AMS | BOOK OF ABSTRACTS

AMS 9TH ANNUAL RESEARCH MEETING
2 APRIL 2026, KIT AMSTERDAM

Amsterdam Movement Sciences

VU VRIJE UNIVERSITEIT AMSTERDAM

Amsterdam UMC

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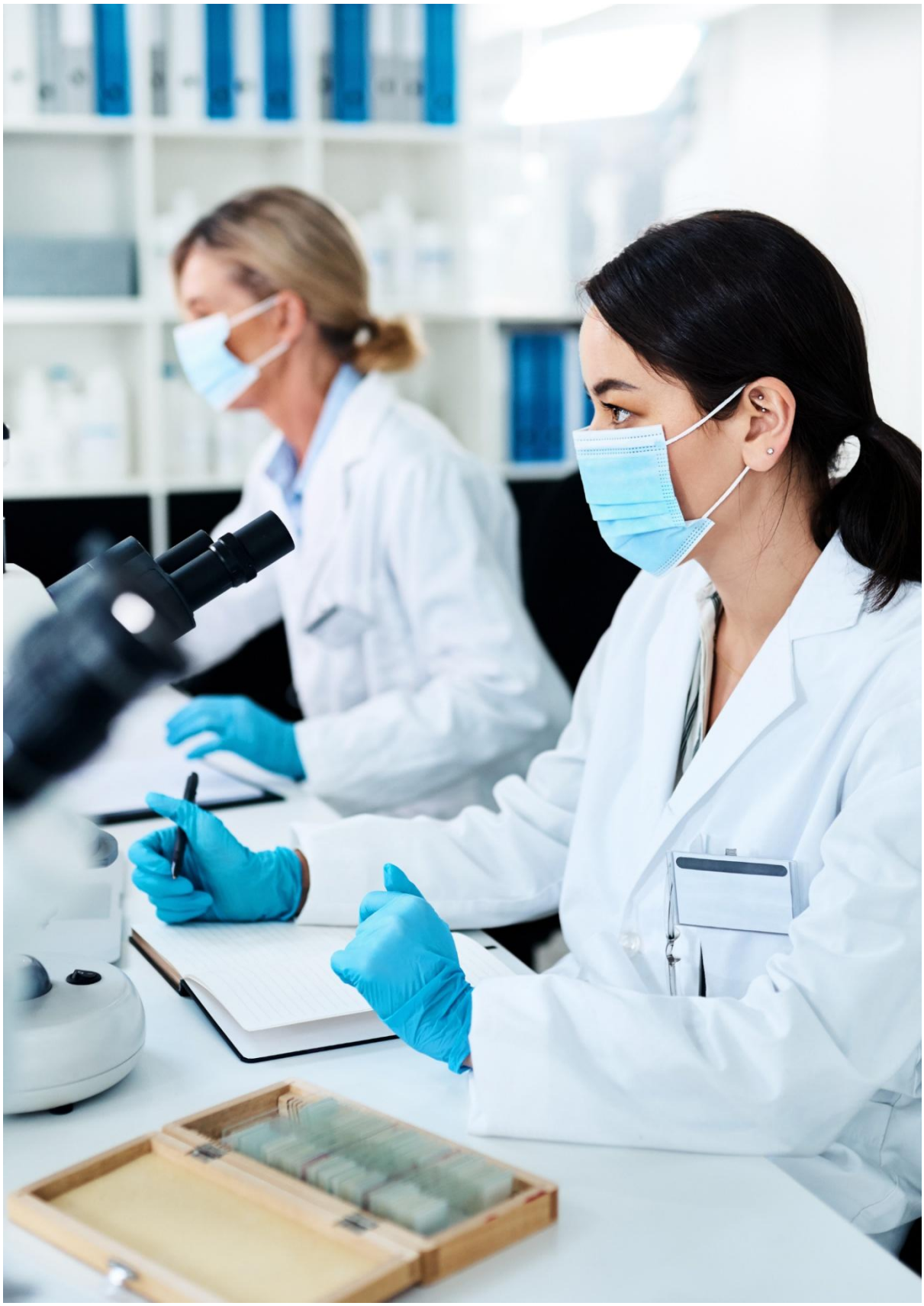
Fundamental Research



F1 – Leopold Kalemba

THE WARBURG EFFECT IN ELECTRICALLY PULSE-STIMULATED MYOTUBES: INSIGHTS FROM ^{13}C-GLUCOSE FLUX ANALYSIS

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Introduction - Skeletal muscle is a key regulator of whole-body glucose homeostasis, accounting for most postprandial glucose uptake, and loss of muscle mass is strongly associated with insulin resistance, metabolic disease, and increased all-cause mortality. Beyond this regulatory role, glucose metabolism itself provides energy and biosynthetic precursors required for muscle growth and maintenance, indicating a close interaction between muscle mass and glucose utilization. Skeletal muscle hypertrophy is associated with a metabolic shift toward increased glycolysis despite sufficient oxygen availability, reminiscent of the Warburg effect described in cancer cells. In this state, glucose-derived carbons are redirected from energy production toward biosynthetic pathways that support cellular growth. While anabolic stimuli such as insulin-like growth factor 1 (IGF-1) and muscle contraction promote this metabolic reprogramming, inflammatory stress induces catabolic signaling and muscle atrophy. However, the metabolic mechanisms by which anabolic, inflammatory, and contractile stimuli differentially redirect intracellular glucose-derived carbon fluxes across specific pathways remain incompletely understood. The purpose of this study is to investigate how IGF-1, Lipopolysaccharide as an inflammatory stimulus, and Electrical Pulse Stimulation as an in vitro model of muscle contraction, applied individually or in combination, reprogram glucose metabolism in C2C12 myotubes. By directly tracing carbon flow from glucose, this study aims to identify metabolic features that distinguish anabolic, inflammatory, and contraction-induced states in muscle cells.

Methods - Differentiated C2C12 myotubes will be exposed to six experimental conditions: Control, IGF-1, Lipopolysaccharide, Electrical Pulse Stimulation, IGF-1 + Electrical Pulse Stimulation, and Lipopolysaccharide + Electrical Pulse Stimulation. Following the treatments, cells will be incubated with [U-$^{13}C_6$]glucose. Liquid chromatography-mass spectrometry (LC-MS)-based ^{13}C metabolic flux analysis will be used to quantify labeling patterns in key intracellular metabolites, allowing pathway-specific assessment of glucose utilization across glycolysis, the tricarboxylic acid cycle, and anabolic pathways such as the pentose phosphate and serine biosynthesis pathways. In parallel, glucose and lactate concentrations will be measured in the medium at two timepoints to assess extracellular metabolic fluxes. Anabolic signaling will be evaluated by analyzing mTORC1-related proteins and global protein synthesis rates, while gene expression analyses will provide insight into metabolic and catabolic adaptations. Myotube diameter will be measured as a structural indicator of hypertrophy or atrophy.

Results - Data collection and initial analyses are ongoing, with first results expected by mid-February. This timeline allows for the presentation of preliminary findings at the AMS Annual Research Meeting. It is expected that IGF-1 and Electrical Pulse Stimulation will increase glucose uptake and promote the redirection of glucose-derived carbons into biosynthetic pathways associated with cellular growth, resulting in increased myotube diameter. Lipopolysaccharide treatment is expected to induce a more glycolytic phenotype while impairing anabolic signaling and reducing myotube size. Combined IGF-1 + Electrical Pulse Stimulation treatment is anticipated to show additive anabolic effects, characterized by enhanced glucose flux into biomass-producing pathways. In the Lipopolysaccharide + Electrical Pulse Stimulation condition, Electrical Pulse Stimulation is expected to partially counteract inflammatory and catabolic signaling, leading to an improved metabolic balance compared to Lipopolysaccharide alone.

Discussion - This study is expected to show that anabolic growth factor signaling, and contraction-like stimuli not only increase glucose uptake in muscle cells but also influence how glucose is used inside the cell. Specifically, glucose is expected to be directed toward biosynthetic pathways that support

cellular growth and maintenance. In contrast, inflammatory stress is expected to disturb this regulation by promoting aerobic glycolysis while reducing anabolic glucose utilization alongside the activation of catabolic signaling pathways, thereby contributing to muscle atrophy. Crucially, contraction-like activity may preserve metabolic flexibility under inflammatory conditions by improving the balance between glycolytic flux and anabolic glucose utilization. Together, these findings will provide fundamental insight into how exercise-related signals protect muscle mass and metabolic health in conditions associated with inflammation, aging, and metabolic disease.

F2 – Fangxin Xiao

EFFECTS OF LUMBAR DISC INJURY AND NOCICEPTION ON TRUNK MOTOR CONTROL DURING RAT LOCOMOTION

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Introduction. Intervertebral disc (IVD) injury may lead to mechanical instability[1] and contribute to low-back pain. When the IVD is compromised, enhanced activation of paraspinal muscles, such as the multifidus (MF) and longissimus muscles (ML), appears critical for maintaining spine stability. On the other hand, nociception may result in inhibition of these muscles[2]. It is unknown how IVD injury induced instability and additional muscle-derived nociception affect neuromuscular control.

Purpose. To assess the effects of spinal instability caused by IVD injury on trunk motor control, and to assess the effects of muscle-derived nociception on trunk motor control in an unstable spine during locomotion in the rat.

Method. Spine and pelvic kinematics and bilateral EMG activity from MF and ML were recorded in vivo during treadmill locomotion. After baseline measurement, IVD injury was induced by needle puncture at the L4/L5 level. One week later, measurements were repeated before and after induction of muscle-derived nociception via hypertonic saline injection into the lumbar MF.

Results. Spine and pelvic kinematics remained largely similar across conditions. No significant changes were found in stride duration, pelvic, lumbar and spine angles, angle change variability, or movement asymmetry. Muscle activation patterns and intermuscular coordination also remained largely consistent, with MF showing bilateral synchronized activation patterns and ML showing left-right alternating activation patterns. Compared with baseline, IVD injury caused significantly increased mean amplitude and variability of EMG activity in the right MF, indicating localized neuromuscular adaptation. When muscle-derived nociception was added in the unstable spine condition, EMG variability and minimum amplitude were significantly reduced both in the right and left MF.

Conclusions. IVD injury alone or in combination with muscle-derived nociception did not disrupt global trunk and pelvic kinematics. IVD injury elicited subtle and localized adaptations in multifidus activity. Muscle-derived nociception under unstable conditions reduced minimum multifidus activation and attenuated instability-related increases in multifidus mean activation and variability, but did not fully reverse them.

mean amplitude (right) **variability** (right) **minimum amplitude** (left)

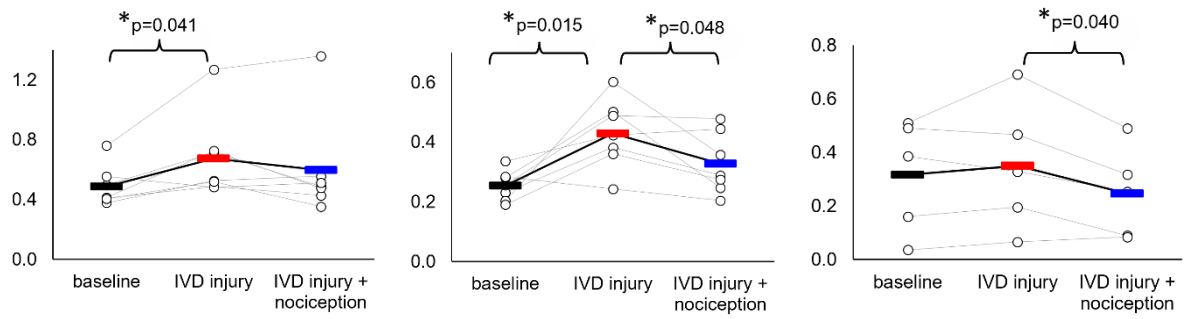

Figure 1. Normalized EMG outcomes of the multifidus muscle during locomotion. Hollow circles represent individual data of each rat, horizontal bars represents the group mean. IVD, intervertebral disc. *, significant difference

[1] Xiao F, et al, Int Biomech. 2025 Dec;12(1):67-80

[2] Xiao F, et al, Exp Brain Res. 2025 Apr 28;243(5):132

F3 – Anastasia Sclocco

DOSE MATTERS: HAPLOINSUFFICIENCY IN OSTEOGENESIS IMPERFECTA

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Abstract

Introduction Osteogenesis imperfecta (OI) is a common genetic disorder of syndromic bone fragility, presenting with variable skeletal and extraskeletal severity. Over the last decades, the deforming types have almost exclusively received all scientific attention, leaving large knowledge gaps about the most prevalent OI type 1. However, recent studies reveal higher unrecognized aspects of disease burden in this large patient population which contrasts with its widely adopted classification as mild OI.

Methods This review is the first to address this unique patient group by recognizing the diverse facets of clinical burden, genetic landscape, bone pathophysiology, quality of life, disease models and emerging treatment options, to identify disease-specific characteristics and critical gaps in current knowledge.

Results OI type 1 is associated with a broad spectrum of skeletal and multisystem complications, and significant psychosocial impact, contrasting sharply with its historical designation as mild OI. Due to their later diagnosis, disease invisibility, increased mobility, and uncharted clinical course, these patients and their treating physicians face with unique healthcare and diagnostic challenges. In contrast to the rest of OI patients, they are primarily characterized by molecular uniformity in the form of collagen type I deficiency. The scarcity of animal and cell models has also contributed to insufficient initiatives to explore OI type 1.

Discussion These patients present distinct clinical, molecular features, necessitating personalized clinical approaches and dedicated research. Our review aims to break this vicious cycle of OI type 1 obscurity by highlighting its true disease burden and defining disease gaps for future investigations. Recognizing collagen type I haploinsufficiency as a defining mechanism offers unique opportunities for therapeutic development. We urge with this review the attention of the OI community to HI OI so that this significant patient group can also benefit from adequate research and care.

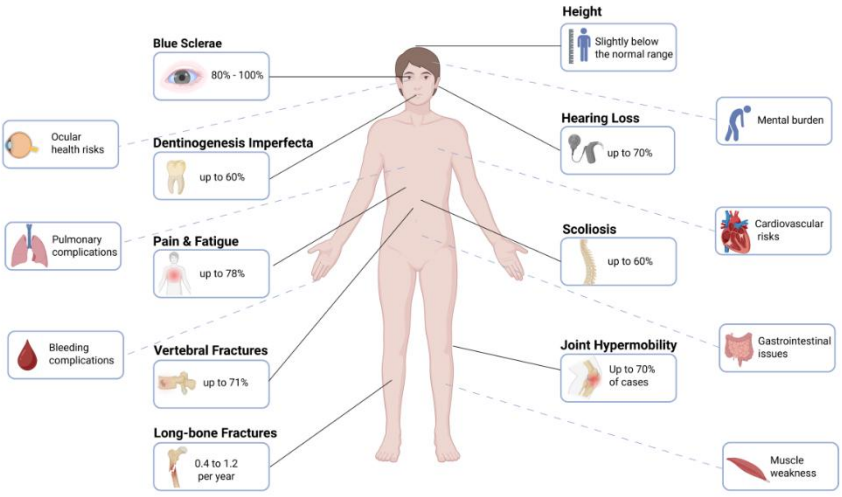

Figure 1 Multisystemic Clinical Manifestations of Osteogenesis Imperfecta Type 1

F4 – Wenya Yang

AGE-DEPENDENT CHANGES IN DENTAL MINERALIZATION IN AN OSTEOGENESIS IMPERFECTA TYPE I MOUSE MODEL ASSESSED BY MICRO–COMPUTED TOMOGRAPHY

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Background: Osteogenesis Imperfecta (OI) type I is a genetic connective tissue disorder characterized by defects in type I collagen, leading to skeletal fragility and altered mineralization of hard tissues. In addition to bone abnormalities, dental tissues such as enamel and dentin are also affected; however, age-related changes in dental mineralization in OI remain insufficiently characterized.

Objective: This study aimed to quantitatively evaluate age-dependent changes in dental mineralization in an OI type I mouse model using micro–computed tomography (micro-CT).

Methods: OI type I mice were examined at 8, 24, and 42 weeks of age. Maxillary and mandibular teeth were scanned using micro-CT. Three-dimensional reconstructions were performed, and mineral density–related parameters of enamel and dentin were quantified based on grayscale value analysis. Comparisons were conducted across age groups to assess temporal changes in dental tissue mineralization.

Results: Micro-CT analysis revealed distinct age-related differences in mineralization patterns of dental tissues in OI type I mice. Compared with the 8-week group, both enamel and dentin showed dynamic changes in mineral density–related parameters at 24 and 42 weeks. Dentin exhibited more pronounced alterations across time points, suggesting a higher sensitivity to collagen-related defects during maturation and aging processes.

Conclusion: Dental tissues in OI type I mice undergo significant age-dependent changes in mineralization, with dentin being particularly affected. Micro-CT provides a sensitive and non-destructive approach to assess dental mineralization in OI models. These findings contribute to a better understanding of craniofacial and dental involvement in OI and may inform future studies on functional implications within the musculoskeletal system.

F5 – Anouk Slaghekke

IMPAIRED SKELETAL MUSCLE OXYGENATION AND MICROVASCULAR DYSFUNCTION IN LONG COVID AND ME/CFS

Anouk Slaghekke [1], *Braeden T Charlton* [1], *Jelle Y Huijts* [1], *Brent Appelman* [2], *Ellen A Breedveld* [1], *Wendy Noort* [1], *Frank W Bloemers* [3], *Paul van Amstel* [3], *Jelle J Posthuma* [4], *Richie P Goulding* [1], *Michèle van Vugt* [5], *Rob C I Wüst* [1]

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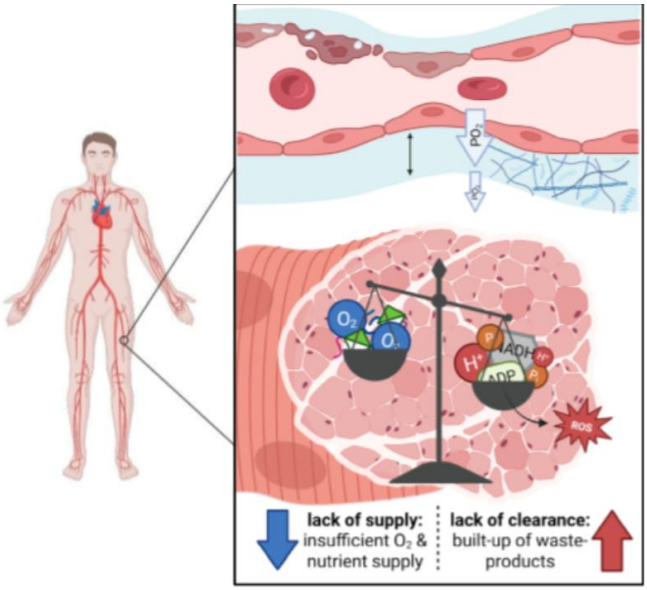
Introduction: Long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) are debilitating multisystem diseases characterized by brain fog, reduced exercise capacity, and post-exertional malaise. Ineffective matching of oxygen delivery to consumption in skeletal muscle can contribute to a lower exercise capacity and fatigue. Therefore, this study examines skeletal muscle oxygenation and possible alterations in skeletal muscle microvasculature.

