendinopathy: effectiveness of eccentric exercise. Br J Sports Med. 2007 Apr;41(4):188-98; discussion 199. doi: 10.1136/bjsm.2006.029769. Epub 2006 Oct 24. PMID: 17062655; PMCID: PMC2658941.

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LECTURE

Mechanisms underlying exercise-dependant remodelling of the sarcotubular system: the role of temperature and pH

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Skeletal muscle function is regulated by intracellular Ca^{2+} levels. Two main mechanisms control movements of Ca^{2+} ions from intracellular stores (i.e. the sarcoplasmic reticulum, SR) and from extracellular space: i) excitation-contraction (EC) coupling; and ii) store-operated Ca^{2+} entry (SOCE). SOCE is a mechanism that allows recovery of external Ca^{2+} when intracellular stores (i.e. the sarcoplasmic reticulum, SR) are depleted. We recently discovered that SOCE is mediated by specialized intracellular junctions named Calcium Entry Units (CEUs), which increase in number and size during exercise. CEUs are formed by two elements: i) SR stacks containing STIM1; and ii) I-band extensions of the transverse tubule (TT) containing Orai1 (1-3). The mechanisms underlying exercise-dependent formation of CEUs remain to be elucidated. First, we verified that functional CEUs can assemble *ex-vivo* in absence of blood supply and innervation, subjecting isolated extensor digitorum longus (EDL) muscles from wild type (WT) mice to an *ex-vivo* exercise protocol. Then, we evaluated if temperature and pH, parameters that are influenced by exercise, may promote the assembly of CEUs. Results collected indicate that higher temperature (36°C vs. 25°C) and lower pH (7.2 vs. 7.4) promote the formation of CEUs increasing the percentage of fibers containing SR stacks, the n. of SR stacks/area, and the elongation of TTs at the I band. Functionally, assembly of CEUs at higher temperature (36°C) or at lower pH (7.2) correlates with increased fatigue resistance of EDL muscles in presence of extracellular Ca^{2+}.

Key words: Exercise; excitation-contraction (EC) coupling; skeletal Muscle; Store-Operated Ca^{2+} Entry (SOCE).

References

1. Boncompagni, S., A. Michelucci, L. Pietrangelo, R. T. Dirksen, and F. Protasi. 2017. Exercise-dependent formation of new junctions that promote STIM1-Orai1 assembly in skeletal muscle. Scientific Reports. 7(1): 14286. PMID: 29079778
2. Michelucci, A., S. Boncompagni, L. Pietrangelo, M. García-Castañeda, T. Takano, S. Malik, R.T. Dirksen, and F. Protasi. 2019. Transverse tubule remodeling enhances Orai1-dependent Ca2+ entry in skeletal muscle. eLife. 8: e47576. PMID: 31657717
3. Protasi, F., L. Pietrangelo, and S. Boncompagni. 2020. Calcium entry units (CEUs): perspectives in skeletal muscle function and disease. J Muscle Res Cell Motil. 42(2): 233-249. PMID: 32812118

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SATURDAY April 1, 2023

Conference Hall, Hotel Petrarca, Thermae of Euganean Hills (Padua) Italy

09:00 AM Session XI:
LBI workshop on muscle rehabilitation - from mouse to elderly

Sandra Zampieri, Feliciano Protasi, Chairs

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Mimicking disuse and rehabilitation in a mouse model

Laura Pietrangelo, Alice Brasile, Barbara Girolami, Feliciano Protasi (1,2)

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Proper skeletal muscle function is controlled by intracellular Ca^{2+} levels and by efficient production of energy (ATP). In the last 15 years our laboratory collected the following results:

a. Short-term (7-15 days) denervation of muscle fibers causes misplacement and damage of membrane structures involved in EC coupling (calcium release units, CRUs) and of the mitochondrial network;[1]
b. Sedentary ageing causes partial disarray/damage of CRUs and of calcium entry units (CEUs, structures involved in SOCE) and loss/misplacement of mitochondria;[2,3]
c. Re-innervation and regular exercise promote rescue/maintenance of the proper architecture of CRUs, CEUs, and mitochondria in both denervation and ageing.[1,3]

All these structural changes were accompanied by related functional changes, i.e. loss/decay in function caused by denervation and ageing, and improved function following re-innervation and exercise. These data suggested that integrity and proper disposition of intracellular organelles deputed to Ca^{2+} handling and aerobic generation of ATP is challenged by inactivity (or reduced activity) and improved following recover of movements.[4] To definitely test this hypothesis, we generated a model of short-term inactivity, and randomly assigned mice to two experimental groups: i) immobilized adult mice, in which inactivity is obtained for 6 days by unilateral immobilization of a hind limb; ii) rehabilitation group, in which mice underwent 15 days of treadmill running after the immobilization procedure. The results collected in this study indicate that: i) even short-term inactivity caused significant alterations to the membrane system and organelles previously discussed; and ii) 2 weeks rehabilitation rescued proper intracellular organization of CRUs, CEUs, and mitochondria.

Key Words: Mitochondria; excitation-contraction coupling; store operated calcium entry; immobilization; exercise.

Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

References
1. Pietrangelo L, Michelucci A, Ambrogini P, Sartini S, Guarnier FA, Fusella A, Zamparo I, Mammucari C, Protasi F, Boncompagni S. Muscle activity prevents the uncoupling of mitochondria from Ca^{2+} Release Units induced by ageing and disuse. Arch Biochem Biophys. 2019 Mar 15;663:22-33. doi: 10.1016/j.abb.2018.12.017. Epub 2018 Dec 20. PMID: 30578752; PMCID: PMC6377823.
2. Zampieri S, Pietrangelo L, Loefler S, Fruhmann H, Vogelauer M, Burggraf S, Pond A, Grim-Stieger M, Cvecka J, Sedliak M, Tirpáková V, Mayr W, Sarabon N, Rossini K, Barberi L, De Rossi M, Romanello V, Boncompagni S, Musarò A, Sandri M, Protasi F, Carraro U, Kern H. Lifelong physical exercise delays age-associated skeletal muscle decline. J Gerontol A Biol Sci Med Sci. 2015 Feb;70(2):163-73. doi: 10.1093/gerona/glu006. Epub 2014 Feb 18. PMID: 24550352.
3. Boncompagni S, Pecorai C, Michelucci A, Pietrangelo L, Protasi F. Long-Term Exercise Reduces Formation of Tubular Aggregates and Promotes Maintenance of Ca^{2+} Entry Units in Aged Muscle. Front Physiol. 2021 Jan 5;11:601057. doi: 10.3389/fphys.2020.601057. PMID: 33469430; PMCID: PMC7813885.
4. Protasi F, Pietrangelo L, Boncompagni S. Improper Remodeling of Organelles Deputed to Ca^{2+} Handling and Aerobic ATP Production Underlies Muscle Dysfunction in Ageing. Int J Mol Sci. 2021 Jun 8;22(12):6195. doi: 10.3390/ijms22126195. PMID: 34201319; PMCID: PMC8228829.

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Molecular biological basis and effects of immobility and training in young and aging

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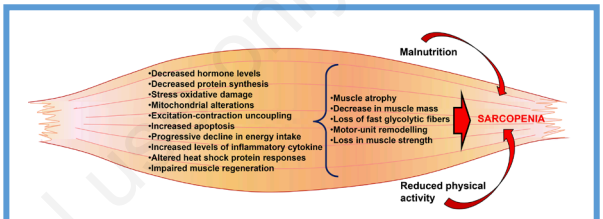
The progressive age-related decline in skeletal muscle mass and strength (sarcopenia), responsible for impaired mobility and disability in elderly is the result of multiple molecular and cellular changes occurring during the aging process, including an imbalance between protein synthesis and degradation, changes in metabolic/hormonal status and in circulating levels of inflammatory mediators.[1,2] Loss of motor units, decrease in structural and functional integrity of neuromuscular junctions, decline in mitochondrial function, and altered autophagic mechanism represent other pathogenic mechanisms of muscle aging.[3] Thus, factors/conditions that increase muscle mass and promote anabolic pathways might be of therapeutic benefit to counteract sarcopenia.[4] Current data, also from our lab, point out that the development of muscle wasting is a multifactorial process and believed to be the result of both intrinsic factors, involving changes in molecular and cellular levels, and extrinsic ones, such as nutrition and exercise. Many factors, including motor-unit remodeling, decreased hormone levels with consequent negative effect on protein synthesis, stress oxidative damage,



Schematic representation of the potential extrinsic factors, such as reduction in nutrition and exercise, and intrinsic ones, involving in muscle wasting and sarcopenia.

alteration in satellite cells activity may all contribute to decrease in muscle mass and functional performance.[5-7] Despite numerous theories and intensive research, the principal molecular mechanisms underlying the process of muscle wasting are still unknown. Here we provide insights into the cellular and molecular mechanisms that control muscle atrophy, adaptation/response of muscle to immobilization/disuse and exercise/training. We explored whether and how long-term physical exercise modulates relevant biomarkers of muscle function, atrophy, and remodeling. To reach this objective we took advantage of using in vivo experimental models of disuse and training and human samples from regularly active, sedentary/regularly active and athlete individuals. The molecular data suggest that regular activity and lifelong physical activity induce molecular adaptations of muscle, counteracting muscle atrophy and improving functional outcomes with positive influence on quality of life.

Key words: Aging; sarcopenia; muscle wasting; physical exercise; molecular mechanisms.

References
1. Larsson L, Degens H, Li M, Salviati L, Lee YI, Thompson W, Kirkland JL, Sandri M. Sarcopenia: Aging-Related Loss of Muscle Mass and Function. Physiol Rev. 2019 Jan 1;99(1):427-511.
2. Barberi L, Scicchitano BM, Musaro A. Molecular and Cellular Mechanisms of Muscle Aging and

Sarcopenia and Effects of Electrical Stimulation in Seniors. Eur J Transl Myol. 2015 Aug 25;25(4):231-6.
3. Franco-Romero A, Sandri M. Role of autophagy in muscle disease. Mol Aspects Med. 2021 Dec; 82:101041.
4. Musarò A. To the heart of the problem. mIGF-1: local effort for global impact. Aging (Albany NY). 2012.
5. Musarò A, Scicchitano BM. Counteracting sarcopenia: the role of IGF-1 isoforms. Aging (Albany NY). 2019 Jun 13;11(11):3410-3411.
6. Ascenzi F, Barberi L, Dobrowolny G, Villa Nova Bacurau A, Nicoletti C, Rizzuto E, Rosenthal N, Scicchitano BM, Musarò A. Effects of IGF-1 isoforms on muscle growth and sarcopenia. Aging Cell. 2019 Jun;18(3): e12954.
7. Scicchitano BM, Pelosi L, Sica G, Musarò A. The physiopathologic role of oxidative stress in skeletal muscle. Mech Ageing Dev. 2018 Mar; 170:37-44

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C-Terminal Agrin Fragment as a biomarker of muscle wasting and weakness in aging and disuse