Methods: Markers of skeletal muscle microcirculation were assessed in Long COVID (n=24), ME/CFS (pre-2020 diagnosis, n=26), and healthy controls (n=30). Participants underwent a maximal cycling exercise test for determination of maximal oxygen uptake (VO2max) with simultaneous muscle oxygenation assessment (near-infrared spectroscopy). Vastus lateralis muscle biopsies were analysed using immunohistology and electron microscopy to assess capillary ultrastructure, capillarization, and basal membrane thickness.

Results: Both patient groups obtained lower VO2max ($p<0.0001$) and peak power output ($p<0.0001$), despite no alterations in maximal heart rate or ventilatory equivalents. Tissue O_2 uptake ($p=0.001$) and vasodilatory capacity ($p=0.011$) were lower in Long COVID and ME/CFS patients. Even though capillarization was only lower in ME/CFS patients ($p<0.0005$), both patient groups showed significantly lower capillary contact lengths ($p<0.0001$), primarily driven by decreased capillary tortuosity ($p<0.0001$). Additionally, both patient groups displayed substantial capillary basement membrane thickening ($p<0.0001$), with a maximum of 62.7% in healthy controls and a minimum of 63.2% in patients. Ultrastructural analysis further confirmed basement membrane thickening alongside multiple markers of endothelial dysfunction, including microvacuolization, endothelial hypertrophy, and signs of degeneration.



Conclusion: Microvascular impairments in patients with Long COVID and ME/CFS suggest inadequate skeletal muscle oxygenation, contributing to fatigue and post-exertional malaise. The pronounced basement membrane thickening may serve as a novel diagnostic biomarker and provide new insights into the pathophysiology of Long COVID and ME/CFS.

F6 – Roland Bumbuc

THE ACUTE PHASE RESPONSE TO BURN INJURY: AN IN-SILICO MODELING APPROACH

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Background: Burn injuries cause complex events, such as acute inflammation, which play a crucial role in tissue repair and regeneration. The activation of the complement system after burn injury is essential to the inflammatory response and mediates various immune pathways during healing.

Objective: Develop and validate a computational model that simulates the acute inflammatory phase during the first 18 days post burn injury by using animal data.

Methods: Our Agent Based Cellular Potts model approach includes different cell types as individual agents, cytokines and growth factors that interact within a defined tissue environment on a two-dimensional wound simulation. This model considers systemic factors such as the concentration of cytokines and chemokines immune cell recruitment, and local factors including Damage Associated Molecular patterns that signal tissue damage. We incorporated experimental data from animal burn models from the literature to validate the interactions of key players within the acute inflammation cascade, seeking to create a representation of complement activation, inflammatory events and the associated consequences over time.

Results: Through simulation, we investigated how different factors, such as the severity of burn injury, the prolonged inflammation, and changes in the concentration of complement factors, affect the dynamics of the acute inflammatory phase. Furthermore, we explored the interaction between complement activation and other signalling pathways involved in burn wound healing, such as IL-6, IL-8, IL-1β, TNF-α and TGF-β1 concentration with increasing CRP concentration (in blood and wound) and complement activation.

Conclusion: This computational model provides insight into the spatio-temporal dynamics of acute inflammation driving factors after burn injuries.

F7 – Jelle Huijts

Shared features of lipofuscin and microclots in skeletal muscle from post-COVID and ME patients

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In this study, we set out the question what amyloid-containing deposits in skeletal muscle and blood are. Using electron microscopy, we searched for amyloid-containing deposits in a subset of patients with post-COVID syndrome(n=6/24) and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS, n=6/26), and age- and sex-matched healthy controls (n=16/30). Experiments are still ongoing to increase sample size.

We observed subsarcolemmal, extracellular and intracellular accumulation of lipofuscin in skeletal muscle tissue. Its pattern and distribution matched with our earlier observations of the ThT staining. A dual staining using correlative light and electron microscopy (CLEM) confirmed a near-perfect overlap between ThT and lipofuscin deposits in skeletal muscle.

There was a significantly higher skeletal muscle lipofuscin concentration in post-COVID (1.66±0.68/fiber, $P<0.001$) and ME/CFS (3.94±0.48 /fiber; $P<0.001$) patients compared to controls (0.56±0.57 /fiber). There was an age-dependent increase in lipofuscin concentration in healthy controls (n=16, $R^2=0.50$, $P=0.002$), but this was absent in post-COVID ($P=0.68$) and ME/CFS ($P=0.28$).

ThT-positive microclot levels are elevated in the blood of patients with post-COVID. Across all three conditions studied, microclot abundance increased in response to acute, but returned to baseline within 24 hours, making it unlikely that microclots are directly involved in PEM. Using CLEM, we have identified two distinct populations of ThT positive microclots: predominantly smaller, lipid-rich clots with morphology resembling lipofuscin, and larger, more protein-rich clots. Whether these microclots correlate with circulating lipofuscin is currently still unknow.

These findings suggest that post-COVID and ME/CFS are associated with an accumulation of misfolded proteins and cellular waste products within lipofuscin deposits, resembling accelerated aging. Although microclot levels increase following acute exercise in the blood, their relationship to lipfuscin is currently still unknow. Further studies are required to determine the mechanisms underlying the presence, removal rates, overlap and role of lipofuscin and microclots in post-COVID and ME/CFS.

F8 – Koen Zwetsloot

LASER MICRODISSECTION-BASED SPATIAL PROTEOMICS REVEAL FIBRE-SPECIFIC DISTINCTION IN PROTEASOMAL, SARCOMERIC, AND METABOLIC PATHWAYS IN THE GASTROCNEMIUS MEDIALIS

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Introduction & Methods:

Fibre type-dependent differences are often studied by comparing muscles dominated by specific fibre types. However, such fibre type specificity may be confounded by overall muscle activation profiles. Direct intramuscular comparisons are rare but essential to understand intrinsic differences in the proteome. To study this, C57BL/6N mice (N=6) were terminated, and the gastrocnemius medialis muscle (mixed fibre type composition) was dissected, sectioned and stained for succinate dehydrogenase to distinguish between fibres. Laser microdissection was used to isolate glycolytic and oxidative fibres for LC-MS/MS proteomics, and subsequent gene set enrichment analysis. Functional confirmation of proteomics results was performed using high-resolution mitochondrial respirometry.

Results:

The myosin thick filament proteins and the Na/K-ATPase protein confirmed that the distinguishment based on oxidative capacity was similar to the distinguishment between fast, and slow-twitch fibres. Interestingly, proteins of the M-band, actin thin filament, and Z-disc proteins titin (TTN) & PDLIM7 were more abundant in the glycolytic fibres, while Z-disc proteins myotilin (MYOT), and titin-cap (TCAP) were more abundant in oxidative fibres. Proteins of the ubiquitin-proteasomal system were more abundant in the glycolytic fibres, particularly the ATP-independent regulator (lid) 19s unit (PSMD1/2/8/11/13) the ATP-dependent cataclysmic 20s unit (PSMB5, chymotrypsin-activity), subunits of the 26s complex (PSMC2), and ubiquitin (RPS27A).

Despite the strong distinction of fibres based on mitochondrial capacity, three mitochondrial proteins were more abundant in the glycolytic fibres: GPD2, SQOR, and SFXN3. These proteins are implicated in the glycerol-3-phosphate shuttle, sulphate-, and serine metabolism, respectively. GPD2 could have a role in the glycerol-phosphate shuttle as a reactive oxygen species (ROS) protective mechanism in glycolytic fibres and a by-pass from the glycolysis directly to the oxidative phosphorylation system. High-resolution respirometry confirmed the functional contribution of the glycerol-3-phosphate shuttle to mitochondrial respiration, with an increased respiration during ROS exposure (with pyrogallol producing H_2O_2) in the EDL (+410%, $p<0.05$) compared to the soleus (+17,7%, non-significant).

Conclusion:

Muscle fibre type distinction based on oxidative capacity proved effective and revealed unexpected fibre type-specific expression of sarcomeric proteins. Contrary to literature, glycolytic fibres showed higher abundance of proteasomal components. The glycerol-3-phosphate shuttle appears crucial in these fibres for both energy metabolism and ROS protection. Further study on the potential role for hydrogen

sulphide metabolism is needed. Together these findings highlight the value of intramuscular fibre type proteome analyses in uncovering biologically relevant differences that may be overlooked by bulk tissue approaches.

F9 – Hadi Seddiqi

PERFUSION CELL CULTURE INDUCES OXYGEN DIFFUSION AND OSTEOGENIC ACTIVITY IN MULTI-CHANNELED CRITICAL-SIZE SILK FIBROIN SCAFFOLDS WITH PRE-OSTEOBLASTS: EXPERIMENTAL AND FINITE ELEMENT MODELING STUDY

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Introduction: The development of 3D-scaffolds to treat critical-size bone defects in orthopedic and reconstructive surgery remains a challenge due to low oxygen diffusion causing cell death in the core of the scaffolds. Perfusion cell culture and fluid-conducting hollow channels might be critically important to enhance oxygen diffusion.

Purpose: we aimed to test whether perfusion cell culture synergistically improves oxygen diffusion and osteogenic activity in multi-channeled 3D-porous silk fibroin scaffolds with pre- osteoblasts using experiments and finite-element modeling.

Methods: Pre-osteoblasts were cultured on scaffolds without or with channels (diameter: 0.5 or 1 mm) up to 21 days in perfusion or static bioreactors. The scaffolds' physicomechanical properties, oxygen diffusion, and pre-osteoblast activity were evaluated.

Results: Channeling did not change the scaffolds' porous structure, biodegradation rate, or compressive modulus, but decreased compressive strength. Finite element modeling showed that all scaffolds remained resilient under 2%-compressive strain, which is below their yield stress. Channeled scaffolds showed uniform oxygen diffusion and cell distribution in static and perfusion bioreactors. Experimentally, channeling increased gene expression of *Fgf2, Ki67, Runx2,* and *Ocn*, and oxygen concentration in a static bioreactor. In a perfusion bioreactor, channeling markedly increased cell number, collagen deposition, and matrix mineralization.

Conclusion: Perfusion cell culture in combination with multi-channeling of 3D-porous silk fibroin scaffolds with pre-osteoblasts significantly enhanced oxygen diffusion, cell infiltration, and osteogenic activity without affecting the physicomechanical properties of the scaffolds, which may help to further improve and overcome insufficient oxygen diffusion and cell activity in the core of critical-size 3D-scaffolds for bone defects *in vivo* (Fig. 1).

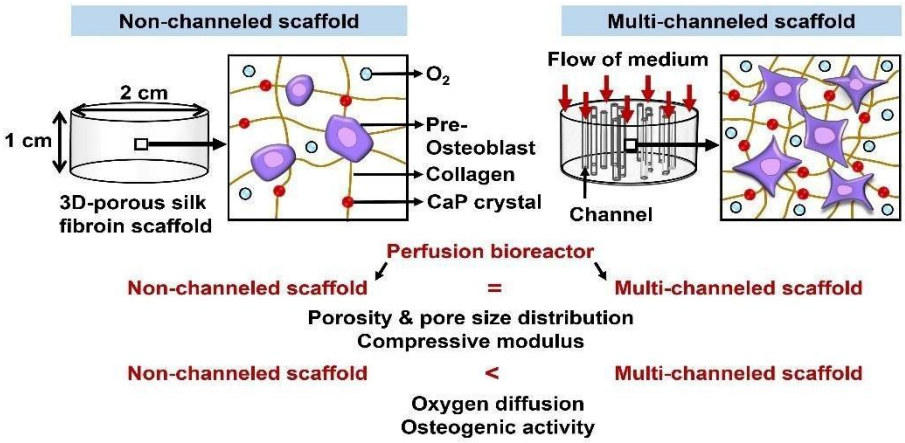

Fig. 1. Perfusion cell culture induces oxygen diffusion and osteogenic activity in multi- channeled critical- size silk fibroin scaffolds with pre-osteoblasts.

F10 – Tom Kerkhoff

The effects of serum, containing myositis-specific autoantibodies, on muscle fiber contractility in Immune-Mediated Necrotizing Myopathy.

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** These authors contributed equally.*

Abstract - Pathogenesis of inflammatory myopathy

Background – Immune-mediated necrotizing myopathy (IMNM) is the most severe myositis subtype in terms of muscle weakness. Immunosuppressive therapies are often insufficient and there is a need for better therapies. IMNM is associated with myositis-specific autoantibodies (MSAs) against signal recognition protein-54 (SRP) and 3-hydroxy-3-methylglutaryl CoA reductase (HMGCR), which have been suggested to play a pathogenic role. We have previously shown that the force generating capacity of non-necrotic muscle fibers from untreated IMNM patients is impaired. This may be caused by serological constituents; more specifically IgGs and MSAs, this is however unknown.

Methods – Serum was drawn from treatment naive anti-SRP$^+$, anti-HMGCR$^+$ or seronegative IMNM patients and healthy controls. Subsequently, IgG was isolated from the serum to obtain total IgG and IgG-depleted serum. Healthy intact muscle fibers from the Flexor Digitorum Brevis (FDB) muscle of mice were isolated. After 1 day of culture (to allow the muscle fibers to recover from isolation), fibers were exposed to (IgG-depleted) serum for 2 hours. The muscle fibers were permeabilized and mounted between a force transducer and length motor; the fibers were then exposed to solutions with incremental Ca^{2+}-concentrations and force was measured.

Results – Our data suggest that muscle contractility is altered after a 2-hour exposure to serum of IMNM patients compared to healthy controls. Maximum normalized force of healthy muscle fibers is lower after exposure to serum from IMNM patients compared to force generated by fibers exposed to serum from healthy controls, whereas Ca^{2+}-sensitivity of force was not altered. Preliminary data from fibers exposed to IgG-depleted patient serum exposure did not replicate the differences as seen after serum exposure, suggesting that IgGs contribute to the force depression.

Conclusion – Serum of IMNM patients has a direct impact on muscle fiber contractility. Since the preliminary data suggest that IgG depleted serum does not affect muscle contractility, it is likely that the IgG of these patients cause the observed effect. To further examine that MSAs play a role in impaired muscle fiber contractility, experiments are ongoing with the IgG and IgG-depleted serum of these patients followed up with purified MSA exposure.

Keywords – Myofiber contractility, Myositis specific autoantibody exposure

F11 – Brian Chen

A Skeletal Muscle–Specific snRNA-seq Analysis Pipeline Reveals Improved Myonuclear Resolution

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Introduction
Over the past decade, next-generation sequencing studies of skeletal muscle have expanded rapidly. Due to the multinucleated nature of myofibers, single-nuclear RNA sequencing (snRNA-seq) has become a novel approach for capturing myonuclear transcriptomic information, that is cell-type specific. However, the experimental complexity of snRNA-seq and the unique architecture of skeletal muscle pose challenges for batch-effect correction and accurate cell type identification. The aim of this study is to evaluate different analytic pipelines and provide a skeletal muscle–specific analysis guideline.

Methods
Human vastus lateralis muscle biopsies were processed for snRNA-seq using an optimized nuclei isolation workflow including mechanical dissociation, detergent based nuclear release, and droplet based sequencing on the 10x Genomics platform. We compared the standard Seurat workflow described in open source documentation with a customized scVI based pipeline. The Seurat workflow integrates datasets using canonical correlation analysis followed by Louvain clustering. In contrast, our customized pipeline employs scVI, a neural network based variational autoencoder trained on raw gene counts, combining highly variable genes with curated skeletal muscle marker genes, followed by Leiden clustering.

Results
The standard Seurat workflow achieved strong batch alignment but resulted in overmixing of myonuclei, flattened condition specific effects, and poor resolution of hybrid myonuclear populations. In contrast, the biologically informed scVI-based integration strategy produced improved cluster coherence and clearer separation of Type I, Type II, and hybrid myonuclei (Fig. 1).

Conclusion
These findings demonstrate that CCA based integration can obscure myonuclear heterogeneity, whereas a biologically informed scVI-based integration pipeline preserves myonuclear diversity and improves the separation of fiber type and hybrid myonuclei.

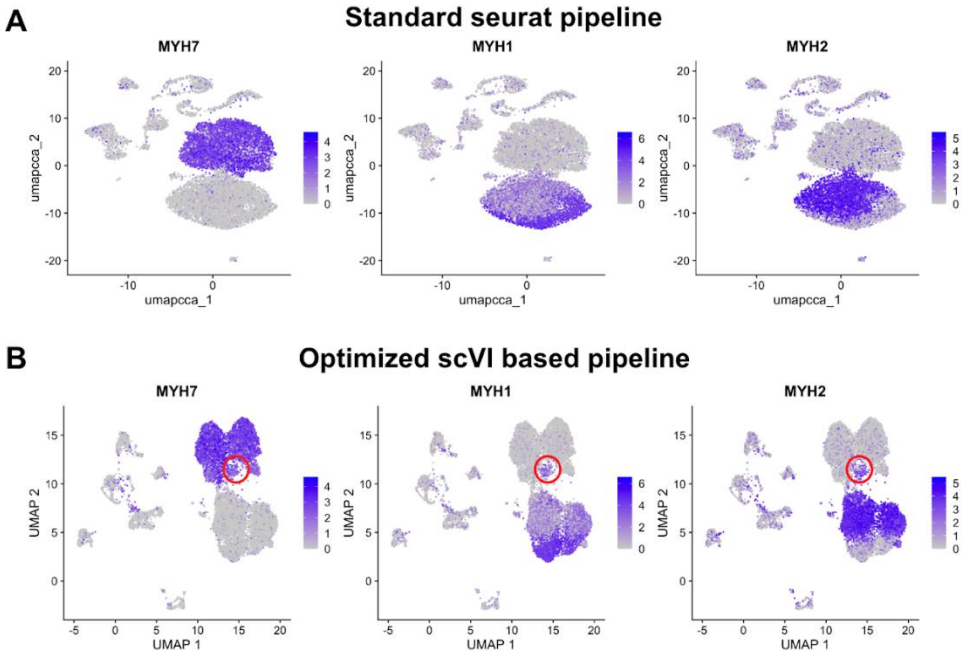

Figure 1.
Comparison of standard Seurat and optimized scVI based pipeline for skeletal muscle snRNA-seq. A) In the standard CCA-based Seurat pipeline, nuclei expressing MYH7 (Type I) or MYH1/MYH2 (Type IIa/IIx) are forced into two dominant groups, and nuclei with mixed MYH7 and MYH1/MYH2 expression cannot be distinguished as a separate population. B) In contrast, the optimized scVI-based pipeline clearly separates MYH7-high Type I, MYH1/MYH2-high Type IIa/IIx, and a distinct population of nuclei co-expressing MYH7 and MYH1/MYH2, consistent with hybrid myonuclei (red circles).

F12 – Yunxin Chen

AGEING AFFECTS MECHANOSENSITIVITY OF HUMAN OSTEOCYTES

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Introduction

With increasing age the human skeleton changes its composition and decreases in density, thereby compromising its load-bearing capacity. Embedded in the bone matrix are mechanosensitive osteocytes, which orchestrate bone adaptation to mechanical loading by regulating osteoblast and osteoclast activity. Whether age-related alterations in the bone matrix are reflected by a decrease in the mechanosensitivity of osteocytes is currently unknown. This study aimed to assess whether ageing affects osteocyte mechanosensitivity.