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In the last decades, the extended human longevity resulted in increasing numbers of senior individuals in the general population. Ageing is accompanied by a progressive decline in muscle mass and function. It is associated with increased risk of adverse outcomes including knee or hip injuries and degeneration, falls, or bone fractures, possibly determining the onset of a clinical syndrome termed sarcopenia. Sarcopenia is not only caused by ageing (primary sarcopenia) but may be linked to the presence of several co-morbidities (secondary sarcopenia), such as disuse/inactivity, advanced organ failure, or inadequate intake of energy/proteins. Denervation and NMJ impairment have been proposed as key determinants of age-related muscle wasting and weakness. Thus, screening, monitoring and prevention of those conditions inducing muscle dysfunction is essential to improve the quality of life, potentially reducing ageing and sarcopenia-related social and economic costs. To this aim, the reliability and accessibility of non-invasive blood derived biomarkers is being evaluated. C-terminal Agrin Fragment (CAF), a circulating C-22 kDa peptide resulting from the proteolytic cleavage of agrin, a protein responsible for the neuromuscular junction (NMJ) assembly and maintenance, has been widely investigated by us and numerous other groups as circulating NMJ-related biomarker of muscle dysfunction. Essentially, serum CAF concentration was observed to increase with age and in sarcopenic individuals when compared to age-matched, medically stable peers. Serum CAF was reported also to raise following chronic inactivity or disuse and seemed to be lowered or maintained by exercise training. Finally, CAF was found to correlate with appendicular lean mass, handgrip and gait speed. Therefore, CAF seems to be a specific biomarker for screening and monitoring muscle wasting and weakness. It may be a useful tool for tailored approaches of muscle rehabilitation and for prevention or rescue of muscle dysfunction. When findings will be confirmed on larger cohort of subjects, future guidelines may be implemented for introducing CAF as a biomarker in clinical settings.
Key Words: C-terminal Agrin Fragment; aging; sarcopenia; muscle wasting; muscle weakness.
References
1. Hettwer S, Dahinden P, Kucsera S, Farina C, Ahmed S, Fariello R, Drey M, Sieber CC, Vrijbloed JW. Elevated levels of a C-terminal agrin fragment identifies a new subset of sarcopenia patients. Exp Gerontol. 2013 Jan;48(1):69-75. doi: 10.1016/j.exger.2012.03.002. Epub 2012 Mar 11. PMID: 22433628.
2. Gonzalez-Freire M, de Cabo R, Studenski SA, Ferrucci L. The Neuromuscular Junction: Aging at the Crossroad between Nerves and Muscle. Front Aging Neurosci. 2014 Aug 11;6:208. doi: 10.3389/fnagi.2014.00208. PMID: 25157231; PMCID: PMC4127816.
3. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. Age

Ageing. 2019 Jan 1;48(1):16-31. doi: 10.1093/ageing/afy169. Erratum in: Age Ageing. 2019 Jul 1;48(4):601. PMID: 30312372; PMCID: PMC6322506.
4. Stephan A, Mateos JM, Kozlov SV, Cinelli P, Kistler AD, Hettwer S, Rülicke T, Streit P, Kunz B, Sonderegger P. Neurotrypsin cleaves agrin locally at the synapse. FASEB J. 2008 Jun;22(6):1861-73. doi: 10.1096/fj.07-100008. Epub 2008 Jan 29. PMID: 18230682.
5. Monti E, Sarto F, Sartori R, Zanchettin G, Lofler S, Kern H, Narici M, Zampieri S. C-terminal agrin fragment as a biomarker of muscle wasting and weakness: a narrative review. Journal of Cachexia, Sarcopenia and Muscle, 2023 in press. DOI: 10.1002/jcsm.13189.

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Exercise intervention in elderly: a novel system within the Centre of Active Aging in Bratislava

Jan Cvecka, University of Bratislava, Slovakia

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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Relationship between 24-hour movement behaviour and physical performance in older adults: A cross-sectional insight into the Centre of active ageing data

Nejc Sarabon, University of Primorska, Slovenia

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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AMB-REMOB – results of an early outpatient rehabilitation program

Stefan Loefler, Helmut Kern, LBI Rehabilitation Research, Vienna, Austria

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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Outcomes of early rehabilitation in elderly patients

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In recent years, the prevalence of chronic diseases has increased, especially in the aging population. Rehabilitation plays a key role in alleviating and even preventing the physical limitations associated with aging and living with chronic diseases. Unfortunately, many older people who could benefit from inpatient follow-up rehabilitation (WHO Phase II) do not have access to it because of their fragile health status after hospitalization. To bridge the gap between primary/acute care and rehabilitation, the concept of transitional rehabilitative care was introduced. This has allowed patients to spend fewer days in the hospital, avoiding long hospital stays and the need for long-term care. To evaluate the effectiveness of this transitional care, a pilot project was conducted in 2022 with 114 patients. Of these, 50 patients participated in at least three measurement time points (with a mean length of stay of 7 ± 3 weeks), and 36 patients were followed up 24 weeks after admission (t4). The sample had a mean age of 82 ± 7 years, with 88% of patients being female. The results of the study showed significant improvements in care needs (Barthel Index, HAQ), quality of life (pain, EQ-VAS), and physical mobility (Timed Up-and-Go Test, 10m gait speed) from the beginning (t1) to the end (t3) of the stay. This was especially true for the first three weeks of treatment (t1-t2). However, at follow-up 24 weeks after admission (t4), there was a marked deterioration in quality of life. Nevertheless, after six months, more than 80% of geriatric patients received both private (5 ± 7 hours per week) and/or professional (13 ± 12 hours per week) care at home, and only 15% of patients were in a long-term care facility. Qualified transitional care and rehabilitation is essential to enable elderly, multimorbid patients to return to independent living at home. The results of this study provide evidence for this and will be used to develop an evidence-based treatment pathway for early rehabilitation of geriatric patients.
Key Words: Chronic diseases; ageing; transitional care; geriatrics; rehabilitation.

Eur J Transl Myol 33 (1) 11247. doi: 10.4081/ejtm.2023.11247

References
1. Grote V, Unger A, Böttcher E, Muntean M, Puff H, Marktl W, Mur E, Kullich W, Holasek S, Hofmann P, Lackner HK, Goswami N, Moser M. General and Disease-Specific Health Indicator Changes Associated with Inpatient Rehabilitation. J Am Med Dir Assoc. 2020 Dec;21(12):2017.e10-2017.e27. doi: 10.1016/j.jamda.2020.05.034. Epub 2020 Jul 28. PMID: 32736990.
2. Grote V, Böttcher E, Unger A, Hofmann P, Moser M, Fischer MJ. Observational study of an inpatient program for musculoskeletal disorders: The effects of gender and physical activity. Medicine (Baltimore). 2021 Oct 29;100(43):e27594. doi: 10.1097/MD.0000000000027594. PMID: 34713836; PMCID: PMC8556041.
3. Tschuggnall M, Grote V, Pirchl M, Holzner B, Rumpold G, Fischer MJ. Machine learning approaches to predict rehabilitation success based on clinical and patient-reported outcome measures. Informatics in Medicine Unlocked 2021, 24, 100598, doi:10.1016/j.imu.2021.100598.
4. Wagner B, Zdravkovic A, Pirchl M, Puhan MA, Zwick RH, Grote V, Crevenna R, Fischer MJ. Performance Score (T2D)-A New Perspective in the Assessment of Six-Minute Walking Tests in Pulmonary Rehabilitation. Diagnostics (Basel). 2022 Oct 3;12(10):2402. doi: 10.3390/diagnostics 12102402. PMID: 36292092; PMCID: PMC9601141.
5. Zdravkovic A, Grote V, Pirchl M, Stockinger M, Crevenna R, Fischer MJ. Comparison of patient- and clinician-reported outcome measures in lower back rehabilitation: introducing a new integrated performance measure (t2D). Qual Life Res. 2022 Jan;31(1):303-315. doi: 10.1007/s11136-021-02905-2. Epub 2021 Jun 15. PMID: 34129172; PMCID: PMC8800917.

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LECTURE

Underwather physiotherapy after knee replacement

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On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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Case Study: The use of Balneotherapy in a comprehensive integrative medicine treatment plan for Fibromyalgia

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The successful treatment of Fibromyalgia is multifaceted and requires a patient specific approach.
The addition of Balneotherapy into the treatment plan for Fibromyalgia represents a multi-system intervention that can be incorporated alongside conventional and integrative therapies. The rationale for Balneotherapy will be reviewed along with the synergistic applications between Balneotherapy and integrative treatment plans.[1-5] A case review will be presented highlighting the use of a Health Resort intervention focusing on Balneotherapy in the on-going management of a patient with Fibromyalgia, and case management concepts will be presented for discussion.

The Springs Resort, Pagosa Springs, Colorado, USA

Key Words: Balneotherapy; fibromyalgia; health resort medicine; integrative medicine; physical medicine.
References
1. Evcik D, Kizilay B, Gökçen E. The effects of balneotherapy on fibromyalgia patients. Rheumatol Int. 2002 Jun;22(2):56-9. doi: 10.1007/s00296-002-0189-8. Epub 2002 Mar 29. PMID: 12070676.
2. Ardiç F, Ozgen M, Aybek H, Rota S, Cubukçu D, Gökgöz A. Effects of balneotherapy on serum IL-1, PGE2 and LTB4 levels in fibromyalgia patients. Rheumatol Int. 2007 Mar;27(5):441-6. doi: 10.1007/s00296-006-0237-x. PMID: 17033835.
3. Fraioli A, Grassi M, Mennuni G, Geraci A, Petraccia L, Fontana M, Conte S, Serio A. Clinical researches on the efficacy of spa therapy in fibromyalgia. A

systematic review. Ann Ist Super Sanita. 2013;49(2):219-29. doi: 10.4415/ANN_13_02_13. PMID: 23771266.
4. Cao CF, Ma KL, Li QL, Luan FJ, Wang QB, Zhang MH, Viswanath O, Myrcik D, Varrassi G, Wang HQ. Balneotherapy for Fibromyalgia Syndrome: A Systematic Review and Meta-Analysis. J Clin Med. 2021 Apr 3;10(7):1493. doi: 10.3390/jcm10071493. PMID: 33916744; PMCID: PMC8038322.
5. Clauw DJ. Fibromyalgia: a clinical review. JAMA. 2014 Apr 16;311(15):1547-55. doi: 10.1001/jama.2014.3266. PMID: 24737367.

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World Thermal Clusters

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On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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Health Resort Medicine and rehabilitation in the Euganean Hills Thermae: Building the future

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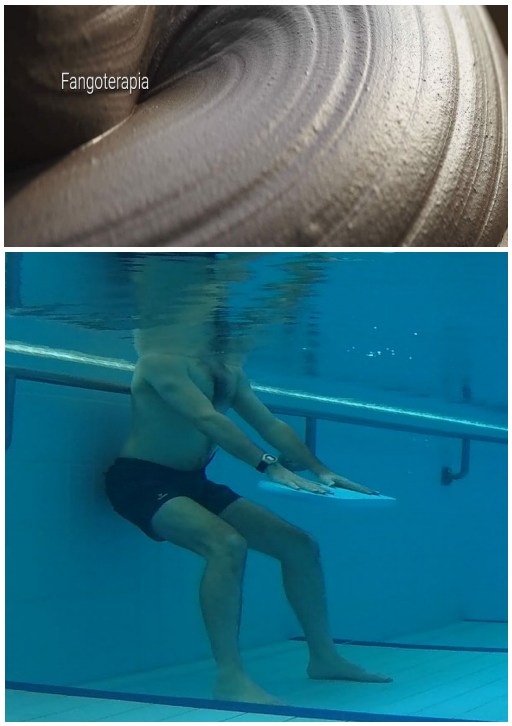
In recent years rapid and epoch-making changes have taken place in all the medicine fields. Rehabilitation has been one of the areas most affected by these changes, accelerated also by the COVID-19 pandemic. In this context, it is essential to determine new rehabilitation settings, which can represent appropriate alternatives to the hospital setting, closer to the community. Health resort facilities, thanks to the presence of a multidisciplinary staff and the possibility of exploiting synergies between traditional spa treatments and rehabilitative interventions (physical energies, respiratory, balance and muscle strengthening exercises, water massage, therapeutic massage, etc.),[1] can be appropriate rehabilitative settings for patients suffering from musculoskeletal, cardiorespiratory and neurological disabilities.1 Aquatic exercise has several well-known therapeutic effects due to the physical properties of the immersion in water. To these, the anti-inflammatory, myorelaxant and antalgic effects of the thermal mineral-rich waters must be added. Rehabilitation programs conducted in the Health Resort settings also have a positive impact on quality of life, as the environment itself promotes patients' sociality and general well-being. Innovative rehabilitative approaches can be proposed in the Health Resort setting due to its many properties. Recently, research projects that broaden the horizons of Health Resort Medicine are being conducted at the Euganean Hills Thermae with the scientific support of the University of Padua. Innovative rehabilitation protocols have been proposed for the management of patients with musculoskeletal disabilities resulting from orthopedic surgery, for patients suffering of movement disorders secondary to neurodegenerative diseases and for subjects with Long Covid outcomes.[2-5] All protocols allow integration between traditional spa treatments (Figure) and advanced technologies, including Telerehabilitation, and demonstrated positive effects in ameliorating patients motor function and quality of life. The increasing development of innovative rehabilitation protocols in the Health Resort setting may have significant social, health



Fango (mud, top) and balneo physiotherapy for the hands (bottom) at the Thermae of Euganean Hills, Padua, Italy

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and economic consequences. Therefore, in the future comprehensive scientific research should be conducted in order to confirm their efficacy and safety.