Methods

Human cortical bone samples were retrieved from 39 donors (age: 23-82 yrs, 25 male, 14 female). Osteocytes were either isolated and cultured as monolayer, or kept in their native matrix in bone explants. Isolated osteocytes were treated by pulsating fluid flow (PFF; 0.7±0.3 Pa, 5 Hz, 1 h), and post-cultured for 6 and 24 h. Nitric oxide (NO) release was quantified during PFF treatment using Griess reagent. Bone explants containing osteocytes in their native matrix were mechanically loaded by three-point bending (2000 microstrain, 1 Hz, 5 min), and post-cultured for 6 and 24 h. Bone stiffness was determined using a force-displacement modulus curve. Mechanosensitivity-related gene expression (cyclooxygenase-2 (*COX-2*), sclerostin (*SOST*), dentin matrix protein-1 (*DMP1*), interleukin 6 (*IL-6*) was assessed in isolated osteocytes and explants during post-culture by RT-PCR. Linear regression analysis was used to assess a possible relationship between age and osteocyte mechanosensitivity.

Results

Isolated cell cultures responded to PFF with enhanced release of NO (2.6-fold, $p<0.001$), independent of age. Ageing did not change cortical bone stiffness in bone explants. There was a positive association between age and PFF-induced gene expression of *IL-6* ($R^2=0.38$, $p<0.05$; cell cultures from older donors showing a higher response than cultures from younger donors), but not expression of *COX-2*, *SOST* and *DMP1* in isolated osteocytes. In bone explants, age and mechanical load-induced gene expression was not significantly correlated.

Conclusion

Osteocytes isolated from aged matrix increased their ability to respond to PFF, while osteocytes in aged bone explants did not show such an effect. This suggests that alterations in structure and/or composition of the ageing bone matrix may affect osteocyte mechanosensitivity, which could, at least in part, be responsible for bone fragility leading to bone fractures during ageing.

F13 – Antong Wu

Metformin alleviates temporomandibular joint osteoarthritis by targeting chondrocyte senescence through FoxO1-mediated autophagy

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Abstract

Objectives: Temporomandibular joint osteoarthritis (TMJ-OA) is a degenerative disorder driven by inflammation and chondrocyte senescence, leading to cartilage and bone destruction. Metformin is a medication used to treat diabetes that also exhibits anti-inflammatory and anti-aging properties. Here, we investigated the potential of metformin to mitigate TMJ-OA and its underlying mechanism. **Methods:** Metformin (200 mg/kg) was administered to monosodium iodoacetate (MIA)-induced TMJ-OA rats *via* gavage. Cartilage degeneration and subchondral bone changes were assessed using histology and micro-CT. Serum levels of senescence-associated secretory phenotype (SASP) factors were measured via cytokine assays. RNA sequencing (RNA-seq) identified key pathways. *In vitro*, IL-1β-stimulated chondrocytes were treated with metformin, with or without forkhead box O1 (FoxO1) inhibition (AS1842856). Senescence markers (p53 and p21), autophagy markers, and inflammatory factors were analyzed using RT-qPCR, Western Blotting, SA-β-gal staining, and immunostaining. **Results:** Metformin significantly reduced cartilage degradation, subchondral bone loss, and SASP production in TMJ-OA rats. Metformin downregulated senescence markers (P53/P21) while enhancing autophagy. RNA-seq linked metformin's effects to FoxO1 activation. *In vitro*, metformin counteracted IL-1β-induced senescence and inflammation in chondrocytes by promoting FoxO1-dependent autophagy. FoxO1 inhibition abolished these protective effects. **Conclusions:** Metformin attenuates TMJ-OA by suppressing inflammation-driven chondrocyte senescence through the activation of autophagy. These findings highlight metformin as a promising therapeutic agent for TMJ-OA, particularly in cases where inflammaging plays a principal pathogenic role.

Keywords: Metformin; Temporomandibular joint osteoarthritis; FoxO1; Inflammation; Autophagy; Cellular senescence

F14 – Alexandra Dorn

Treating hypercontractility in Dutch nemaline myopathy mice with myosin inhibitors

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Nemaline myopathy (NEM) is among the most common non-dystrophic congenital myopathies. Nemaline myopathy type 6 (NEM6) is caused by variants in Kelch-repeat-and-BTB-(POZ)-Domain-containg-13 (KBTBD13). Majority of NEM6 patients harbor the Dutch founder mutation KBTBD13R408C (c.1222C>T, p.Arg408Cys), which results in a hypercontractile phenotype caused by impaired sarcomere-based relaxation. Histological characteristics of NEM6 patients include the presence of nemaline bodies, and the presence of cores indicating the absence of complex I (NADH) activity and mitochondrial dysfunction. Previously, we have conducted a natural history study in homozygous Kbtbd13R408C-knockin mice (NEM6 mouse model) to investigate the phenotype of this mouse model at different ages. At one month of age we saw no NEM6 phenotype, an onset of dysfunction was seen at three months, and this dysfunction got progressively worse at nine months old.

In this study, we aimed to counteract the hypercontractility and mitochondrial damage seen in NEM6 with the administration of a fast-twitch myosin inhibitor. We first conducted the acute effect of a myosin inhibitor, EDG-4131 a fast-twitch myosin inhibitor currently in phase 2 of clinical trials for Duchenne muscular dystrophy, in Flexor Digitorum Brevi of the NEM6 mouse model. Acute administration of EDG-4131 showed to successfully shortened the percentage of shortening seen during contraction. Following this, we assessed the chronic effect of EDG-4131 on our NEM6 mouse model starting from the age of one month old, at which no NEM6 phenotype is present in the mice. After eight weeks of treatment, we observed a significant increase the *in vitro* mitochondrial respiration, and a significant decrease in the formation of cores.

To conclude, this study shows the potential of myosin inhibitors to prevent the onset of mitochondrial dysfunction in our NEM6 mouse model.

F15 – Mica Menks

THE ORIGIN OF ALTERED MECHANICAL PROPERTIES OF GASTROCNEMIUS MUSCLE-TENDON UNIT IN SPASTIC RATS – AN ANALYSIS ACROSS MULTIPLE LEVELS OF ORGANISATION

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Muscle spasticity has been defined as a velocity-dependent increase in tonic stretch reflexes caused by hyperexcitability of the stretch reflex [1]. In the spastic Han-Wistar mutant rat model, ankle plantar flexion contractures develop similarly as found in humans with spastic lower legs [2]. In these rats, changes in muscle-tendon unit (MTU) length-force characteristics of the gastrocnemius were observed; specifically, a narrower active length-force curve and a reduced maximal active force were found [3]. These changes may be the result of altered properties of the various structures within the MTU, but how each of these structures contribute is currently unknown. This study aims to identify the mechanisms that cause the changes in gastrocnemius MTU length-force characteristics of spastic Han-Wistar rats.

Two groups of Han-Wistar rats were measured: spastic (n=9) and typically developing siblings (n=7). MTU length-force characteristics of the gastrocnemius were measured in situ. In addition, the length-force characteristics of only the muscle belly were assessed. After the in situ experiment, fiber bundles of medial gastrocnemius (MG) were harvested for later assessment of length-force characteristics and specific tension of individual muscle fibers.

We found a reduced maximal active force in the gastrocnemius MTU and muscle belly of spastic rats. Muscle mass was lower, but physiological cross-sectional area (PCSA) did not differ between groups. The specific tension of the single muscle fibers of spastic rats was 21% lower than that of typically developing rats, but this was not significant. As the PCSA was the same, specific tension (a measure of fiber quality) is a possible factor explaining the lower muscle force. While a narrower active length-force curve was found for the MTU, this width did not differ between groups for the muscle belly. This suggests that the difference in the MTU can be explained by changes in tendon properties. In conclusion, the gastrocnemius MTU length-force properties in spastic rats may be explained by different tendon properties and a lower specific tension of its muscle fibers. Other parameters, such as fiber type composition and connective tissue content, are currently being assessed.

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F16 – Zhenjia Zhong

In Vitro Characterization of Three Muscle Models for Examining MenopauseRelated Effects on Skeletal Muscle

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Background

Menopause is the permanent end of the menstrual cycle and is caused by a declined estrogen (E2) production by the ovaria. It is associated with decreased muscle strength, endurance and altered intrinsic muscle capacity to generate energy through Oxidative Phosphorylation (OxPhos). Up until today it remains unclear how a decline in hormones like E2 causes such effects and *in-vitro* muscle models that replicate pre- and post-menopause conditions aren't well developed yet.

Objectives

(i) Characterize 3 *in-vitro* muscle models to evaluate their suitability to study menopause-related effects on skeletal muscle;

(ii) Test how IGF-1 (100 ng/ml) affects muscle mass, and gene expression of genes linked to cell growth, protein synthesis, and degradation in the 3 different *in-vitro* muscle models;

(iii) Test how physiological concentration of E2 (1nM) affect muscle mitochondrial oxidative phosphorylation (OxPhos) complex content *in vitro*.

Method

Myotubes (Myot) generated from human induced Pluripotent Stem Cells (H iPS) derived myoblasts, human primary (H primary) myoblasts, or immortalized mouse myoblasts (C2C12), were incubated with or without IGF-1 (100ng/ml) to mimic pre- and post-menopausal IGF-1 conditions (N=6/ group).

Bright-field images were taken to measure myotube diameter, as outcome measure for muscle mass.

Gene expression was assessed for muscle cell-proliferation (CCND1, c-MYC, and PKM2), protein synthesis (PHGDH) and protein degradation (MAFbx) with qPCR (N=6/ group). ERα and GLUT4 protein level were evaluated in H primary Myot, H iPS Myot, and H iPS 3D bundles, using MCF-7 human breast cancer cell lines and human skeletal muscle (SKM) as positive controls, respectively.

Protein content of OxPhos complexes were evaluated in H primary Myot and C2C12 Myot with or without physiological level (1nM) E2 for 24h (n= 3/group). Values are expressed as means±SD.

Results

IGF-1 increased muscle size in H primary Myot (13.9 ±13.13%) and boosted CCND1 levels (41.45 ± 26.07%), with a slight decrease trend in MAFbx (31.32 ±28.68%). In C2C12 Myot, IGF-1 reduced gene-expression of MAFbx (48.53 ±7.88%) and c-MYC (27.94 ±27.09%), and increased PHGDH (33.85 ±17.44%), CCND1 (91.72 ±26.96%), PKM2 (44.48 ±14.23%). Changes in C2C12 Myot were stronger than in H primary Myot. IGF-1 had no effect on H iPS Myot.

H iPS Myot and 3D bundles exhibited significantly lower levels of ERα isoforms, classic 66 kDa (iPS Myot: 60.20 ±14.62%; iPS 3D bundles: 85.03 ±14.62%) and 81 kDa (42.29 ±16.37%; 75.99 ±16.37%), than H primary Myot, while GLUT4 expression present no difference.

OxPhos complex V and III decreased by 37.32 ±18.16% and 39.34 ±26.16% in human primary Myot, respectively after 24h of 1nM E2. C2C12 showed no changes in OxPhos content in response to E2.

Conclusion

This study demonstrated *in-vitro* muscle model-specific differences in IGF-1 sensitivity, ERα content and E2 effect on mitochondrial OxPhos complex content between human primary, iPS and C2C12 Myot or 3D bundles for *in vitro* skeletal muscle research. Based on responsiveness to IGF-1 and E2, we tend to think human primary Myot is a better model used to research menopause-related effects. It can ultimately improve the knowledge of how IGF-1 and other menopause-related hormones play a role in menopause-associated skeletal muscle dysfunction.

F17 – Babette Mooijekind

GASTROCNEMIUS MEDIALIS MUSCLE MORPHOLOGY AND FUNCTION AFTER LENGTHENING SURGERY IN ADOLESCENTS WITH CEREBRAL PALSY

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Introduction

Plantarflexion contracture is a common deformity in children with cerebral palsy (CP). Surgical gastrocsoleus aponeurotic lengthening can improve ankle range of motion (ROM). However, effects on muscle morphology are not yet known. Therefore, we assessed the effects of gastrocsoleus lengthening on gastrocnemius medialis (GM) morphology and ankle ROM during gait in CP.

Methods

Eight individuals with spastic CP (12-19 years) were assessed before and one year after gastrocsoleus Vulpius surgery. All had a 3D ultrasound of the GM, clinical examination, and 3D clinical gait analysis (six with a multi-segment foot model, two with a mono-segment foot model). Outcomes were compared before and after surgery using Wilcoxon signed rank tests.

Results

After surgery, tendon length normalized by tibia length increased by 11.4% [5.6:32.6%] (*median [min:max])*, p=.01), while normalized fascicle length decreased by -14.2% [-44.7:-5.5%], p=.02. The pennation angle increased by 7.2°[0.1:14.6°], p=.02. Muscle volume normalized to body mass did not change, but increased in 5/7 individuals. The Physiological Cross-Sectional Area normalized by body mass$^{2/3}$ increased by 48.1% [8.8:96.8%], p=.03. The maximum passive ankle dorsiflexion increased significantly by 12.5° [+0:+55°] (p=.02). Active ankle ROM during gait decreased in 7/8 individuals, by median 3.7° [-9.2:+14.2°] after surgery, although not significant (p=.20). Power absorption during early stance significantly decreased by 0.92 [-0.0073:-1.46] Watt/kg (p=.02), but push-off power did not increase (0.13 [-0.40:+0.45] Watt/kg, p=.58).

Discussion

Surgical gastrocsoleus aponeurotic lengthening resulted in an increase in passive ankle dorsiflexion in adolescents with cerebral palsy due to tendon lengthening. However, we observed a trend toward a reduced range of motion during gait, possibly related to shortened muscle fascicles following surgery. This suggests that improvements in foot and ankle alignment do not necessarily coincide with recovery of muscle morphology and function. Together with the large interindividual variability, this underscores the importance of a personalized treatment approach that also incorporates muscle-specific outcome measures.

F18 – Merve Ceylan

OSTEOGENIC DIFFERENTIATION of GINGIVAL and PERIODONTAL LIGAMENT FIBROBLASTS INHIBITS OSTEOCLAST FORMATION in 2D and 3D FIBRIN CULTURES

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ABSTRACT

Bone regeneration involves multiple cell types responding to biochemical and biomechanical cues from the extracellular matrix (ECM) in a temporospatial manner. Gingival fibroblasts (GFs) and periodontal ligament fibroblasts (PDLFs) play key roles in wound healing and regeneration, as they can differentiate into osteoblast-like cells and induce osteoclastogenesis from precursor cells. However, it remains unclear whether these two fibroblast populations contribute equally to bone regeneration and how ECM properties modulate their osteogenic differentiation and subsequent osteoclast-inducing capacity. Here, we compared the osteogenic potential of 12 GFs and 12 PDLFs cultured in 2D monolayers or 3D fibrin hydrogels under normal or osteogenic conditions and assessed how fibroblast-conditioned media regulates osteoclast formation from peripheral blood mononuclear cells (PBMCs). Both fibroblast populations underwent osteogenic differentiation, as evidenced by increased alkaline phosphatase (ALP) activity, calcium deposition, and robust mineral nodule formation in 3D fibrin hydrogels. Osteogenic stimulation reduced macrophage colony-stimulating factor (M-CSF) release and increased osteoprotegerin (OPG) release. Functionally, conditioned media from non-osteogenic cultures promoted formation of multinucleated TRAcP-positive osteoclasts and upregulated osteoclast differentiation markers TRACP, RANK and Cathepsin Kand fusion marker DC-STAMP. In contrast, media from osteogenically preconditioned fibroblasts did not induce osteoclast formation. Across all parameters, GFs and PDLFs exhibited broadly comparable osteogenic and osteoclast-modulating phenotypes. These findings indicate that osteogenic differentiation acts as a functional switch that attenuates the osteoclast-inductive capacity of oral fibroblasts and support the interchangeable use of GFs and PDLFs in periodontal regenerative strategies.

F19 – Siem Muusz

FROM MOTION TO MUSCLE FORCES: DEVELOPMENT OF A BIPEDAL MUSCULOSKELETAL RAT MODEL

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Introduction - Muscles are the only actuators in movement, therefore individual muscle forces are central to understanding movement mechanics. Yet, we cannot measure individual muscle forces of all muscles simultaneously through experimental- and ethical limitations. Musculoskeletal models present a valuable tool to get estimates of how all muscles collectively determine movement. Well-established *in vivo* and *in situ* methods to determine intrinsic muscle dynamics provide fundamental validation of musculoskeletal computer models at individual muscles. Here, we integrate kinematics, kinetics, electromyography, with *in vivo* muscle dynamics into a musculoskeletal model of a rat, a go-to model species in (bio)medical research, to inform and evaluate predicted muscle behaviour during locomotion.

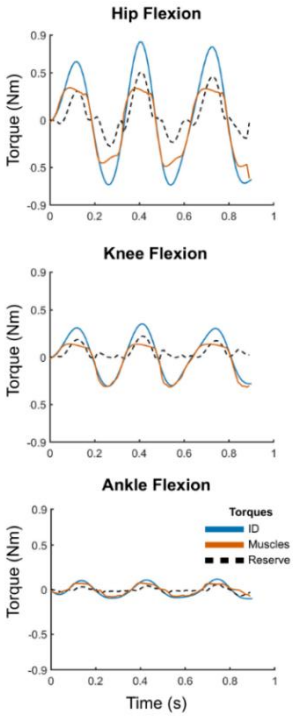

Figure 1: Joint torques obtained using inverse dynamics (ID, blue), muscle-driven torques (orange), and reserve actuator torques (black dashed) during inverse simulations of three consecutive steps.

Methods - We remodelled an incomplete but existing one-legged muscle model of the rat[1], to include toe segments and all major muscles of the limbs, resulting in 36 actuators. We updated segmental parameters (i.e., length, weight, centre-of-mass location, rotational inertia) based on rat cadaver dissections. We simplified the model by adjusting tendon slack lengths and wrapping surfaces to reduce unrealistic passive forces and to maintain physiologically realistic relationships between muscle-tendon complex length and joint angle. We estimated muscle parameters – tendon slack length and optimal fibre length – using an optimization-based method, with a generic literature-based model as the baseline[2].

Results - Segmental inertial properties and centres-of-mass followed expected trends, with larger inertias in heavier segments and more proximal mass distributions in the femur and tibia. Updating segment masses and inertial properties improved the feasibility. The model yields physiologically plausible estimates of inverse dynamics torques at the primary joints and is currently being refined to reduce reliance on reserve actuators (**Fig. 1**). Developing this initial model was a prerequisite for incorporating in-house *in vivo* and *in situ* data to explore the relative contributions of muscle mechanics and sensory feedback to agile locomotion.

Discussion - The model we present captures inverse kinematics and dynamics of current data[3], however it exhibits relatively high reserve actuator contributions. This discrepancy likely arises from inconsistencies between kinematic and kinetic data derived from different studies. We are confident that the model will perform better when applied to in-house data that we will collect in the spring of 2026, as part of ongoing study. The fully updated bipedal model will provide a valuable tool to investigate the muscle dynamics of the major leg muscles during rat locomotion, and has strong potential to increase confidence in musculoskeletal simulations applied to human movement, by enabling validation of core modelling assumptions under controlled experimental conditions.