Key Words: Balneotherapy; aquatic exercise, telerehabilitation, long covid, COVID-19 pandemic syndrome.

References

1. Tognolo L, Coraci D, Fioravanti A, Tenti S, Scanu A, Magro G, Maccarone MC, Masiero S. Clinical Impact of Balneotherapy and Therapeutic Exercise in Rheumatic Diseases: A Lexical Analysis and Scoping Review. Applied Sciences. 2022; 12(15):7379.
2. Lobanov AA, Irina A Grishechkina, Andronov SV, Gleb N Barashkov, Andrey I Popov, Anatoliy D Fesyun, Elena P Ivanova, Maccarone MC, Stefano Masiero. Can aquatic exercises contribute to the improvement of the gait stereotype function in patients with Long COVID outcomes? Eur J Transl Myol. 2022 Jul 14;32(3):10698. doi: 10.4081/ejtm.2022.10698. PMID: 35833897; PMCID: PMC9580543.
3. Masiero S, Maccarone MC. Health resort therapy interventions in the COVID-19 pandemic era: what next? Int J Biometeorol. 2021 Nov;65(11):1995-1997. doi: 10.1007/s00484-021-02134-9. Epub 2021 Apr 21. PMID: 33880643; PMCID: PMC8057917.
4. Maccarone MC, Masiero S. Can spa rehabilitative interventions play a role for patients suffering from neurodegenerative disorders at the early stages? A scoping review. Int J Biometeorol. 2022 Dec;66(12):2369-2377. doi: 10.1007/s00484-022-02369-0. Epub 2022 Sep 21. PMID: 36129582; PMCID: PMC9684286
5. Maccarone MC, Magro G, Albertin C, Barbetta G, Barone S, Castaldelli C, Manica P, Marcoli S, Mediati M, Minuto D, Poli P, Sigurtà C, Raffaetà G, Masiero S. Short-time effects of spa rehabilitation on pain, mood and quality of life among patients with degenerative or post-surgery musculoskeletal disorders. Int J Biometeorol. 2023 Jan;67(1):29-36. doi: 10.1007/s00484-022-02381-4. Epub 2022 Oct 8. PMID: 36207541; PMCID: PMC9546417.

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2023Pdm3 April 1 - Abstract 92

Technological transition of different rehabilitation approaches: challenges and answers

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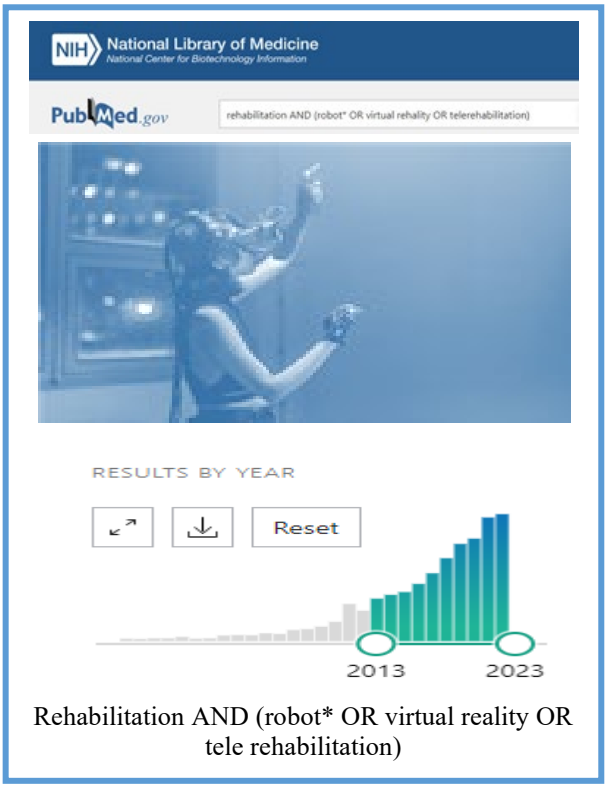
Medicine, in its history, has shown important innovations fundamental for increasing life duration and for implementing quality of life. In the last decades, Medicine has seen a constant transformation, with a larger and larger dialogue between physicians and high-tech tools. Rehabilitation is an emblematic field where this technological innovation is regularly present. Indeed, in rehabilitation, we have a lot of new tools useful for evaluation and treatment. However, one of the main issues only poorly analyzed in research is the implications for society and policies of the technological transition. In fact, the simple adaptation of an industrial device (for example a robot) for medical application does not necessarily imply a real clinical and efficient applicability for patients. A complex relationship of multiple systems on multiple levels is required: different networks (research, industrial, cultural, financial, user-related) mutually interact and they interact with the sociotechnical progress. Concerning the technologies used in rehabilitation, this complex interaction should be assessed to understand how single innovations can transform the medical and social systems and how the worldwide recent challenges (pandemic, war, economic/financial crisis) can modulate the future technological transformation of Medicine. We analyzed the literature data about three common technology-based rehabilitation approaches: robotics, virtual reality and telerehabilitation (including rehabilitation in additional



Rehabilitation AND (robot* OR virtual reality OR tele rehabilitation)

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settings, like the thermae). The analysis was performed in order to assess the consequences on the medical and social systems of the approaches. The analysis revealed a continuous high interest in the approaches but confirms the rare estimation of their consequences from a multi-system point of view. In conclusion, rehabilitation should have a key role in the future development of Medicine, but we need a large implementation of our vision. Future research should focus on the factors determining the applicability and the success of the different rehabilitation approaches to get a real and efficient technological transition.