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F20 – Xuedan Zhao

Alterations in Muscle–Tendon Structure and Function in a Mouse Model of Osteogenesis Imperfecta with Type I Collagen Haploinsufficiency

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Introduction: Osteogenesis imperfecta (OI) is a rare inherited disorder most commonly caused by pathogenic variants in type I collagen genes (*COL1A1* and *COL1A2*), which are associated with bone fragility, muscle weakness, tendon rupture susceptibility, and joint hypermobility[1-3]. A mouse model carrying a heterozygous deletion of the *Col1a1* allele that recapitulates haploinsufficient (HI) OI type 1 was recently developed[4]. This hiOI model shows collagen deficiency, evidenced by a reduced *Col1a1/Col1a2* mRNA ratio and decreased collagen biosynthesis marker procollagen type I N-terminal propeptide (P1NP). These mice display reduced bone volume and compromised bone structure and mechanics. Since intramuscular connective tissue and tendons are largely composed of type I collagen, this study aimed to assess whether and how collagen HI in this mouse model affects muscle and tendon structure and function.

Methods: Gastrocnemius muscles (GM) from 8-week-old wild-type (WT) and hiOI mice were analyzed for muscle mass, fiber-type composition (immunofluorescence), oxidative capacity (succinate dehydrogenase, SDH, staining) and connective tissue content (Picrosirius Red staining). Achilles tendons from 24-week-old WT and hiOI mice were subjected to 8% cyclic strain loading and pull-to-failure testing. Gene expression in muscle and tendon tissues was assessed by RT-qPCR. Data were analyzed using two-way ANOVA with genotype and sex as factors.

Results: GM mass was reduced by 15.9% in hiOI mice. In the high oxidative region, muscle fiber-type distribution differed between sexes, with male mice exhibiting lower percentage of type IIB fibers and higher percentage of type IIA and type IIX fibers than females. SDH activity was lower in females. Fiber cross-sectional area (CSA) was 19.4% larger in hiOI mice, and integrated SDH was higher in male mice. The connective tissue volume fraction in GM muscle, estimated from CSA measurements, was 16.2% reduced in hiOI mice and was lower in females than in males. However, endomysium and perimysium thickness exhibited a sex effect only, being larger in males. *Tgfb1* mRNA expression in GM was higher in hiOI mice.

Cyclic loading of Achilles tendons revealed lower maximum force and stiffness in hiOI mice compared with WT mice, while hysteresis was unaffected. Pull-to-failure testing indicated a 26.5% reduction in stiffness and 37.3% increased in strain at rupture in hiOI tendons. Regarding sex differences, only maximum failure force differed, with males resisting higher forces at failure than females.

All reported differences were statistically significant, with the exception of the *Col1a1/Col1a2* mRNA ratio in muscles and tendons (genotype effect: $p<0.15$).

Conclusions: Type I collagen haploinsufficiency in hiOI mice is associated with reduced gastrocnemius muscle mass and intramuscular connective tissue content, accompanied by decreased Achilles tendon stiffness and increased extensibility. These hiOI mouse muscle–tendon alterations are consistent with the muscle weakness and reduced tendon mechanical competence in individuals with OI. Our findings provide experimental support for muscle–tendon involvement in phenotypic characteristics of patients with OI.

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F21 – Daniel van Etteger

NOT FOR COMPETITION

GLUTAMINE IN THE POST-EXERCISE WARBURG EFFECT

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Sarcopenia and disuse induced muscle wasting are strongly associated with increased morbidity, making resistance exercise essential for maintaining physical health. Despite standardized training protocols, individuals exhibit significant variability in hypertrophic adaptations [1], the molecular causes of which remain poorly understood.

Muscle fiber types with high oxidative capacity have features like high mitochondrial density that associate with high protein synthesis rates, compared to more glycolytic muscle fiber types, this would suggest that high oxidative muscle fibers have greater anabolic potential. Yet the opposite is the case, as glycolytic fiber types have a greater anabolic capacity instead [2]. Recent research demonstrates that after hypertrophic stimulus, glycolytic fiber types have the ability to shift their metabolism to a 'Warburg-like' state. This metabolic reprogramming results in increased glycolytic flux and shunts glycolytic intermediates into anabolic pathways, such as the serine synthesis pathway [3], thereby elevating amino acid and nucleotide synthesis rates.

Paradoxically a study investigating mRNA expression in relationship to lean mass gains after a twelve week training regime has reported that mitochondrial related genes were most strongly associated with lean mass gains [4]. A potential factor reconciling this paradox, could be the availability of glutamine within muscle fibers. In proliferative cells glutamine catabolism (glutaminolysis) in mitochondria contributes to the production of glycolytic intermediates and to serine synthesis [5]. Consistently, A drop in both intramuscular and plasma glutamine has been observed after, but not during exercise [6][7]. We hypothesize that this drop reflects an increase in glutaminolysis after hypertrophic stimulus exposure. Yet whether glutaminolysis contributes to the hypertrophic response or if it prevents atrophy of post-mitotic muscle fibers remains elusive.

The aim of this study is to determine whether glutamine availability and utilization serves as a link between the Warburg-like metabolism and the crucial involvement of mitochondrial gene expression in post-exercise muscle fibers. We hypothesize that glutamine availability will be a limiting factor for myotube diameter growth and will upregulate the expression of genes associated with glycolysis and branching anabolic pathways.

To test this hypothesis, we propose experiments exposing differentiated myotubes to varying glutamine concentrations in the presence of growth-stimulating factors like IGF-1. As both glutamine availability and mitochondrial gene expression in response to resistance exercise varies between individuals, this could help explain differences in hypertrophic response between individuals. Understanding these mechanisms provides a foundation to optimize interventions to counterbalance muscle wasting and sarcopenia.

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F22 — Lois Boadu

OSTEOGENIC DIFFERENTIATION OF PRE-OSTEOBLASTS ON TITANIUM DIOXIDE NANOTUBES UNDER HYPERGLYCEMIC CONDITIONS

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ABSTRACT
Background: Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia. In diabetic patients, dental implant failure rates are reported to be significantly higher (≈14%) compared to non-diabetic individuals (2–5%). Reduced implant success in diabetic patients is mainly caused by impaired bone healing and altered cellular responses due to chronic hyperglycemia. Therefore, this study aims to investigate the effect of titanium dioxide (TiO_2) nanotubes on osteoblast differentiation under hyperglycemic conditions. **Methods:** MC3T3-E1 pre-osteoblasts were cultured under varying glucose concentrations on glass slide (5.5, 8, 12, or 24 mM) and Ti surface (5.5 or 24 mM) without/with nanotubes fabricated by anodization for 1 and 7 days. Cell morphology were observed by light microscopy and scanning electron microscopy. Pre-osteoblast metabolic activity, DNA content, alkaline phosphatase (ALP) activity, and gene expression assays were performed. **Results:** *Cells cultured on on glass slides:* MC3T3-E1 cells treated with different glucose concentrations spread well on glass slides at day 1 and 7. Cell metabolic activity was increased under 24 mM glucose compared to 5.5 mM (1.2-fold) and 8 mM (1.1-fold) glucose at day 1, but decreased by 24 mM glucose compared to 5.5 mM (0.7-fold), 8 mM (0.6-fold) and 12 mM (0.6-fold) glucose at day 7. *Cells cultured on Ti surface (Figure 1):* Cells cultured under 5.5 and 24 mM glucose spread well on a surface without/with nanotubes at day 1 and 7. Importantly, *Ki67* gene expression was not affected by the presence of nanotubes under 24 mM glucose at day 1 and 7. *Bmp2* gene expression was increased by 24 mM glucose in cells cultured on a surface with nanotubes (5.3-fold compared to 24 mM glucose without nanotubes at day 1; 7.1-fold compared to 5.5 mM glucose with nanotubes at day 1; 4.8-fold compared to 5.5 mM glucose with nanotubes at day 7). *Cox2* gene expression was decreased under 5.5 mM glucose in cells cultured on a surface with nanotubes (0.4-fold compared to 24 mM glucose without nanotubes; 0.4-fold compared to 24 mM glucose with nanotubes) at day 1, but was not affected at day 7. Notably, *Opn* gene expression was decreased under 5.5 mM glucose in cells cultured on a surface with nanotubes (0.5-fold compared to 24 mM glucose without nanotubes; 0.5-fold compared to 24 mM glucose with nanotubes) at day 1, but was increased (1.7-fold) at day 7, compared to the 24 mM glucose condition without nanotubes. **Conclusion:** These findings indicate that the biological performance on implants with nanoscale is sensitive to glucose levels, highlighting the importance of considering metabolic conditions in the development of bone-contacting materials. Understanding these interactions may help optimize titanium implant success and osseointegration strategies for diabetic patients.

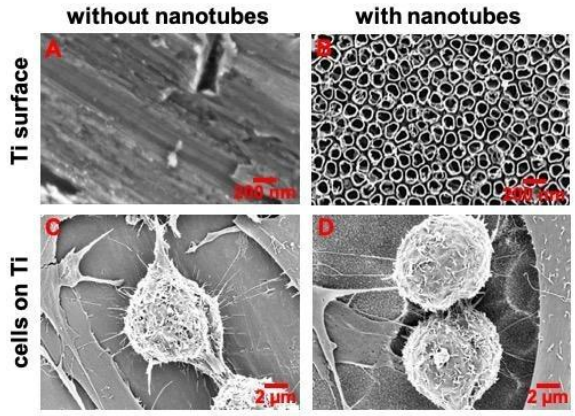

Figure 1. Titanium surface topography and cell morphology on titanium surfaces without and with nanotubes observed by scanning electron microscopy. (A) Titanium surface topography without nanotubes. (B) Titanium surface topography with nanotubes. (C) Cells on titanium surface without nanotubes. (D) Cells on titanium surface with nanotubes. Ti: titanium.

Sports & Health Research

S1 – Marijke de Leeuwerk

Implementation fidelity of a blended physical activity and nutritional intervention to optimize physical recovery after oncological surgery: Evaluation alongside the Optimal Physical Recovery After Hospitalization (OPRAH) randomized controlled trial

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Background: Blended interventions–combining e-health tools with remote coaching–offer a potentially sustainable and effective approach to support physical recovery after oncological surgery. To ensure such interventions achieve their intended outcomes, it is essential to evaluate implementation fidelity. The aim of this study was to evaluate the implementation fidelity of a blended intervention aimed at optimizing physical recovery following major abdominal oncological surgery, involving dietitians, physiotherapists, and patients.

Methods: Implementation fidelity was evaluated alongside a Randomized Controlled Trial investigating the effect of the Optimal Physical Recovery After Hospitalization (OPRAH) intervention. For three months post-discharge, dietitians and physiotherapists remotely coached patients using data on physical activity and protein intake collected via a smartphone application and activity tracker. Carroll's framework guided the evaluation of the two key components of the intervention: (1) self-monitoring and (2) remote coaching. Adherence and moderating factors were evaluated using both quantitative and qualitative data.

Results: Patient adherence to wearing the activity tracker and monitoring protein intake was high. All patients received coaching from at least one of the two professionals. A negative moderating factor was that the OPRAH intervention was difficult to implement in daily work routine. Positive moderating factors included positive responsiveness of physiotherapists, dieticians, and patients, well-functioning technology, and facilitation strategies that effectively engaged physiotherapists and dieticians.

Conclusion: Both patients and healthcare professionals demonstrated high adherence to the key components of the OPRAH intervention. For long-term implementation, the main challenge include embedding the intervention into routine care and maintaining facilitation strategies that promote effective collaboration between physiotherapists and dietitians.

S2 – Rijk Dersjant

REPEATED 12-WEEK FUNCTIONAL POWER TRAINING PROGRAMS YIELD ADDITIONAL AEROBIC AND ANAEROBIC IMPROVEMENTS IN AMBULANT CHILDREN WITH CEREBRAL PALSY

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5. Amsterdam Rehabilitation Research Center, Reade, Amsterdam, the Netherlands.

Introduction Functional power training (FPT) improves aerobic endurance and anaerobic capacity in children with cerebral palsy (CP). However, it remains unknown whether repeated intensive FPT programs show similar improvements over time.

Methods Retrospective data was used from twenty-one children with CP (ages 4–10; GMFCS I-II) who completed two 12-week FPT programs, with an average 1.30 ± 0.95 year gap between programs. Anaerobic capacity (Muscle Power Sprint Test, MPST) and aerobic endurance (10-Meter Shuttle Run Test, SRT) were measured before and after each program. Absolute changes in MPST and SRT performance due to training were compared between both training periods, using Wilcoxon tests, and paired-t tests, respectively.

Results Average MPST performance increased from 24.9 to 46.1 W during the first program, and from 42.8 to 77.3 W during the second program. Increases in MPST performance were significantly greater ($p=0.014$) during the second program. Average SRT performance increased from 5 to 9.2 shuttles during the first program, and from 8.2 to 11.8 shuttles during the second program, with no significant difference ($p=0.289$) between programs. A significant decline in SRT ($p=0.046$), but not MPST performance ($p=0.305$) occurred during the training gap.

Conclusion Repeated intensive FPT programs yield additional benefits in anaerobic capacity and aerobic endurance for children with CP, with a drop-off in aerobic but not anaerobic performance during the training gap. However, aerobic and anaerobic performance were expected to increase due to physical growth during the training gap. We intend to further evaluate how physical growth impacted these observed training effects.

S3 – Antoinette Houtkooper

IMPACT OF NEOPRENE WETSUITS ON LUNG VOLUMES AND WORK OF BREATHING: IMPLICATIONS FOR DIVER SAFETY AND PERFORMANCE.

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Introduction

Scuba diving is a physically demanding activity that exposes divers to unique environmental stressors, including hydrostatic pressure, equipment-related constraints, and thermal challenges. Neoprene wetsuits, essential for thermal insulation and buoyancy, may also impose mechanical restrictions on the chest wall and abdomen, potentially altering respiratory mechanics. While previous studies have reported reduction in dynamic lung volumes (e.g., forced vital capacity [FVC] and forced expiratory volume in 1 second [FEV1]) due to wetsuit use, the broader impact on static lung volumes, airway resistance, and work of breathing (WOB) remains poorly understood. These effects could have significant implications for diver safety, performance, and operational efficiency, particularly among military divers who operate under strenuous conditions.

This study aimed to investigate the influence of neoprene wetsuits on respiratory parameters, including dynamic and static lung volumes, airway resistance, and diffusion capacity. The primary goal was to assess how wetsuits alter respiratory mechanics and WOB.

Methods

A prospective, randomized crossover trial was conducted at the Royal Netherlands Navy Diving Medical Centre with 31 healthy male divers (age: 40.7 ± 11.1 years). Participants underwent pulmonary function testing, including spirometry, body plethysmography, and diffusion capacity for carbon monoxide (DLCO), both with and without a standardized 5 mm neoprene wetsuit. Primary outcomes included changes in FVC, FEV1, functional residual capacity (FRC), expiratory reserve volume (ERV), airway resistance (Raw), and WOB. Statistical analyses were performed using paired t-tests or Wilcoxon Signed-Rank tests, with significance set at $p < 0.05$.

Results

Wearing a neoprene wetsuit led to statistically significant reductions in FVC (2.8%, $p < 0.05$), forced expiration in 1 second (2.9%, $p < 0.05$), FRC (4.0%, $p < 0.05$), and expiratory reserve volume (10.9%, $p < 0.05$), alongside increases in inspiratory capacity and tidal volume. Raw increased significantly ($p < 0.05$), while DLCO remained unchanged.

Discussion and conclusion

Neoprene wetsuits induce mechanically restrictive effects on the chest wall, reducing static and dynamic lung volumes and increasing WOB. While these changes may not be clinically relevant at rest, they could compound respiratory demands during strenuous or prolonged dives, particularly when combined with other equipment that limits thoracic excursions. Future research should explore these effects under immersed conditions to better understand their operational impact on diver performance and safety.

S4 – Timo van den Bogaard

RESPONSIVENESS OF THE CALERA RESEARCH SENSOR TO HEAT-ACCLIMATION-INDUCED REDUCTIONS IN RECTAL TEMPERATURE

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Introduction. Military personnel and athletes increasingly use non-invasive methods to estimate body core temperature (T_c) during heat acclimation (HA). This study determined the responsiveness of the CALERA Research Sensor (CRS) to changes in resting and end-exercise T_c induced by HA as well as the criterion validity for determining the thermal dose, defined as time spent with a $T_c \geq 38.5$ °C.

Methods. Fifteen participants completed a nine-day controlled-hyperthermia HA protocol. T_c was continuously monitored prior to and during heat exposures using both the CRS (T_{crs}) and a rectal temperature (T_{re}) probe. This study assessed the responsiveness and criterion validity using a Bland-Altman analysis and intraclass correlation coefficient (ICC). Additionally, the analyses included a linear mixed model to further analyse the responsiveness.

Results. T_{crs} showed poor responsiveness to HA-induced changes in resting and end-exercise T_{re} with substantial bias (≥ 0.10 °C, limits of agreement from ≤ -0.40 °C to ≥ 0.60 °C) and poor agreement (ICC ≤ 0.23). Additionally, resting and end-exercise T_{re} decreased to a greater extent than T_{crs} during the nine-day HA ($P < 0.001$), which is shown in figure 1. The CRS underestimated thermal dose (-20 minutes, limits of agreement from -61 to 21 minutes) and showed poor agreement with T_{re} (ICC = 0.30). in estimating the thermal dose.

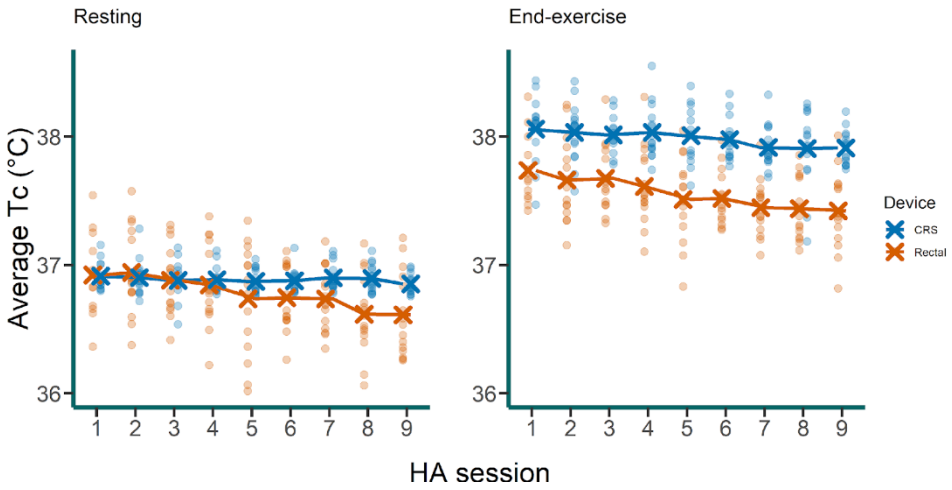

Figure 1: Average body core temperature for fifteen participants across heat acclimation sessions. The average body core temperature (T_c) during rest (left panel) and end-exercise (right panel) across nine heat acclimation (HA) sessions reduces to a greater extend when measured with a rectal probe (T_{re}, orange) compared to the CALERA Research Sensor (TCRS, blue). Dots represent mean values of each participant and symbol X represents the mean value of that HA session.

Conclusions. These results indicate that the current version of the CRS is not suitable to detect HA-induced changes in either resting and end-exercise T_{re} and to quantify the thermal dose.

S5 – Paul Voorn

THE EFFECT OF PROLONGED WALKING ON DAILY-LIFE GAIT QUALITY IN COMMUNITY-DWELLING OLDER ADULTS

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Introduction

Physical activity, including prolonged walking, is encouraged for all ages. Nonetheless, both inactive and highly active older adults show an increased risk of falling, particularly when engaged in bouted activities of ten minutes or more. This suggests that prolonged walking might increase fall risk in older adults. A potential contributing factor is a decline in gait quality, possibly due to exercise-induced fatigue. We investigated whether gait quality changes during daily-life prolonged walking in community-dwelling older adults. As we expect physically active older adults to be less fatigable, we also investigated whether their physical activity level (PAL) affects the expected changes in gait quality.

Method

Gait quality, gait quantity and PAL data of 229 older adults (mean age 76 years, 76% female) were collected using tri-axial inertial sensors worn on the lower back for one week. Long walking bouts (≥10 minutes) were extracted, and gait quality measures, including local dynamic stability and walking speed, were calculated for every ten seconds of these walking bouts. A mixed-linear-model was performed to analyse the relation between walking duration, gait quality, and walking speed, including sensor-based PAL as a moderator.

Results

From this cohort, 319 walking bouts (≥10minutes) were extracted. We found no significant change in walking speed, nor in gait stability over time during walking episodes of up to sixteen minutes. PAL did not moderate the relation between walking duration and gait stability.

Conclusion

Our preliminary findings suggest that, in real-world conditions, gait stability remains consistent during walking bouts of up to sixteen minutes, and this was not affected by changes in gait speed, nor by participant's PAL. Additional cohort data, and additional gait quality parameters are currently analysed to further explore the effect of prolonged walking on daily-life gait quality parameters.

S6 – Larissa Heideman

Feasibility of home-based assessments using wearable sensors and videos in children with GNAO1-related movement disorders: A pilot study

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Background: Movement disorders in GNAO1-associated disorder (GNAO1-RMD) are common, with dystonia being the most prevalent. Dystonia is characterized by involuntary movements and/or postural changes. Currently, clinical scales are used to monitor dystonia. However, this approach lacks objectivity. Assessments using wearable technology show promising results, but are scarcely tested in children. Therefore, our aim is to investigate feasibility of home-based assessments of dystonia in GNAO1-RMD using wearable sensors and videos.

Methods: Children with GNAO1-RMD wore five sensors around the wrists, ankles and head, all connected to a mobile device. Using the MODYS@home app – developed to synchronize video and sensor data –, children were filmed performing standardized tasks by parents/caregivers. An online survey was distributed to parents/caregivers for evaluation. Answers were given using a 5-points Likert scale for satisfaction and difficulty levels. All videos were scored for dystonia severity in five-seconds time-windows by three examinators, using the Burke-Fahn-Marsden-Dystonia-Rating-Scale and Barry-Albright-Dystonia-Scale. Inter-rater reliability (IRR) was calculated using the intraclass correlation coefficient (ICC).

Results: Three girls and four boys were included. Median age was 11 years (range: 10-14 years). All participants completed the survey (n=6). Two participants were satisfied with the overall experience of home-based assessments, four voted neutral. Difficulty levels of tasks varied amongst participants (very difficult, n=1; difficult, n=2; neutral, n=2; easy, n=1). Scoring and IRR are currently being executed.

Implications: Our results contribute to developing an objective, reliable measure to monitor GNAO1-RMD. Home-based assessments provide physicians with valuable *real-life* information, ultimately to track disease progression accurately and timely adjust treatment strategies.

S7 – Tamara de Haas

CAN EXISTING PREDICTIVE EQUATIONS ACCURATELY ESTIMATE RESTING ENERGY EXPENDITURE IN INDIVIDUALS WITH NEUROMUSCULAR DISEASES?

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3. Amsterdam UMC, Nutrition and Dietetics, Amsterdam, the Netherlands;
4. Amsterdam UMC, Gastroenterology Endocrinology Metabolism, Amsterdam, the Netherlands;
5. Amsterdam Movement Sciences, Aging & Vitality, Amsterdam, the Netherlands.

Introduction Accurate estimation of resting energy expenditure (REE) in individuals with neuromuscular diseases (NMD) is essential to prevent and manage both overweight and malnutrition, which are prevalent in this population. While indirect calorimetry is the reference standard for measuring REE, it is not routinely available in clinical practice, making healthcare providers reliant on predictive equations with unknown accuracy.

Purpose To evaluate the accuracy of frequently used predictive equations for estimating REE in individuals with NMD by comparing them to indirect calorimetry.

Methods REE and anthropometric data were cross-sectionally collected in participants with different NMD. Body weight and fat-free mass (FFM) were measured by air-displacement plethysmography. REE (kcal/day) was measured by indirect calorimetry using a ventilated hood and compared to five frequently used predictive equations: the equations from the World Health Organization (WHO weight + height), Harris & Benedict (1918), Henry, Mifflin-St Jeor (Mifflin), and Cunningham. Equation performance was assessed by the percentage of participants with accurate predictions, defined as a calculated REE within 90-110% of the measured REE. Root mean squared errors (RMSE) were calculated per equation to evaluate the overall fit. For each equation, characteristics (age, sex, BMI, diagnosis, muscle function and FFM-index) of participants with accurate and inaccurate predictions were compared with independent samples t-tests, Mann-Whitney U tests, or Chi-square tests.

Results Forty-nine participants with post-polio syndrome, Charcot-Marie-Tooth disease and inclusion body myositis were included (aged 32-79 years, 45% female). The Cunningham equation based on FFM had the highest proportion of accurate predictions, with 75% of participants accurately predicted (RMSE 209 kcal/day). Other equations ranged from 63% accuracy (WHO, RMSE 219 kcal/day) to 71% (Harris & Benedict, RMSE 195 kcal/day). For all equations, inaccurate predictions included both under- and overestimations of REE. Comparison of participant characteristics between accurate and inaccurate predictions showed no differences between groups for any equations, except for the Mifflin equation, where accurately estimated participants had a lower FFM-index compared to inaccurately estimated participants (15.9 ± 1.8 kg/m^2 vs. 17.9 ± 1.9 kg/m^2, $p<0.001$).

Conclusion The Cunningham equation provided the most accurate REE predictions in individuals with NMD. When FFM cannot be determined, the Harris & Benedict equation appears to be the most suitable alternative. Based on comparisons of participant characteristics between accurate and inaccurate predictions, no clear evidence was found to identify which individuals were more likely to be inaccurately predicted by the equations. Overall, the equations performed relatively well and can be used for individuals with NMD with reasonable confidence.

S8 – Bram Hoogerheide

Bi-directional associations between physical functioning and trajectories of five physical activity components in community dwelling older adults.

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Purpose:
Physical activity (PA) and physical functioning influence each other throughout life. When functioning declines during aging, it becomes harder to stay active, and when activity decreases, functioning often worsens. However, this bi-relationship is usually studied through a focus on one of these directions, rather than accounting for both directions of the association. Building on findings from the Longitudinal Aging Study Amsterdam (LASA), which identified long-term trajectories in each of five PA components (duration, intensity, strength, mechanical strain, and turning actions), this study is the first to examine the bi-directional association between ten-year activity trajectories of multiple PA components and physical functioning.

Methods:
Longitudinal Aging Study Amsterdam data includes a representative cohort of older Dutch adults. Previously identified PA trajectories were linked to measures of physical functioning (self-reported functional limitations and objective physical performance tests) for 4,963 participants (52% women; mean age = 66 years, SD = 8.6). Analyses were performed in two steps: first it was studied whether baseline physical performance and baseline functional limitations are associated with membership of PA trajectories with multinomial logistic regression; second, it was studied whether PA trajectory membership were associated with later-life physical performance with linear regression and functional limitations with multinomial logistic regression. All analyses were stratified by sex and adjusted for demographic, health, and lifestyle factors.

Results/findings:
Preliminary results show that higher baseline physical performance increased the odds of belonging to a more active PA trajectory, while higher baseline functional limitations decreased these odds. These associations held after adjustment for confounders and did not show marked differences between sex or PA components. After ten years of follow-up, membership in more active trajectories for duration, intensity, and strength predicted higher physical performance scores, except for intensity in men and strength in women. Trajectories for mechanical strain and turning actions were not associated with physical performance.

Conclusions:
These findings support a bidirectional relationship between physical activity and functioning. Better functioning increases the likelihood of remaining active, while maintaining higher intensity, strength, or longer activity duration is linked to better functional outcomes. Understanding these two-way associations can help refine strategies to promote independence and healthy aging.

S9 – Karlijn Kooijman

TRIGGER-FINGER BEHAVIOUR AND VISUAL ATTENTION DURING HIGH-RISK FIREARM DECISION-MAKING

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Special interventions operators respond to high-risk incidents that involve dangerous situations to the public, the subject and the officers and are often required to use their firearms. The use of firearms carries inherent risk including involuntary firearm discharges (IFD). While IFDs present an operational risk, not much is known about the perceptual-motor processes associated with them. Triggerfinger movements represent the final motor action leading to discharge, making them a valuable observable behaviour for understanding the mechanisms underlying IFDs.

This exploratory study investigated whether deviations in triggerfinger behaviour are associated with differences in gaze behaviour. Twenty-eight operators performed short reality-based shoot/don't-shoot scenarios under varying levels of ambiguity (low vs. high) and firearm procedures (SUL vs. holster) while wearing Pupil Invisible eye-trackers. To compare trials with and without triggerfinger deviations, "matched trials" were created: pairs of trials executed by the same participant with identical ambiguity, starting position, and decision outcome, but differing in triggerfinger behaviour.

Gaze behaviour was analysed using multiple metrics, including mean fixation duration, search rate, and fixation location. Analyses were conducted across entire scenarios and at the moment of triggerfinger deviation. Additionally, scan paths and timeseries graphs were created to examine gaze patterns. At the time of submission, data analyses are ongoing.

These analyses will provide insight into the perceptual-motor and attentional processes underlying triggerfinger movements in high-risk situations. Understanding these processes may inform training interventions aimed at reducing the risk of IFDs and enhancing operational safety.

S10 – Michel de Haan

DISENTANGLING THE RELATIONSHIPS BETWEEN MUSCLE CHARACTERISTICS AND PHYSICAL CAPACITIES IN YOUNG ELITE SOCCER PLAYERS

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Abstract

This study examines how *m. vastus lateralis* (VL) morphology relates to explosive (sprint capacity and jump capacity) and endurance capacity in young elite players. Twenty-four soccer players performed 20-meter sprints, a treadmill test to measure maximal oxygen uptake ($\dot{V}O_{2max}$), and countermovement jumps (CMJ) to measure jump height and peak push-off power. $\dot{V}O_{2max}$ and jump peak power were normalized to lean body mass$^{2/3}$ to adjust for body size. VL morphology was assessed using 3D ultrasound imaging. Relationships between explosive and endurance capacities were examined using Deming regression. Associations between VL morphology and physical capacity were assessed using linear and stepwise regression, and *k*-means clustering was used to identify specific subgroups based on VL characteristics. Normalized CMJ peak power and normalized $\dot{V}O_{2max}$ were inversely related, while average 20-meter sprint speed and normalized $\dot{V}O_{2max}$ showed no relationship. At the muscle level, volume was associated with increased sprint, jump and power capacities while physiological cross-sectional area was positively correlated to jump height. No morphological variables were linked to normalized $\dot{V}O_{2max}$. Clustering identified three distinct morphological profiles, which were associated with different physical capacities. In young elite soccer players, peak power, but not sprint speed, seemed to be mutually exclusive with endurance capacity. Muscle morphology influences physical capacity, with larger muscle volume and PCSA relating to higher sprint and jump outcomes. Furthermore, distinct morphological profiles of soccer players were identified and combining these profiles with insights into the relationships between morphology and physical capacity may enable more individualized training and player monitoring strategies.

Keywords: 3D-ultrasound, clustering, football, machine learning, $\dot{V}O_{2max}$

S11 – Elze Geurts

EIGHT OUT OF TEN PATIENTS PARTICIPATE AT THEIR DESIRED LEVEL OF SPORTS AFTER TALAR OSTEOPERIOSTIC GRAFTING FROM THE ILIAC CREST FOR LARGE OSTEOCHONDRAL LESIONS OF THE TALUS

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Background:
The Talar OsteoPeriostic grafting from the Iliac Crest (TOPIC) procedure shows successful clinical outcomes up-to 2-years follow-up for large osteochondral lesions of the talus (OLT). However, sports outcomes remain unknown.

Purpose/Hypothesis:
The purpose of this study was to prospectively evaluate sport outcomes for patients with large OLTs treated with the TOPIC procedure. Our hypotheses were that the TOPIC procedure would result in adequate (return to/participation in) sports outcomes and improvements of pain scores during running at 1 and 2 years after surgery.

Study design: prospective case series; Level 3.

Methods:
Sixty-one patients who underwent the TOPIC procedure for a symptomatic OLT were prospectively included with at least 24 months follow-up. Using digital questionnaires and an in-depth qualitative telephone interview, participation in desired level of sport at 1 and 2 years (primary outcome) was assessed. Secondary outcomes included different levels of return to- and participation in sports rates, as well as the Numeric Rating Scale (NRS) for pain during running and the Ankle Activity Score (AAS) at 1 and 2 years postoperatively.

Results:
59% and 82% of patients participated at their desired level of sport, at 1 and 2 years after TOPIC, respectively. Furthermore, 2 years postoperatively, the return to any level of sports was 96%, the return to preoperative level of sports was 93%, and the return to preinjury level of sports was 59%. The AAS significantly increased from 2 (IQR: 2-3) preoperatively to 5 (IQR: 5-6.5), 2 years postoperatively ($p<0.05$). The NRS for pain during running improved significantly from 9 (IQR:8-10) points preoperatively to 5 (IQR: 1-8) points at 2 years postoperatively($p<0.05$). At two years of follow-up, the reoperation rate was 38%.

Conclusion:
Almost all patients returned to sports, 8 out of 10 returned to their desired level of sport two years after the TOPIC procedure. Ankle activity significantly improved, and pain during running significantly decreased. Moderate symptoms, mostly unrelated to the graft, persisted in some patients, and 1 in 3 required reoperation.

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S12 – Karen Stolk

THE ADDED VALUE OF A SMARTPHONE APPLICATION AND THERAPIST DASHBOARD IN SELF-MANAGEMENT OF CANCER RELATED FATIGUE

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Introduction

Cancer related fatigue (CRF) is a highly prevalent and debilitating symptom following cancer treatment. Smartphone applications integrating wearable data and brief questionnaires may empower patients to self-manage CRF by providing insights and feedback on factors influencing their fatigue. Such applications could also enable tailored guidance from healthcare professionals. This study evaluates the perspectives of patients and their therapists on the usability and added value of a smartphone application combined with a therapist dashboard for self-management or therapy of CRF.

Methods

A mixed-methods feasibility study was conducted between May and December 2025. The smartphone application and therapist dashboard were developed in collaboration with patients and therapists. Patients with CRF were included via their oncological physical or occupational therapists. Patients completed the daily questionnaires in the smartphone app and were asked to wear a smartwatch. Data were accessible to both patients, via their smartphone application, and therapists, via their dashboard. Data collection included pre- and post-intervention surveys including demographic questions and assessing patients' CRF severity. The post-intervention survey, completed after 6 to 9 weeks of app usage, assessed usability, motivation, and overall satisfaction. Semi-structured interviews were performed after completion of the post-intervention survey and explored user experiences and perceived value. Quantitative data were analysed descriptively and qualitative data were analysed using template analysis.

Results

Twenty-one patients and 10 therapists participated. The System Usability Scale showed a reasonable usability (average score of 69), the intrinsic motivation was moderate and the Net Promoter Score was acceptable (average score of patients 15.79). Interviews revealed generally positive attitudes, however perceived added value varied. Therapists saw potential for this innovation to promote self-management of patients, as they became more responsible for their own rehabilitation process and gained insight into their fatigue. Patient interviews revealed that they were more aware of their energy management throughout the day or week due to completing the daily questionnaires.

Discussion

Our findings suggest possible benefits for self-management, but also highlight how perceived benefits vary strongly across individuals and contexts. Both patients and therapists see potential in the idea of a smartphone application combined with smartwatch data and a therapist dashboard, however they are doubtful about continue using this innovation themselves, probably due to not enough added clinical value.

S13 – Ilse Boot

THE IMPACT OF ANKLE IMMOBILITY ON SPRINT CYCLING PERFORMANCE: IMPLICATIONS FOR PARA-CYCLING CLASSIFICATION

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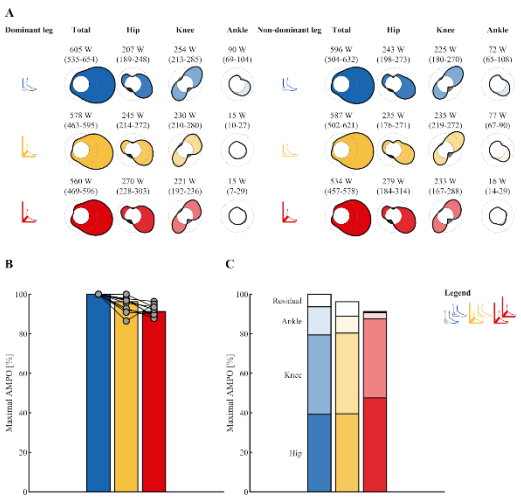
Introduction The International Paralympic Committee mandates the development of evidence-based classification systems for Paralympic sports, which minimize the impact of impairments on competition outcomes[1,2]. Recent research showed an overlap in track time trial performance between C3-C4[3] and C4-C5[4]. Ankle immobility is among the key determinants for classification in C3-C5[5]. This overlap may therefore be caused by insufficient knowledge of the impact of ankle immobility on cycling performance.

Purpose We investigated the impact of ankle immobility on cycling performance, quantified by the maximal average mechanical power output (AMPO) relative to that without ankle immobility.

Methods Ten well-trained able-bodied cyclists performed all-out seated sprints on a cycle ergometer with and without ankle foot orthoses (AFOs) immobilizing the ankle joint in neutral position (Fig. 1). The participants performed two 6-second isokinetic sprints per condition. Cadence was set to 120 rpm.

Power output was measured by SRM pedals, an SRM crank and the ergometer. Pedal forces were measured by the SRM pedals. An inverse dynamics analysis was performed using the measured cycling kinematics and pedal forces. The amount of muscle activation for four leg muscles was determined from EMG data. Non-parametric statistical tests were performed to test whether maximal AMPO, joint AMPO, and amount of muscle activation significantly differed across conditions.

Results Maximal AMPO significantly differed across conditions. Maximal AMPO with 1 AFO and 2 AFOs was 96 (92-97)% and 91 (89-94)% of 0 AFOs. Ankle joint AMPO was significantly lower with 2 AFOs than with 0 AFOs. It was only 19 (16-26)% of 0 AFOs. In contrast, hip joint AMPO was significantly higher with 2 AFOs than with 0 AFOs. It was 113 (106-127)% of 0 AFOs. Due to this increase in hip joint AMPO, the decrease in maximal AMPO with ankle immobilization was less than the decrease in ankle joint AMPO (Fig. 2). No significant differences in the amount of muscle activation across conditions were found.