Key Words: Rehabilitaation; robotics; virtual reality; tele-rehabilitation; technology transition.

References

1. McLeish C, Johnstone P, Schot J. The changing landscape of deep transitions: Sociotechnical imprinting and chemical warfare. Environmental Innovation and Societal Transitions 2022;43:146-159.
2. Coraci D, Capobianco SV, Romano M, Calvaruso S, Vecchio M, Giovannini S, Loreti C, Fusco A, Masiero S, Santilli V, Padua L. Neuropathic Pain and Ultrasonography: A Multiperspective Literature Evaluation. Diagnostics (Basel). 2021 Sep 17;11(9):1705. doi: 10.3390/diagnostics11091705. PMID: 34574046; PMCID: PMC8470278.

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2023Pdm3 April 1 - Abstract 93

Balneotherapy - prospects for the development of health tourism in Bulgaria

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Balneological resorts offerd different rehabilitation proceedures with mineral water, hydrotherapy, showers, pearl and mud baths, tangentor, jacuzzi, balneotherapy, etc.

European countries are among the most popular health tourism destinations worldwide. Currently, the European health market is undergoing intense processes of transformation and the identification of new trends for this type of tourism in conditions of great competition. Their research is essential in order to draw attention to balneo resorts and to support Bulgarian health (medical) tourism. Bulgaria has significant potential to develop health tourism with an emphasis on balneology (Medical SPA and Wellness SPA). The results of the systematic review in the scientific databases PubMed, Scopus, Medline, etc., indicate that among the European countries with the largest number of balneo resorts and developed rehabilitation tourism are Italy (180), Germany (131) and Spain (106). These countries also have the largest number of patients who used the services of spa and wellness resorts. There are 47 balneological resorts in Bulgaria with over 225 mineral springs of different composition and temperature. The healing properties of the waters have a scientifically proven effect in the treatment of a wide range of diseases. Currently, the prices of the medical services offered in our country are extremely attractive, and our country has the potential to receive patients from other countries. The climate, mineral springs, nature and cultural attractions allow combining rest and prevention with treatment and rehabilitation of a number of socially significant diseases. Promoting health SPA treatments as preventive medicine and enhancing specific rehabilitation training programs are the future perspective of developing health tourism in Bulgaria.

Key Words: Balneotherapy; health tourism; spa and wellness; rehabilitation; hydrotherapy.

References

1. Yurcu G, Wellness and Spa Tourism. J Tourism Hospit. 2017;6:2 DOI: 10.4172/2167-0269.1000274 ISSN: 2167-0269.
2. https://globalwellnessinstitute.org/wpcontent/uploads/2018/10/Dr.-Natalia-Tchaourskaia-European-Association-of-Patients-and-Users-of-Thermal-Centers-Activities-and-Programs.pdf (Visited 18.01.2023)

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3. https://www.mh.government.bg/bg/informaciya-za-grazhdani/rehabilitaciya-i-balneoturizm/spisk-na-bazite-za-rehabilitaciya/ (Visited 18.01.2023)
4. https://www.tourism.government.bg/bg/kategorii/strategicheski-dokumenti/nacionalna-strategiya-za-ustoychivo-razvitie-na-turizma-v (Visited 19.01.2023)
5. https://www.eaptc.net/ (Visited 19.01.2023)

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2023Pdm3 April 1 - Abstract 94

Modern methods of neuro-rehabilitation

Andrey Rachin,
Rehabilitation and Balneology Center, Moscow, Russia

On-site presentation of unpublished results. The author denied Zoom circulation, recording and post-meeting dissemination by YOUTUBE

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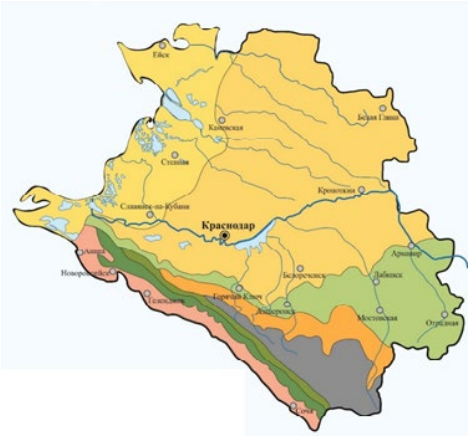
Correction of increased meteosensitivity of obese patients when using Terrainkur, taking into account the bioclimatic characteristics during stay in health resorts

Maxim Yu. Yakovlev, Anatoliy D. Fesyun, Irina A. Grishechkina, Igor P. Bobrovnitkyi, Andrey A. Parfenov, Elena A. Valtseva, Michail V. Nikitin, Sergey A. Pavlovskyi

National medical research center for rehabilitation and balneology, Moscow, Russia

Obesity (overweight) is a common multifactorial multisystem disease associated with a high incidence of cardiovascular diseases.[1,2] Graduated physical exercise is the main therapeutic intervention.[3] The combination of exercise with climatotherapy (terrainkur) cumulates the therapeutic effect. However, external meteorological conditions and meteotropic reactions that occur in the patient must be taken into account, which can neutralise the achieved therapeutic effect.[4] The aim of the work is to improve the effectiveness and safety of the use of the health resort in the treatment of overweight patients by using digital bioclimatic prediction technology and microclimatic zoning. Evaluation of the bioclimatic potential of Krasnodar territory and microzonation of the area where “Vulan” sanatorium and resort complex is located. Verbal and communicative examination of 735 patients in “Vulan” sanatorium and resort complex using "Method of evaluation of human meteosensitivity" (Patent No. 2736612 C1 of 19.11.2020) was carried out. Based on data from weather stations in Gelendzhik, Novorossiysk, Krasnodar and Vulan sanatorium and resort complex, a risk model for the development of hypertensive crisis was made for the first time for this area. It has been established that the macroclimatic characteristics of Krasnodar territory vary over a wide range throughout the year, which is due to the physical and geographical features of the region, namely a sharp transition from a continental dry climate in Taman and on the border with Stavropol territory to a moderately continental one in the Kuban lowlands, from a cold climate in the highlands to a subtropical one on the Black Sea coast (Figure).