Conclusion Relative maximal AMPO with 1 AFO and 2 AFOs was substantially higher than that estimated for athletes classified in C4 (96% instead of the estimated 70%) and C3 (91% instead of the estimated 64%)[4]. Thus, our findings may imply that the impact of ankle immobility on cycling performance may be smaller than that of other impairments classified in the corresponding classes.

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S14 – Liza van Dijk

SELECTION CRITERIA AND PREOPERATIVE PREDICTORS OF MOTOR OUTCOMES AFTER SELECTIVE DORSAL RHIZOTOMY: A SCOPING REVIEW

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Introduction: Selective dorsal rhizotomy (SDR) is a neurosurgical procedure that reduces lower limb spasticity, aiming to enhance motor function in ambulatory individuals or improve comfort and care for non-ambulatory individuals. Optimal treatment outcomes depend on careful selection. Current selection criteria primarily rely on expert opinion, hampering clinical decision-making and expectation management. This scoping review aims to map and synthesise the literature on SDR selection criteria, and to explore the empirical evidence supporting these criteria in relation to (functional) motor outcomes.

Methods: Following PRISMA-ScR guidelines, five databases were searched. Studies were included if they outlined SDR selection criteria or examined the relationship between preoperative patient factors and postoperative motor outcomes. A distinction was made between studies reporting selection criteria for ambulant and non-ambulant individuals.

Results: A total of 126 studies were included. Of these, 104 reported SDR selection criteria (n=67 for ambulant individuals, n=14 for non-ambulant individuals, n=33 for mixed), and 53 examined preoperative factors related to postoperative outcomes. Most of the selection criteria were reported within the International Classification of Functioning, Disability and Health (ICF) domain of 'Body Functions and Structures' for both ambulant and non-ambulant individuals. Two good-quality studies found no clear associations between several baseline characteristics and changes in gross motor functioning after SDR.

Conclusion: Current selection criteria are diverse, and although there is general agreement on the underlying key concepts as relevant criteria, there are considerable differences in how these concepts are operationalized in practice, which limits reproducibility. Empirical good-quality evidence linking preoperative factors to postoperative motor outcomes is scarce, limiting the development of robust, evidence-based selection criteria. To enable future meta-analyses and the development of evidence-based guidelines for this irreversible intervention, SDR selection criteria and outcome measures should be better harmonised. A Delphi study would be a good approach for developing a core set of selection criteria and outcome measures. The outcome of this review provides a decent basis for such a procedure.

S15 – Yvette Keij

EFFECTS OF STIFFNESS-OPTIMIZED ANKLE-FOOT ORTHOSES ON PATIENT-REPORTED OUTCOME AND EXPERIENCE MEASURES IN PEOPLE WITH CALF MUSCLE WEAKNESS

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Introduction

People with calf muscle weakness due to neuromuscular disorders often use ankle-foot orthoses (AFOs) to improve walking. To maximize the effects of AFOs for walking, it is important to individually optimize their bending stiffness. [1] Optimizing AFO bending stiffness has been shown to significantly reduce the energy cost of walking and increase comfortable walking speed compared to standard, non-optimized AFOs in individuals involving calf muscle weakness [1] [2]. However, the effects of individually optimized AFOs on patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) are unknown. To fully understand the impact of AFO stiffness optimization it is important to also determine the effects on user relevant outcomes in individuals with calf muscle weakness.

Purpose

What are the effects of stiffness-optimized AFOs on PROMs and PREMs compared to usual care AFOs in people with calf muscle weakness.

Method

We analyzed data of people with calf muscle weakness form a previous randomized controlled trial who received a standard care AFO (n=25) or a stiffness-optimized AFO (n=12) [3], in combination with data of 22 patients who received a stiffness-optimized AFO as part of usual orthotic care in Amsterdam UMC.

Both in the RCT and in usual care, outcomes were measured at baseline and 3 months after provision of the (stiffness-optimized) AFO. [4] The following outcomes were assessed: personal treatment goals (assessed with the goal-attainment scale (GAS)), perceived fatigue (Fatigue severity scale (FSS), range 9-36), physical functioning (Short Form-36 (SF36)), range 0-100), AFO satisfaction (D-Quest, range 0-5), pain (range 0-10), stability (range 0-10) and perceived walking effort (10-point BORG-scale). Outcomes were analyzed as change from baseline to 3 months follow up with independent t-tests or Mann-Whitney U-test for normally and non-normally data, respectively.

Results

In total, 25 patients received a standard care AFO (17 males, mean age of 64.9 ± 14.2 years) and 34 patients received a stiffness-optimized AFO (16 males, mean age of 67.4 ± 10.6 years). Outcome at baseline and at 3 months follow up for both groups, as well the change over time between groups is presented in Table 1. In the stiffness-optimized AFO group, 81% improved their GAS score by at least 2 points with a median score of 0 (desired goal attainment), compared to 33% for the control group with a median score of -1.5 (between unchanged and less than expected, $p = 0.016$). Furthermore, perceived stability improved significantly for the stiffness-optimized AFO group ($p = 0.048$). For all other outcomes, no significance differences were found between stiffness-optimized and standard care AFOs (all $p>0.190$).

Discussion

Our results indicate that patients who received a stiffness-optimized AFO showed greater improvement in their treatment goals and experienced stability compared to the control group, with desired goals being attained rather than remaining unchanged or being achieved to a lesser extent than expected in the control group. Stiffness-optimized AFOs were also superior in improving perceived stability. These results highlight the importance of including these patients reported outcomes in future AFO research. In addition to objective measures such as energy cost of walking and walking speed that are currently emphasized.

Table 1. Effects of stiffness-optimized AFOs compared to standard AFOs in PROMs and PREMs.

	Stiffness-optimized AFO group (n = 34)		**Standard care AFO group (n = 25)**		**Delta change over time between groups**	
	T1	T2	T1	T2	Mean ± SD or median [IQR]	*p-value*
Goal Attainment Scale	n.a.	0.0 [0.0 – 1.0]	n.a.	-1.5 [-2.0 – 0.0]	n.a.	**0.016***
Fatigue sum (FSS, range 9-36)	41.9 ± 11.9	40.1 ± 14.0	40.4 ± 11.0	39.0 ± 13.8	0.43 ± 2.62	0.678
Stability (NRS, range 0-10)	5.0 ± 1.7	7.2 ± 1.9	4.6 ± 1.8	5.6 ± 1.9	-1.20 ± 0.68	**0.048***
Pain (NRS, range 0-10)	2.5 ± 2.4	2.2 ± 2.0	2.6 ± 2.5	2.5 ± 2.4	0.23 ± 0.58	0.190
Physical functioning (SF36-PF, range 0-100)	46.0 ± 19.4	52.7 ± 20.2	48.4 ± 18.1	51.04 ± 20.4	-5.21 ± 4.07	0.309
Falls per year	1.0 [0.0 – 9.0]	0.0 [0.0 – 0.0]	3.0 [1.5 – 12.0]	3.5 [1.0 – 10.3]	-1.0 [-6.0 – 0.5]	0.212
Perceived intensity (BORG, range 0-10)	4.7 ± 2.6	4.0 ± 2.3	5.1 ± 2.0	4.4 ± 2.1	-0.02 ± 0.65	0.831
D-Quest aids av (range 0-5)	3.49 ± 0.41	4.16 ± 0.78	3.37 ± 0.52	3.67 ± 0.85	-0.32 ± 0.25	0.224
D-Quest services av (range 0-5)	3.62 ± 0.61	3.83 ± 0.51	3.63 ± 0.76	3.31 ± 0.55	-0.14 ± 0.31	0.689

D-Quest overall score (range 0-5)	3.89 ± 0.62	3.83 ± 0.55	3.73 ± 0.81	3.52 ± 0.67	0.10 ± 0.22	0.246

*Statistical significance was set at p-value<0.05. Outcomes are presented as mean ± Standard deviation or as median [interquartile range]

Abbreviations: SD = standard deviation, IQR = Inter quartile range, n.a. = not applicable, FSS = Fatigue severity scale, NRS = Numerical rating scale, SF36-PF = Short Form-36 physical functioning, D-Quest = Dutch version of the Quebec User Evaluation of satisfaction with assistive technology

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S16 – Isabella Gigante

FOOTWEAR EFFECTS ON BIOMECHANICAL AND USER-RELATED OUTCOMES, IN INDIVIDUALS WITH DIABETES AT MODERATE-TO-HIGH RISK OF FOOT ULCERATION AND OTHER POPULATIONS: A SYSTEMATIC REVIEW

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Introduction: Therapeutic footwear is recommended for individuals with diabetes at moderate-to-high risk of foot ulceration to reduce mechanical stress and protect the feet. Previous systematic reviews have focused on either the insole or the overall shoe, in relation to biomechanical or user-related outcomes, separately, without integrating these outcomes across the full range of footwear design components. This lack of combining specific components across both outcome categories makes it more difficult to translate evidence into footwear designs that are both mechanically effective and fulfil the user's needs. We aimed to systematically review biomechanical and user-related effects of footwear in people with diabetes at moderate-to-high ulceration risk (i.e. target population) and in other populations.

Methods: We conducted a PRISMA-guided systematic review in PubMed and Embase. Included studies were categorised by population, components, and outcomes, including pressure, shear stress, stability, adherence, usability, and quality of life. Studies involving the target population were classified as direct evidence, while others were considered indirect evidence. Risk of bias was assessed using the Critical Appraisal Skills Programme.

Results: Of 6303 screened studies, 288 were included (11 qualitative, 185 cross-sectional, 38 cohort, 54 RCTs), with 43 providing direct evidence. Stiffened rocker soles improved comfort and reduced plantar pressures at the forefoot and heel by 30-50% in direct evidence. However, indirect evidence showed that this component increased instability. Insoles with metatarsal pads reduced forefoot pressure by up to 57% in direct evidence. Pressure reductions were associated with foot pain relief in indirect evidence, however, these benefits compromised comfort and walking convenience. Upper-related components were not assessed in direct evidence and were rarely evaluated in indirect evidence. Overall, footwear adherence was most consistently associated with comfort, fit, and satisfaction rather than biomechanical performance. There was limited evidence on shear stress across all footwear components and populations.

Discussion: The results show that footwear components can affect biomechanical and user-related outcomes in different and sometimes opposing ways, such as rocker soles and metatarsal pads, which can improve offloading but decrease balance or comfort. Also, user-related outcomes, such as adherence, were strongly associated with comfort, fit, and satisfaction rather than biomechanical performance. Limited evidence on upper components and shear stress restricts the understanding of their effects on outcomes.

Conclusion: This review provides an overview of how footwear components impact biomechanical and user-related outcomes in populations with and without moderate-to-high ulceration risk. The trade-offs

between biomechanical and user-related outcomes highlight the need to combine both in designing footwear for individuals with diabetes at moderate-to-high risk of foot ulceration. These findings offer guidance for clinicians and technicians in selecting appropriate footwear features for the target population.

S17 – Silvia Bargeri

GENDER IMPACT ON PHYSICAL ACTIVITY IN MUSCULOSKELETAL DISORDERS PREVENTION: A SURVEY-BASED CROSS-SECTIONAL STUDY IN LOMBARDY REGION, ITALY (WEMOVEFORHEALTH)

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Background and aims: Musculoskeletal (MSK) disorders are among the leading causes of disability worldwide, and regular physical activity is essential for MSK prevention and rehabilitation. The 2020 World Health Organization (WHO) guidelines on physical activity and sedentary behaviour provide evidence-based recommendations on the amount of physical activity needed for health benefits. However, a substantial proportion of European adults remain insufficiently active, especially women. This gap appears particularly pronounced in Southern European countries (e.g., Italy), where structural and socio-environmental determinants may further constrain opportunities for physical activity. Therefore, we aim to investigate gender differences in adherence to WHO recommendations among adults living in the Lombardy Region (Northern Italy), and to explore associated socio-environmental characteristics and perceived barriers.

Methods: This cross-sectional study was based on an online survey (WeMoveForHealth), conducted at Galeazzi-Sant'Ambrogio Hospital, Milan (ClinicalTrials.gov: NCT06747052). Eligibility criteria were adults of any gender aged 18-64 years residing in Lombardy. The survey was open for 6 months (February-August 2025) and disseminated through social media, emails, flyers, and collaborations with local associations. The primary outcome was adherence to WHO physical activity recommendations. Socio-environmental factors, beliefs on the preventive role of physical activity for MSK disorders, and perceived barriers were also collected. Descriptive analyses and multivariable logistic regression were performed using STATA. We reported results comparing women and men because the number of gender-minority participants was too small for meaningful analysis.

Results: The survey webpage was accessed by 1,412 individuals; 1,283 (90.9%) provided informed consent and 1,202 (85.1%) met the inclusion criteria. In total, 1,113 participants completed the whole questionnaire (completion rate 92.6%). The sample included 75.1% women, 24.4% men, and 0.5% gender-minority participants, with a median age of 42 years. Overall, 46.8% adhered to WHO recommendations, with higher adherence among men (64.4%) compared with women (40.9%). Gender differences were observed in domestic workload distribution (54.5% women vs 21.6% men), caregiving responsibilities (17.2% vs 10.4%), and full-time employment (69.2% vs 81.5%). In multivariable analysis, female gender was independently associated with lower adherence to WHO recommendations (OR 0.31, 95% CI 0.22-0.43). Beliefs regarding the preventive role of physical activity were positive across all groups (99%). The most frequently reported barriers were lack of time (59.4% women vs 63.9% men), lack of

motivation (42.9% vs 61.1%), fatigue due to commitments (40.0% vs 36.1%), and family responsibilities (21.8% vs 13.9%).

Conclusion: In this adult sample from Northern Italy, adherence to WHO physical activity recommendations was substantially lower among women than men. These findings are relevant to European MSK prevention and rehabilitation agendas, supporting gender-sensitive strategies that address caregiving burden and socio-environmental barriers. Future studies should use targeted recruitment to better understand needs among gender-minority groups.

S18 – Stijn Wolters

HEMODYNAMIC RESPONSES AND AUTONOMIC SYMPTOM BURDEN DURING SUPINE-TO-STAND TESTING IN POST ACUTE INFECTION SYNDROMES

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Background:
Post-Acute Infection Syndromes (PAIS), such as Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) and Long COVID, are characterized by chronic symptoms after an acute viral infection, with severe fatigue, muscle pain and cognitive dysfunction amongst the most reported symptoms. Dysautonomia, which is increasingly recognized as an important part of both conditions, has been proven to manifest itself in patients as orthostatic intolerance (OI). OI is defined as the inability to tolerate an upright position and is typically assessed using supine-to-stand tests, e.g. the NASA Lean test. Different OI phenotypes such as postural tachycardia syndrome (POTS) or orthostatic hypotension (OH) can be derived from this test, through the analysis of hemodynamic changes like blood pressure and heart rate. Previous studies have indicated that not all patients with OI symptoms display OI during supine-to stand tests. However, these studies have not focused on differences in the severity of subjective symptoms in the patients without a testing OI diagnosis and this has also not been compared across different PAIS.

Objective:
This study aims to evaluate the presence and characteristics of OI in patients with ME/CFS and Long COVID compared to healthy controls, using both hemodynamic responses from NASA Lean Testing and patient-reported symptom burden. As well as evaluating symptom burden in those not able to complete the testing protocol or those without a tested OI diagnosis.

Methods:
The used dataset was obtained from the Dutch ME/CFS Cohort and Biobank (NMCB), comprising 250 participants, among which are patients with ME/CFS (n=88), Long COVID (n=95), and healthy controls (n=67). All participants underwent NASA Lean Testing as part of standard biobank protocol. Autonomic and general symptom burden were assessed using validated questionnaires, including the Composite Autonomic Symptom Scale-31 (COMPASS-31), the DePaul Symptom Questionnaire (DSQ), and the 36-item Short Form Health Survey (SF-36). Hemodynamic responses and symptom profiles will be compared across groups.

Results:
All analyses will be completed prior to the AMS annual meeting. It is expected that both ME/CFS and Long COVID patients will demonstrate a higher prevalence of OI based on physical testing and autonomic symptom burden compared to healthy controls, with potential differences between the two patient groups.

Discussion:
The results of this study could contribute to an improved understanding of OI in ME/CFS and Long COVID and create a basis for future studies to see whether other parameters (e.g. heart rate variability) that are measured during physical testing could provide more information about OI in these patient populations.

S19 – Miguel Cifuentes Santamaria

Cortico-synergy coherence under gravitational unloading in adult locomotion

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Understanding how the brain, spinal cord, and sensory systems interact is essential for improving mobility in clinical rehabilitation and in altered-gravity environments. Body-weight support (BWS) provides a unique experimental framework to investigate these interactions, as it partially unloads the body while preserving natural walking patterns, allowing systematic probing of sensorimotor adaptations as sensory feedback is gradually reduced. In this project I will investigate how cortical and spinal networks interact to sustain stable gait across a wide range of unloading levels (0–100%). Electroencephalography, multi-muscle electromyography, and full-body motion-capture recordings will serve to unravel the temporal entrainment of rhythmic cortical activity and the coordinated activation of muscle groups, known as muscle synergies. For this we will focus on beta-frequency coherence (13–30 Hz), an indicator of sensorimotor communication between cortical and spinal circuits. Data collection and analysis will be a collaborative effort at VU Amsterdam and the Laboratory of Neuromotor Physiology at the IRCCS Santa Lucia Foundation Hospital in Rome. It combines complementary expertise in cortical analysis, gait neuroscience, and body unloading technology, creating a valuable exchange of knowledge and methodology between the Department of Human Movement Sciences, the AMS research institute, and one of Europe's leading gait laboratories. The overarching aims is to advance our understanding of sensorimotor integration in locomotion. My results are expected to inform the development of personalized gait-training strategies in neurological rehabilitation and contribute to research on movement control in reduced-gravity environments relevant for space exploration.

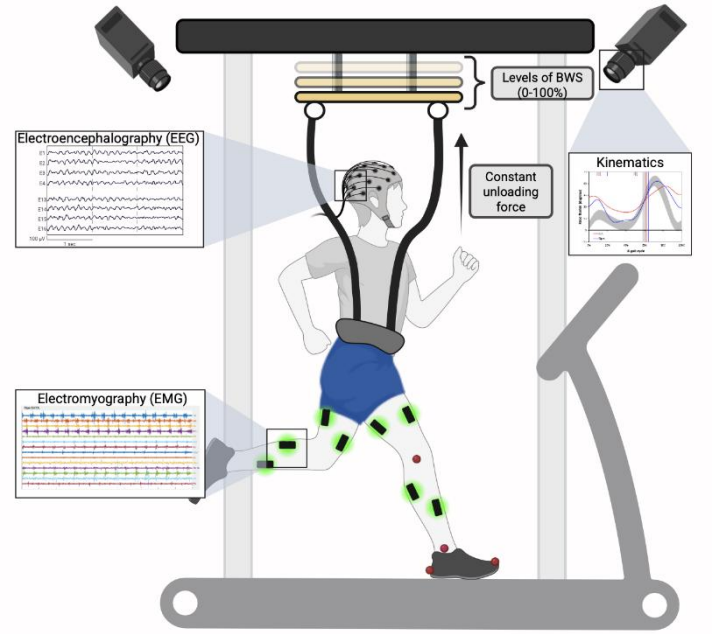

Figure 1. Experimental setup. Participants will walk on a treadmill under different levels of Body-Weight Support (BWS) from 0-100%, while kinematics, surface electromyography (EMG) and electroencephalography (EEG) are recorded. *Created with BioRender.com*.

S20 – Alessandro Vicentini

The Long-term Effects of a Personalized Multimodal Intervention on Plantar Pressure, Physical Activity, and Footwear Adherence in People with Diabetes at High Ulcer Risk: a preliminary analysis

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Background: In people with diabetes, mechanical loading of the foot contributes to ulcer development and recurrence. The factors contributing to mechanical loading (plantar pressure, physical activity and footwear adherence) are mostly assessed at one moment in time, but if and how they change over time remains poorly understood. This study aims to assess these factors between two care models using data from a subsample of a multicenter randomized controlled trial (DIASSIST).

Methods: From the 126 participants enrolled in the DIASSIST trial, 32 with complete plantar pressure, physical activity, and adherence data were included (usual care [UC]: n = 13, age 71.1 ± 6.3 years, BMI 27.9 ± 3.8 kg/m^2; enhanced care [EC]: n = 19, age 69.5 ± 10.6 years, BMI 29.0 ± 7.4 kg/m^2). Enhanced care comprised pressure-optimized footwear, custom-made indoor shoes, daily foot temperature monitoring, and tailored education, while usual care followed standard clinical guidelines. In-shoe and barefoot plantar pressure were assessed during walking and standing at baseline and 12 months. Physical activity (steps and standing duration) was measured using a tri-axial accelerometer, and footwear adherence using a shoe-embedded temperature sensor. Pressure–time integral (PTI) was calculated per foot region, and cumulative plantar tissue stress (CPTS) was computed using a validated model integrating PTI, physical activity, and adherence. Within-group changes were analysed using paired t-tests with effect sizes (Cohen's d), and between-group differences were assessed using independent t-tests.

Results: At 12 months, in-shoe PTI during walking was slightly lower in the EC group at the heel (77.6 vs 80.4 kPa·s) and metatarsals 2–5 (59.5–60.7 vs 62.7–68.2 kPa·s), but higher at the hallux (56.4 vs 46.9 kPa·s) and metatarsal 1 (54.4 vs 51.2 kPa·s). During in-shoe standing, PTI was lower at metatarsals 2–5 (41.3–49.5 vs 45.1–50.6 kPa·s). No significant in-shoe PTI differences were observed. For barefoot PTI, a baseline difference was observed at metatarsals 4–5 during walking (EC: 207 vs UC: 330 kPa·s; p = 0.046). Change-score analysis showed a significant group difference at metatarsals 2–3 (From 256 to 308 kPa·s in EC; from 356 to 334 kPa·s in UC; p = 0.046). The EC group showed higher physical activity, with step counts of 6077 ± 4315 vs 3815 ± 2232 at baseline and 5481 ± 3293 vs 3442 ± 2507 at final visit, as well as longer standing duration (8249 ± 2668 vs 6333 ± 2841 s at baseline). Footwear adherence declined in both groups, with walking adherence decreasing from 62% to 50% in the UC group and from 66% to 53% in the EC group. Total CPTS decreased in the UC group, significantly at metatarsal 1 (from 895 ± 783 to 741 ± 617 MPa·s/day; p = 0.028), while increasing across all regions in the EC group (e.g., metatarsal 1: from 780 ± 390 to 853 ± 536 MPa·s/day). Near-significant group differences were observed at metatarsal 1 (p = 0.053) and metatarsals 4–5 (p = 0.089).

Discussion: No statistically significant differences were found between UC and EC for PTI, physical activity, or footwear adherence across groups or time points. Overall, the intervention did not clearly alter individual loading-related factors, although the small sample size of this sub-analysis may have limited the findings. CPTS was generally higher in the EC group, suggesting that behavioural factors, (e.g., physical activity and footwear adherence), may have outweighed biomechanical factors in determining

cumulative plantar loading. The analysis of the full DIASSIST cohort (n = 126) is warranted to more effectively investigate the long-term effects of a personalized intervention on cumulative plantar loading.

S21 – Peifeng Zheng

MRI Radiomics and Machine Learning Models for Return-to-Sport Prediction after Hamstring Injury

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Introduction : Acute hamstring injury is a frequent sports injury, yet predicting return-to-sport (RTS) remains challenging. Conventional MRI grading provides limited prognostic value. Radiomics, which quantifies image features beyond visual assessment, may enhance prediction accuracy. This study aimed to identify the optimal MRI modality and machine learning model for predicting RTS in acute hamstring injuries.

Materials & Methods: This is a retrospective study, analyzing data from a previous randomized clinical trial (NTR2771), involving single-center 80 patients with acute hamstring injury. Baseline 1.5 Tesla MRI scans (T1-weighted [T1w], T2-weighted [T2w], and Short Tau Inversion Recovery [STIR] sequences) were acquired within 5 days post-injury. Binary RTS outcome was defined using a data-driven threshold at the cohort median to achieve 1:1 class balance. Six algorithms (random forest, eXtreme Gradient Boosting [XGBoost], support vector machine [SVM], Naive Bayes, decision tree, logistic regression) were applied using radiomic features from these sequences. Performance was evaluated by Area Under the Curve (AUC), accuracy, precision, sensitivity, specificity, Brier score, and decision curve analysis (DCA); AUC differences assessed by Wilcoxon signed-rank test ($p < 0.05$).

Result: A total of 80 participants (age 29.0 ± 7.5 years, 76 male and 4 female) were included, and 321 radiomic features were extracted for screening and model development. Each of the evaluated models predicting RTS exhibited unstable predictive performance across 10 repeated runs, with mean AUC values below 0.7. The best-performing STIR+T2w-SVM model achieved an AUC of 0.63 ± 0.16 (95% CI [0.25, 0.88]), and a clinical decision curve benefit (delta net benefit star) of 0.07, outperforming all other models ($p < 0.05$).

Conclusion: SVM model outperformed other models for predicting RTS after hamstring injury, with the STIR-based model showing the best performance.

S22 – Ítalo de Paula

NOT FOR COMPETITION

PLACEBO EFFECT OF MOUTH RINSE ON PHYSICAL PERFORMANCE

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Introduction: Caffeine mouth rinse is one fast strategy to increase corticospinal excitability, motor unit recruitment, and activation of motor regions in the brain, resulting in improved exercise performance. As positive effects on physical performance are popular with supplementation of caffeine (CAF), some people improve their performance just by believing they used CAF, a phenomenon known as the placebo effect. The effects on the reward circuit, motor planning, and opioid system are suggested as characteristics of this placebo effect. Thus, the objective of this study is to investigate the effects of caffeine mouth rinse on exercise performance and the contribution of the placebo effect to this supplementation strategy. Preliminary data will be presented of a first sample of participants.

Methods (Preliminary Data): 9 participants (3 women and 6 men) came to the laboratory and completed two familiarization and two experimental trials (1-Isometric test at 80% MVC with mouthrinse of CAF; 2-Isometric test at 80% MVC with mouthrinse of placebo (PLA)). During each experimental visit, the participants performed two isometric tests: one before (pre) and one after (post) mouth rinse (either with CAF or PLA). The mouth rinse protocol consisted of 4 x 10 seconds of rinsing without ingestion of the substance. Participants also performed the rinse immediately before and during the isometric test. The participants received 25 ml drinks per mouthrinse session containing either CAF (90 mg) or PLA (0.25 mg Teacrine). Physical performance was measured by the time to exhaustion on the isometric tests. An ANOVA 2x2 ($p<0.05$) was used to analyze the difference in time to exhaustion, comparing the main effects of moment (pre vs. post mouth rinse) and condition (CAF vs. PLA), as well as their interaction.

Results: No main effect for condition was found for time to exhaustion. There was a main effect for moment, evidencing that time to exhaustion post mouthrinse was longer than pre mouthrinse (pretest CAF = 47.67 ± 19.29 sec; posttest CAF = 58.11 ± 17.07 sec; pretest PLA = 47.56 ± 25.02 sec; posttest PLA 80% MVC = 60.3 ± 28.50 sec ($F_{(1,15)}= 14.4$, $p < 0.01$). Finally, no interaction effect was found.

Discussion: The study revealed that performing exercise at high intensity with any mouth rinse led to better performance than in the pre-test with no mouth rinse, but this was independent of caffeine as there was no effect of the specific condition (caffeine vs. placebo). Based on the current results, it could be suggested that mouth rinse effects, caused a placebo effect independent of substance, affecting time to exhaustion. However, only a first sample of participants has been analyzed, and more are being recruited as we speak to obtain the required number for full analysis and interpretation. A confounding factor could be the extent to which participants guess if they receive any treatment or not, and the intensity of exercise.

Clinical Research

C1 – Joyce Burger

A MOTIVATIONAL PARADOX: AN INVESTIGATION OF THE RELATIONSHIP BETWEEN CHALLENGE, PERCEIVED COMPETENCE AND ENJOYMENT IN GAME-BASED PHYSICAL EDUCATION

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Physical education (PE) uniquely enables learning through movement and therefore offers an important opportunity to develop students' physical literacy, including motivation, confidence, physical competence, and knowledge and understanding to support lifelong physical activity. As game-based activities constitute the most prominent activity in PE curricula worldwide, fostering students' motivation to engage in game-based lessons represents a critical first step in supporting physical literacy development. Previous research suggests that teachers can foster motivation by manipulating challenge, however, the literature presents conflicting perspectives on the level of challenge that is most motivating. The extended challenge point framework and self-determination theory suggest that challenge should be set below students' skill levels to stimulate perceived competence and therefore belief in one's own abilities, which increases motivation. In contrast, an inverted-U relationship proposes that moderate tension between challenge and skill is most motivating. This study therefore aimed to isolate the effect of challenge on students' perceived competence and enjoyment in a game-based PE setting to answer the following research question: '*Does challenge influence the perceived competence and enjoyment of first-year-secondary-school students, and if so, what does this look like?'*

A within-subject design was used in which 60 first-year secondary school students participated as attackers in both an easy and difficult version of a game (circle ball). Challenge was manipulated by hoop size (100 cm vs. 50 cm). After each condition, students completed the Intrinsic Motivation Inventory subscales for perceived competence and enjoyment, while the number of successful attacks was recorded by two independent observers for all 10 attacks. Differences between conditions were examined using dependent t-tests. Linear mixed models explored the relationship between successful attacks, perceived competence, and enjoyment, and a mediation analysis tested whether perceived competence mediated the relationship between successful attacks and enjoyment.

No differences in perceived competence or enjoyment were found between the easy and difficult conditions. However, a higher number of successful attacks significantly predicted both perceived competence and enjoyment. Perceived competence fully mediated the relationship between successful attacks and enjoyment.

These findings suggest a linear relationship between challenge and motivation, supporting self-determination theory and the extended challenge point framework rather than an inverted-U relationship. The absence of a quadratic effect may be explained by limited data points at the extreme ends of successful attacks for perceived competence and enjoyment, as well as individual differences in motivational profiles. Future research should incorporate students' perceived challenge and mixed-method approaches to better capture individual motivational differences in game-based PE.

C2 – Jules Cool

RADIATION REDUCTION IN COMPUTER-ASSISTED SPINAL DEFORMITY SURGERY USING 3D AND 2D PEDIATRIC SPECIFIC LOW-DOSE FLUOROSCOPY PROTOCOLS

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Introduction: Computer-assisted navigation (CAN) improves pedicle screw accuracy in adolescent idiopathic scoliosis (AIS) surgery but involves intraoperative radiation exposure. This study evaluated novel low-dose 3D and 2D imaging protocols for AIS surgery by assessing image quality for CAN and quantifying radiation reduction.

Methods: Thirty AIS patients were prospectively included: 10 underwent standard-dose 3D imaging and 20 low-dose 3D imaging. The detector entrance dose was lowered from 0.087 to 0.029 µGy/image to achieve the low-dose protocol. Radiation exposure was quantified using dose-area product (DAP). Image quality was evaluated using signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR), and subjective image quality scores. Additional standard- and low-dose 2D fluoroscopy was used throughout the procedures. The per-frame radiation dose was adjusted from 26 nGy to 4 nGy to achieve the low-dose 2D protocol.

Results: The median 3D radiation dose was significantly lower for the low-dose protocol than for the standard protocol (24.6 vs. 57.7 cGy·cm^2, $p < 0.001$), without significant differences in SNR or CNR, and with both protocols deemed subjectively adequate for pedicle screw navigation. For 2D fluoroscopy, mean total DAP ranged from 18.5-106.7 cGy·cm^2 with the standard protocol and from 15.9-58.3 cGy·cm^2 with the low-dose protocol, depending on the frame rate selected.

Discussion: The low-dose 3D fluoroscopy protocol achieved a radiation reduction of 57%. Although a minor, non-significant degradation in image quality (SNR and CNR) was observed, this did not result in a relevant impact on subjective image quality. This supports the use of the low-dose 3D protocol as standard, offering substantial radiation savings. In addition, 2D fluoroscopy contributed substantially to the total intraoperative radiation dose. The 2D dose can be lowered by reducing per-frame radiation dose, but also other intraoperative measures as the use of the minimum frame rate.

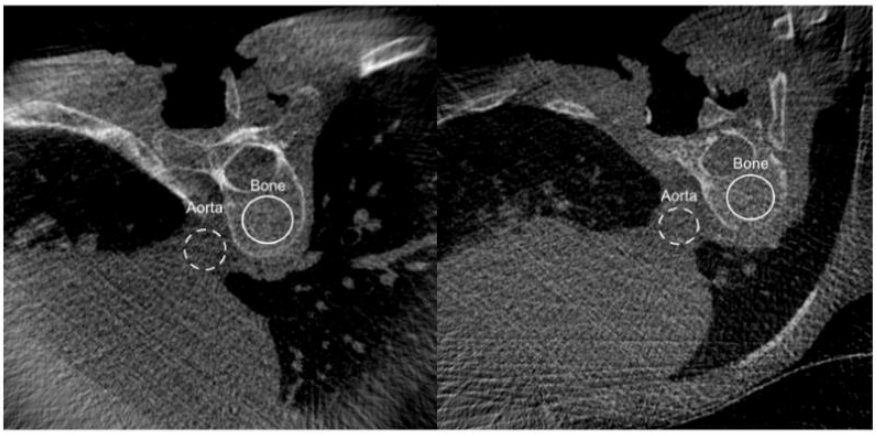

Figure 1: intra-operative 3D-images using the standard (left) and low-dose (right) 3D fluoroscopy protocol

C3 – Charlotte van Westerhuis

OPTIMIZING INTERPROFESSIONAL COLLABORATION IN ONCOLOGICAL PRIMARY CARE REHABILITATION: A QUALITATIVE STUDY AMONG DIETITIANS AND PHYSIOHTERAPISTS

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Abstract

Background: Rehabilitation after gastrointestinal and lung cancer surgery often extends into primary care, where oncology dietitians and physiotherapists support patients with nutritional and physical challenges. Although interprofessional collaboration (IPC) is recognised for enhancing the quality of care and patient outcomes, its implementation in primary care is limited due to unclear roles, negative perceptions, and inadequate interprofessional education. This study explores needs, wishes, and strategies to optimise IPC between primary care oncology dieticians and physiotherapists.

Methods: This qualitative study used a constructivist, semi-structured approach. Fourteen interviews were conducted with primary care oncology dietitians (n = 8) and physiotherapists (n = 6) with a focus on rehabilitation, structured around IPC themes: values and ethics, roles and responsibilities, communication, and teams and teamwork. Reflexive thematic analysis was used to inductively analyse the data.

Results: Four main themes were generated: 1) building trust through recognition as a basis for IPC; 2) clarifying professional boundaries for role clarity; 3) aligning information exchange for coherent care; and 4) future wishes for IPC. The first three highlight needs as well as trust, role clarity, and communication, which are addressed through strategies such as personal engagement, regional networks, and formal agreements. The fourth captures professionals' wishes.

Conclusion: Building trust, clarifying roles, and aligning information exchange between dietitians and physiotherapists is important to optimise IPC. Addressing these needs and implementing proposed strategies may enhance collaboration and improve oncological care outcomes. Results should guide the design of a primary care pathway for oncology dietitians and physiotherapists.

C4 – Jens te Velde

PROGNOSTIC FACTORS FOR HIGH INTRAOPERATIVE BLOOD LOSS IN MULTIPLE MYELOMA-RELATED BONE DISEASE IN THE SPINE

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Introduction: Spine surgery for multiple myeloma (MM) is associated with an increased intraoperative blood loss. Therefore, this study aims to examine prognostic factors for higher intraoperative blood loss in spine surgery for patients with MM.

Methods: In this retrospective multicenter cohort study, 158 adult patients with MM undergoing spine surgery between May 2001 and December 2021 were included. The main outcome for intraoperative blood loss was the Bleeding Index (BI), next to the visually estimated blood loss (EBL). Two separate multivariable generalized linear models (GLMs) were utilized to assess the associations between the predictors and these two outcomes.

Results: The average BI was 4.4 and average EBL was 750 ml. Compared to corpectomy with stabilization, other types of surgery (decompression with stabilization, sole decompression, sole stabilization) were associated with a lower expected BI, ranging from a 26.5% to 39% decrease. A cervical location of surgery was associated with a 40.3% reduction of expected BI compared to a lumbar location (p = 0.006). Lower platelet count (p = 0.003) and longer duration of surgery (p < 0.001) were associated with a higher expected BI. For EBL, ECOG score, surgery type, and duration of surgery were found as independent predictors.

Conclusion: This study identified lower platelet count, type of surgery, location of operated spinal levels, and a longer duration of surgery as independent predictors of higher intraoperative BI in MBD-related spine surgery. These outcomes can be relevant for preoperative screening, shared decision making, and perioperative blood transfusion deliberation or planning.

C5 – Marte Lommerse

A CASE SERIES ON PENG BLOCK USE IN PRE- AND POSTOPERATIVE PAIN MANAGEMENT IN ACETABULAR FRACTURES

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Introduction The pericapsular nerve group (PENG) block, designed to target anterior sensory nerves of the hip capsule while sparing motor function, is a recently developed regional analgetic adjunct to opioid-based postoperative pain management in hip fracture management. This study aimed to evaluate the clinical utility of the pericapsular nerve group (PENG) block for pre- and postoperative pain management in patients undergoing surgical fixation of acetabular fractures.

Methods We conducted a retrospective case series of patients who underwent fixation of an acetabular fracture at a level-1 trauma center (2019–2023) and received a pre- or perioperative PENG block. The primary outcome was pain post-block (Numerical Rating Scale, NRS). Secondary outcomes included opioid use (Morphine Milligram Equivalent, MME), time to mobilization, hospital length of stay, and block-related adverse events.

Results 17 adult patients (mean age 68 years, 65% male) were included. Fractures with an anterior component were present in 88% of cases. Baseline NRS scores at rest were generally low (71% ≤4). Twelve patients (71%) reported unchanged or decreased NRS post-block or post-catheter removal; six patients (35%) achieved ≥2-point reduction, mainly in the catheter group. Median opioid use showed minimal change (single-shot +13 MME; catheter −7.5 MME). Ambulation occurred at median 2 versus 5 days for single-shot versus catheter patients. No major block-related complications were observed.