Based on the meteorological data obtained, a risk model for the development of hypertensive crisis was built. A binary logistic regression formula was obtained, which allows predicting days with an increased risk of hypertensive crisis development and giving individual recommendations to obese patients on physical training and on the selection of a terrainkur route based on the results of the microclimatic zoning. Analysis of subjective evaluation of meteosensitivity showed that overweight patients had meteopathic reactions of the following nature in 95,5% of cases: headache (59,49%), increased blood pressure (47,03%), weakness, decreased activity (42,49%), drowsiness (41,36%), joint pain (40,51%). An association between the severity of meteopathy and the presence of more comorbidities was found ($\chi 2=20.83$, $p < 0.01$). The methods for the correction of increased meteosensitivity using terrainkur, taking into account the bioclimatic characteristics of the weather conditions during the period of stay in health resort in obese patients enable the correction of the emerging weather-related reactions and consequently maintain and enhance the achievable therapeutic effects.



Types of climate in the Krasnodar Territory. The climate of the study area is indicated by colors: pink - dry subtropical climate, black - high-mountain climate, green - mid- and low-mountain temperate continental forest climate

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Key words: Obesity; cardiovascular diseases; meteopathic reactions; weather-related diseases.

References

1. Forouzanfar M.H., Afshin A., Alexander L.T., et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388(10053): 1659-1724.
2. Nguyen NT, Magno CP, Lane K, et al. Association of Hypertension, Diabetes, Dyslipidemia, and Metabolic Syndrome with Obesity: Findings from the National Health and Nutrition Examination Survey, 1999 to 2004. J. Am. Coll. Surg. 2008; 6(207): 928-34
3. Bessesen D., Kushner R. Evaluation & Management of Obesity. Philadelphia: Hanley & Belfus. 2002, 6.
4. Barashkov G.N., Sergeev V.N. Physical training by walking and health path - modern approaches and opportunities at the resort. Vestnik fizioterapii i kurortologii (Bulletin of physiotherapy and balneology). 2020; 26 (1): 47-54. (In Russian).

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Video analysis of patients' gait during Terrainkur in obese people

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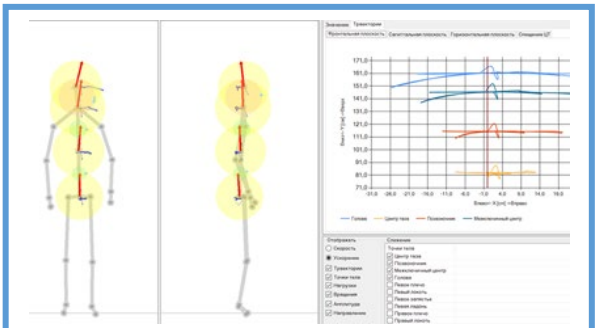
Overweight and obesity is a multifactorial, multisystem disease that the World Health Organization (WHO) declared a global epidemic back in 1997.[1] In Russia, at least 30% of the Russian working-age population is overweight.[2] The use of physical activity as an essential (basic) part of treating obesity and maintaining the body weight achieved during the body weight treatment can provide a durable and long-lasting treatment result, as well as significant changes in body composition (body fat / lean body mass ratio).[3,4] The combination of physical activity (Terrainkur) and climatotherapy results in the cumulation and mutual potentiation of the therapeutic effect. One of the problems in performing physical activity in obese individuals is the difficulty experienced by this category of patients in performing physical activity as a result of impaired walking patterns due to imbalances in the muscular circuits, including the pelvic region, cervical region, which reduces endurance and



Schematic representation of measurement points, the size and deviation of the main directions of movement, the trajectory of movement of the main body parts.

commitment to physical activity.[5,6] The study revealed that the exposure group (Terrainkur) demonstrated lower values of "total fat", "metabolic age", " basic calorie intake" compared to baseline results and the control group; the exposure group (Terrainkur) revealed a decrease in the deviation of the centre of body axis projection from the proper axis, percentage of nonconformity with the proper fluctuations of ankle underextension. These changes contributed to the elimination of restrictions during the terrainkur and, as a result, increased compliance of the patients with the terrainkur exercises.

Key words: Overweight; habilect; walking; gait; software.

References:

1. Guénard, F.; Houde, A., Bouchard, L., Tchernof, A., Deshaies, Y., Biron, S., Lescelleur, O., Biertho, L., Marceau, S., Pérusse, L., Vohl, M.C. Association of LIPA gene polymorphisms with obesity-related metabolic complications among severely obese patients. Obesity (Silver Spring). 2012; 20(10): 2075-82.
2. Mel'nichenko, G.A., Romantsova, T.I. Ozhirenie: epidemiologiya, klassifikatsiya, patogenez, klinicheskaya simptomatika i diagnostika [Obesity: epidemiology, classification, pathogenesis, clinical symptoms and diagnosis]; MIA, Moscow, Russian Federation, 2004. 456 p. [In Russian].
3. Wimalawansa, S.J. Controlling Obesity and Its Complications by Elimination of Causes and Adopting Healthy Habits: «Cause-Driven» Approach. Advances in Medical Sciences. 2014; 3 (1): P. 1-15.
4. Salimgareeva, I.A., Ahmadullin, R.V., Gil'mutdinova, L.T., Gabdullin, N.T. Dietoterapiya ozhireniya v usloviyah sanatoriya [Diet therapy of obesity in a sanatorium]. Actual problems of restorative medicine, balneology and physiotherapy, Proceedings of the International Congress. "All-Russian forum "Zdravnitsa 2003", Moscow, Russian Federation, 2003. P. 172.
5. Platonov, V.N. Sohranenie i ukreplenie zdorov'ya lyudej – prioritetnoe napravlenie sovremennogo

zdravoohraneniya [Preservation and strengthening of people's health is a priority direction of modern health care]. Sportivnaya medicina 2006; 2: P. 3–14.
6. Barieva, Yu.B., Botvineva, L.A., Kajsinova, A.S., Samsonova, N.A. Rol' fizicheskih nagruzok i pit'evyh mineral'nyh vod v profilaktike i lechenii abdominal'nogo ozhireniya - osnovy metabolicheskogo sindroma [The role of physical activity and drinking mineral water in the prevention and treatment of abdominal obesity - the basis of the metabolic syndrome]. Fizioterapiya, bal'neologiya i reabilitaciya 2017; 16 (5): P. 228-233.

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Comparative characteristics of long-term outcomes of rehabilitation programmes in patients with post-COVID syndrome

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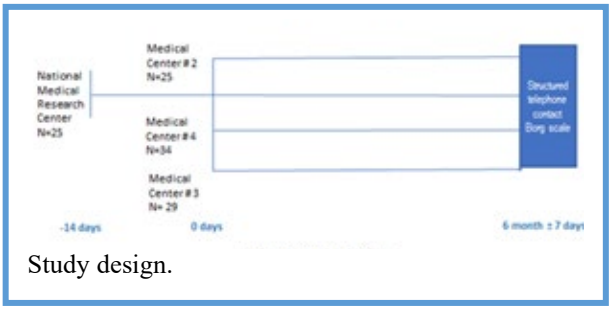
Post-COVID-19 syndrome (Long-COVID-19 syndrome) occurs in persons with a history of probable or confirmed SARS-CoV-2 infection, usually within 3 months of the onset of COVID-19 and characterized by the presence of symptoms for at least 2 months and failure to explain them with an alternative diagnosis.[1] In order to develop rehabilitation programmes for this condition, there have been many studies that focus on short-term data on the effectiveness of different rehabilitation programmes in terms of duration and content, but the data on long-term rehabilitation outcomes are very limited.[2,3] The aim of the study was to evaluate the long-term outcomes of different rehabilitation programmes for post-COVID-19 syndrome. A prospective cohort study was conducted from August 2021 until March 2022, involving 113 patients with post-COVID-19 syndrome (Fig. 1). The patients in the main group (n=25) underwent the rehabilitation programme under study,[4,5] while the patients in the other three groups (n=29, n=34, n=25 respectively) received interventions using rehabilitation protocols other than those under study (Oriental medicine techniques; balneo- and physiotherapy; self-training and



Study design.

physical training). The groups were comparable in terms of gender, age and rehabilitation routing scale. During the follow-up period, the groups recorded: the frequency of hospital admissions due to exacerbation of post-COVID-19 syndrome, death or disability, and the need for other types of care. The patients in the comparison groups were more and more likely to seek therapeutic care for emerging post-COVID syndrome symptoms ($\chi2$=6.635, p=0.001; $\chi2$=13.463, p=0.001; $\chi2$=10.949, p=0.001) and were also more likely to be hospitalized ($\chi2$=5.357, p=0.021; $\chi2$=0.125, p=0.724; $\chi2$=0.856, p=0.355) than those in the main group. The relative risk (RR) of hospital admissions in the observed cohort was 0.143(CI: 0.019; 1.078); 0.580 (CI: 0.056; 6.022); 0.340(CI: 0.040; 2.860). The reduction of the relative risk of hospital admissions when analysing the results of the methods under study compared to alternative rehabilitation methods for patients with post-COVID-19 syndrome was 85.7%; 42.0% and 66.0%, respectively. The best outcomes in patients with 6 months post-COVID were observed after application of rehabilitation programme designed with respiratory rehabilitation principles in mind.

Key Words: Post-COVID-19 syndrome; rehabilitation programs; treatment strategies; exercise therapy; relative risk.

References

1. WHO: Clinical case definition post-COVID-19 by Delphi consensus. 06.10.2021. Available online: URL https://apps.who.int/iris/bitstream/handle/10665/345824/WHO-2019-nCoV-Post-COVID-19-condition-Clinical-case-definition-2021.1-rus.pdf (accessed on 29 May 2022).
2. Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, Walshaw C, Kemp S, Corrado J, Singh R, Collins T, O'Connor RJ, Sivan M Post discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. J of Medical Virology.2021;93(2):1013–1022. doi:10.1002/jmv.
3. Rutsch M, Frommhold J, Buhr-Schinner H, Djeiranachvili L, Gross Th, Schüller Per O, Katalinic A, Deck R Study protocol medical rehabilitation after COVID-19 disease: an observational study with a comparison group with obstructive airway disease / Re_Co. BMC Health Serv Res.2021;21: 373. doi:10.1186/s12913-021-06378-4.

4. Lobanov AA, Irina A Grishechkina, Andronov SV, Gleb N Barashkov, Andrey I Popov, Anatoliy D Fesyun, Elena P Ivanova, Maccarone MC, Stefano Masiero. Can aquatic exercises contribute to the improvement of the gait stereotype function in patients with Long COVID outcomes? Eur J Transl Myol. 2022 Jul 14;32(3):10698. doi: 10.4081/ejtm.2022.10698.
5. Lobanov AA, Grishechkina IA, Fesyun AD, Rachin AP, Yakovlev MYu, Andronov SV, Barashkov GN, Lebedeva OD, Popov AI, Styazhkina EM, Ansokova MA, Vasil'eva VAInvestigation of the Effectiveness and Safety of the Rehabilitation Program for Patients with Long Covid Using Aquatic Training. Bulletin of Rehabilitation Medicine. 2022; 21(3): 45-57. https://doi.org/10.38025/2078-1962-2022-21-3-45-57.

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2023Pdm3 April 1

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Adijo, Adiós, Arrivederci, Auf Wiedersehen, Au revoir, Goodbye to the **2024 Padua Days on Muscle and Mobility Medicine (2024 Pdm3), Padua, Italy March 13-16, 2024.**

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