Conclusions The PENG block provided limited and inconsistent analgesic benefit in acetabular fracture surgery. Pain reduction and opioid-sparing effects were modest, and postoperative opioid use remained necessary. These findings suggest that the PENG block may have limited utility for routine use in this setting. Prospective studies with standardized outcome measures and appropriate comparators are needed to clarify its clinical role.

C6 – Chiel Klein

A LARGER EXTENT OF RADIOLUCENT LINES AROUND TIBIAL COMPONENTS OF TOTAL KNEE ARTHROPLASTY ON CONVENTIONAL RADIOGRAPHS DOES NOT IMPLY MORE LOAD-INDUCED DISPLACEMENT

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Purpose:
After Total Knee Arthroplasty (TKA), radiolucent lines on routine conventional radiographs are commonly interpreted as impaired tibial component fixation, although their relation to implant motion remains unclear. This necessitates a comparison with actual measured component displacement. Recently, a CT-based method measuring load-induced tibial component displacement has been introduced. This study aimed to determine whether the extent of radiolucent lines observed on radiographic imaging shows displacement of tibial components.

Methods:
AP- and lateral conventional radiographs and CT-scans of 50 TKA's were included as part of a long-term post-market follow-up study. The extent of radiolucent lines on conventional radiographs was classified as described by the Modern Knee Society, by two independent raters. Three subgroups were created based on the extent of radiolucent lines along areas of the tibial component: 'none', 'partial', and 'complete'. Subsequently, load-induced implant displacement was quantified using CT-scans of the knee under valgus and varus load. Relative implant displacement was quantified using rotation about the helical axis, Maximum Total Point Motion (MTPM), and mean target registration error (mTRE). Hypothesising similar displacement between subgroups, a Two One-Sided Tests (TOST) procedure, using the Smallest Detectable Change (SDC) as equivalence margins, was conducted. Statistical equivalence would indicate the subgroups showed similar displacement.

Results:
Similar displacement was observed when comparing the subgroups (Figure 1). Statistical equivalence was confirmed in all but one of the comparisons, indicating that the subgroups were similar (Table 1). The comparison of mTRE between the between the 'partial' and 'complete' subgroups did not meet statistical equivalence (p=0.053). The inter-observer Cohen's Kappa for subgroup classification was 0.95 (95%CI:0.84-1.00).

Conclusion:
The subgroups based on the extent of radiolucent lines showed statistically equivalent displacement outcomes. These findings suggest that a greater number of radiolucent lines does not represent more load-induced displacement of tibial components of TKA. This limits the diagnostic value of radiolucent lines for assessing tibial component fixation.

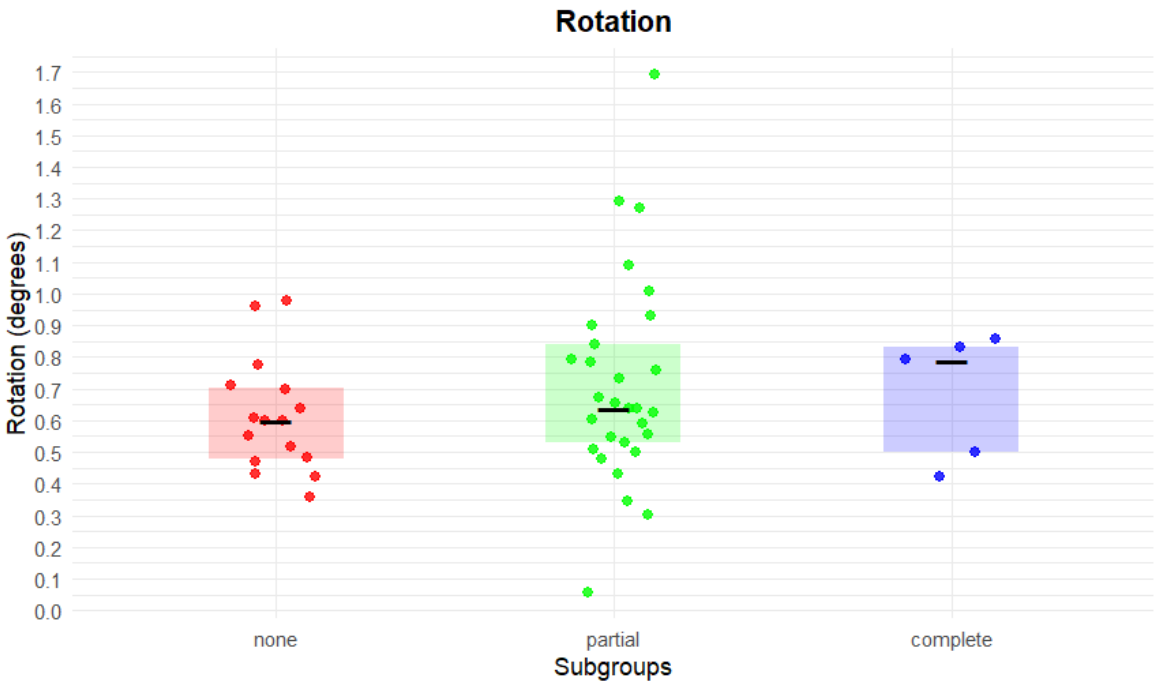

Figure 1. Box- and scatterplot for rotation about the helical axis in degrees per subgroup. Median rotation about the helical axis was 0.60 (IQR: 0.4-0.71), 0.64 (IQR: 0.52-0.87), and 0.79 (IQR: 0.46-0.85) degrees for the 'none', 'partial', and 'complete' subgroups respectively. Statistical equivalence was confirmed by a Two One-Sided Tests (TOST) procedure, indicating the subgroups showed similar displacement within a predefined margin of smallest detectable change (SDC).

Table 2.

Comparison of displacement outcomes between the subgroups within equivalence margins

	'none' vs. 'partial'		**'none' vs. 'complete'**		**'partial' vs. 'complete'**	
Displacement outcomes	*p*-value	Power	*p*-value	Power	*p*-value	Power
Rotation	**<0.001**	1.000	**0.004**	1.000	**0.004**	0.999
MTPM	**<0.001**	0.999	**0.019**	0.998	**0.046**	0.998
mTRE	**<0.001**	0.999	**0.036**	0.996	0.053	0.995

MTPM: maximum total point motion, mTRE: mean target registration error

C7 – Gaia van den Heuvel

QUANTIFYING THE EFFECT OF ORTHOPEDIC FOOT SURGERY IN CEREBRAL PALSY USING WEIGHT-BEARING CT SCANS

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Introduction: In children with cerebral palsy (CP), foot deformities commonly develop due to altered motor control and loading. If these deformities become severe, orthopedic surgery is necessary to correct the alignment of the foot. However, due to the complex anatomy of the foot, accurate assessment of foot posture from 2D imaging is challenging. Weight-bearing CT (WBCT) enables evaluation of foot posture in three dimensions under natural loading and positioning [1]. However, this has not previously been used to evaluate treatment in children with CP. Therefore, our aim was to quantify the effects of surgery on foot posture using WBCT scans.

Methods: WBCT scans have been acquired before and one year after orthopedic foot surgery, according to clinical practice. From this dataset, we present one representative case. The individual with bilateral spastic CP (age 16 years) underwent gastrocsoleus lengthening and plantar fascia release surgery to correct a plantarflexion contracture and cavovarus foot deformity. Local coordinate systems for each foot bone were automatically computed based on the inertial axes of the bones using custom software [2]. Bone translations and rotations relative to the talus, and the differences between these values pre- and postoperatively, were calculated.

Results: The calcaneus, navicular and first metatarsal all translated more lateral relative to the talus post-operatively (Δ = -3.8, -5.0, -20.2 mm, respectively), and more superior (Δ = 0.5, 1.2, 9.5 mm, respectively); see Figure 1. All three bones rotated around the x-axis (mediolateral) more towards dorsiflexion (Δ = -4.5, -4.8, -9.3°, respectively), and around the y-axis (longitudinal) more towards valgus (Δ = 10.2, 15.3, 8.4°, respectively). Around the z-axis (transversal), the navicular and first metatarsal rotated more towards abduction (Δ = -17.7, -16.5°, respectively), while the calcaneus relative to the talus rotated slightly more towards adduction (Δ = 1.3°).

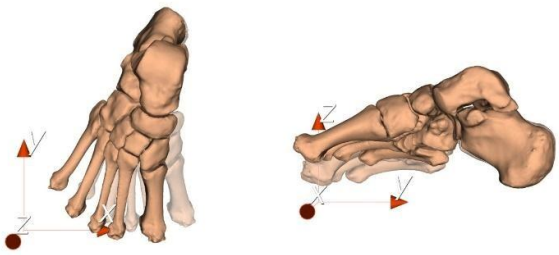

Figure 1. Pre-surgical (semi-transparent) versus post-surgical foot posture (front).

Discussion: We quantified the effect of orthopedic surgery on a cavovarus foot, indicating the bones translate and rotate such that varus and adduction decrease, realigning the foot to a more neutral position. Based on the full dataset, it will be further investigated which foot posture parameters have most clinical relevance for describing foot deformity correction in CP.

References: 1. Wellenberg *et al.*, Skeletal Radiol, 2023; 2. Dobbe *et al.*, IEEE Trans Med Imaging, 2019

C8 – Arianne Gravesteijn

Sustained Benefits of a Multi-Domain Lifestyle Intervention in Multiple Sclerosis in the LIMS study: A 24-Month Follow-Up

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Background and objectives: Multiple sclerosis (MS) often leads to physical, cognitive, and psychological impairments that substantially affect daily functioning and quality of life. As current disease-modifying therapies do not fully prevent disease progression, interest has grown in the potential role of modifiable lifestyle factors. We evaluated (1) whether effects on patient-reported outcomes—including MS impact, quality of life, general health, and MS-related symptoms—were sustained up to 24 months, and (2) long-term changes in lifestyle behaviors following completion of the Lifestyle in Multiple Sclerosis (LIMS) program.

Methods: People with MS participated in a 3-month multimodal lifestyle program followed by a 21-month maintenance phase. Patient-reported outcomes were assessed 3 months prior to the intervention, at baseline, post-intervention, and at 6, 12, 18, and 24 months of follow-up. The primary outcome was MS-related impact on daily functioning (Multiple Sclerosis Impact Scale–29 [MSIS-29]). Secondary outcomes included quality of life, general health, and MS-related symptoms. Longitudinal changes were analyzed using piecewise mixed-effects models, and individual-level change was evaluated using proportions exceeding the smallest detectable change (SDC).

Results: In total, 659 participants were included (mean age 46 years, SD 11; 71% female). During the intervention phase, MSIS-29 physical and psychological scores decreased by approximately 0.8 and 1.1 points per month, respectively, followed by attenuation during long-term follow-up. Despite attenuation, scores remained significantly improved or stable relative to baseline up to 24 months. Only a small proportion of participants exceeded the SDC for MSIS-29 (approximately 4–7%), indicating limited individual-level change. Trajectories were broadly similar across other patient-reported outcomes, with modest short-term improvements and subsequent stabilization. Most pronounced effects were found for dietary adherence which improved substantially during the intervention and remained partially sustained during follow-up, while body mass index decreased modestly, with approximately 20% of participants exceeding the SDC post-intervention. No significant changes were observed in physical activity adherence.

Discussion: In this large, real-world study, a digital multimodal lifestyle intervention was associated with modest, mainly short-term improvements in patient-reported outcomes and more durable changes in dietary behavior and body composition. These findings support a complementary role for lifestyle interventions in long-term MS management.

C9 – Bart Raijmakers

Benefits of microprocessor stance-and-swing-phase-controlled knee-ankle-foot orthoses in a person with knee instability: A case report

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Background

Stance-controlled knee-ankle-foot orthoses (SCKAFOs) are often prescribed to people with proximal leg muscle weakness to improve walking ability. SCKAFOs allow free knee flexion during swing while walking, reducing compensatory movements like hip hiking and circumduction. However, these benefits are mostly limited to walking on level surfaces, and not to walking on uneven terrain, stairs, and/or ramps. Microprocessor-controlled stance and swing phase KAFOs (SSCKAFOs) with hydraulic knee-joints, such as the C-Brace, have shown to improve mobility especially on these uneven surfaces. Recently a new SSCKAFO, the NEURO HiTRONIC, has been introduced, which has not yet been evaluated in daily life use, but may also show these benefits. The aim of this case report was compare walking ability, balance and daily activity performance using the NEURO HiTRONIC and C-Brace microprocessor-controlled SCCKAFOs to a previously provided SCKAFO. Additionally, the effectiveness of the two SCCKAFOs was compared.

Methods

A 68-year-old male with polio who used a NEURO TRONIC SCKAFO in daily life, was consecutively provided with a NEURO HiTRONIC SSCKAFO and C-Brace. Both devices were used for three months in daily life, after which measurements were taken and compared with baseline measurements of the NEURO TRONIC SCKAFO. The measurements included: energy cost of walking, walking speed (both assessed with 6-minute walk test), timed-up-and-go test (TUG), balance performance (Berg Balance scale), balance confidence (activities specific balance confidence scale (ABC)), stair and hill assessment index and daily life functioning (OPUS lower extremity functioning scale (OPUS-LEFS)).

Results

Compared to the NEURO TRONIC SCKAFO, walking with the NEURO HiTRONIC resulted in improvements in walking speed (+13%), energy cost of walking (-11%), balance confidence (+11 ABC points) and daily life functioning (+10 OPUS-LEFS points), Table 1. The results for energy cost of walking and balance performance with the NEURO HiTRONIC and C-Brace were similar. Walking speed, TUG outcome, balance confidence and stair and hill descend improved more with the C-Brace than with the NEURO HiTRONIC SSCKAFO, compared to the NEURO TRONIC SCKAFO.

Discussion

This was the first study to evaluate and compare two microprocessor-controlled SSCKAFOs, the NEURO HiTRONIC and the C-Brace. Both SSCKAFOs were beneficial in improving energy cost of walking, balance confidence and daily life functioning compared to the NEURO TRONIC SCKAFO. The C-Brace showed additional benefits for walking speed and stair and hill descent, when compared to the NEURO HiTRONIC SSCKAFO, which is likely due to the controlled knee flexion resistance functionality of the C-Brace knee-joint.

Table 1

	NEURO TRONIC	NEURO HiTRONIC	C-BRACE
Walking ability			
Walking speed (6MWT)	0.84 m/s	0.95 m/s (+13.1%)	1.03 m/s (+22.6%)
Energy cost (6MWT)	4.92 J/kg/m	4.36 J/kg/m (-11.4%)	4.31 J/kg/m (12.4%)
Stair Assessment Index (0-13)	3	3 (+0)	6 (+3)
Hill Assesment Index (0-11)	5	5 (+0)	7 (+2)
Balance			
Timed-up-and-Go test	15.63 sec	15.20 sec (-2.8%)	10.6 sec (-32.1%)
Berg Balance Scale (0-56)	54	53 (-1)	53 (-1)
ABC Scale (0-100)	59	70 (+11)	86 (+27)
Daily functioning			
OPUS-LEFS (0-80)	37	47 (+10)	51 (+14)

6MWT: 6 minute walking test, m/s: meter/second, J/kg/m: Joule/ kilogram/meter, ABC: Activities Specific Balance Confidence, OPUS-LEFS: Orthotics and Prosthetics User Survey - Lower Extremity Functional Status

C10 – Jesse Brinkman

FRACTURE PROGRESSION AFTER PELVIC FRAGILITY FRACTURES: A SYSTEMATIC REVIEW

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Introduction Pelvic fragility fractures show an increasing prevalence and are associated with substantial mortality and morbidity. Fracture progression represents a clinically significant but under-researched phenomenon specific to pelvic fragility fractures. This review aims to summarize existing evidence for fracture progression.

Methods A systematic literature search was conducted in PubMed, Embase, and Cochrane Library. Studies including older adults with pelvic fragility fractures after low-energy trauma and describing the definition, etiology, incidence, or predictors of fracture progression were eligible for inclusion. Risk of bias was assessed using Joanna Briggs Institute critical appraisal tools.

Results Thirteen studies met the inclusion criteria; ten observational studies, two case reports and one case series. Fracture progression was consistently described with features including a progress of increasing instability, an increasing Rommens fracture classification, the appearance of additional fractures, or progressive dislocation of the fracture site. Etiological factors included increased pelvic ring instability and progressive loss of bone. The average reported incidence of fracture progression was 16.8%, ranging from 3.2% to 38%. Potential predictors for fracture progression included female sex, prolonged pain or immobility, increased dependency, vacuum phenomenon on pelvic CT, early forced mobilization, and specific fracture types and locations.

Conclusions Current literature on fracture progression after pelvic fragility fractures is scarce. Fracture progression can best be defined as “a progress of increasing instability, characterized by an increased Rommens classification, appearance of additional fractures or progressive dislocation of the fracture site”. Fracture progression incidence is high and forms a significant clinical problem for patients with pelvic fragility fractures. Pelvic CT scans are crucial for early detection of fracture progression, thereby enabling timely treatment. Future research with larger multicenter cohorts is needed to clarify etiology and predictors of fracture progression, improve awareness of this phenomenon and support the development of evidence-based guidelines for pelvic fragility fractures.

Level of evidence Level IIb

C11 – Matthijs van der Laan

PERFORMANCE OF A PERSONALIZED SMART CUEING DEVICE TO DETECT FREEZING OF GAIT IN PARKINSON'S DISEASE

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Background

Freezing of gait (FoG) impairs mobility and daily functioning and increases the risk of falls, leading to a reduced quality of life in people with Parkinson's disease (PD). A proven strategy to overcome FoG is external cueing. Typically, external cueing is manually activated or continuously present. However, manual activation is often too late and continuous cueing may be perceived as burdensome. Therefore, the Cue2walk, a medical device for FoG detection and provision of external cues, was developed. In this study we determined 1) the performance to detect FoG of the Cue2walk device and 2) the effect of personal optimization on the performance to detect FoG.

Methods

Twenty-four people with PD and daily FoG completed a gait circuit including FoG-triggering tasks in their own home environment, while wearing a Cue2walk device to collect acceleration data. Two experienced independent raters rated the occurrence of FoG using video annotation. The data set of each participant was split into a training set (60%) and a test set (40%), obtaining an even distribution of FoG episodes. The training set was used to personalize the settings of the algorithm. The test set was used to assess the performance to detect FoG of the standard and personalized setting by calculating sensitivity, specificity and latency (time between onset and detection of FoG).

Results

Sensitivity was 28.2±31.6%, specificity 96.0±4.1%, and latency 1.9±2.4s on the test set with the standard settings. With personalized settings, sensitivity was 89.1±14.8%, specificity 93.3±5.5%, and latency 1.6±2.2s. Sensitivity was significantly higher for the personalized settings ($p<0.001$), while latency and specificity did not differ.

Conclusions

The Cue2walk device showed good performance to detect FoG when using the personalized settings. The clinical and cost-effectiveness of the device need to be determined in future research.

C12 – Esmée van der Velden

IN VITRO MICROMASS MODEL FOR ENCHONDRAL OSSIFICATION USING PERIODONTAL LIGAMENT CELLS FROM PATIENTS WITH FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

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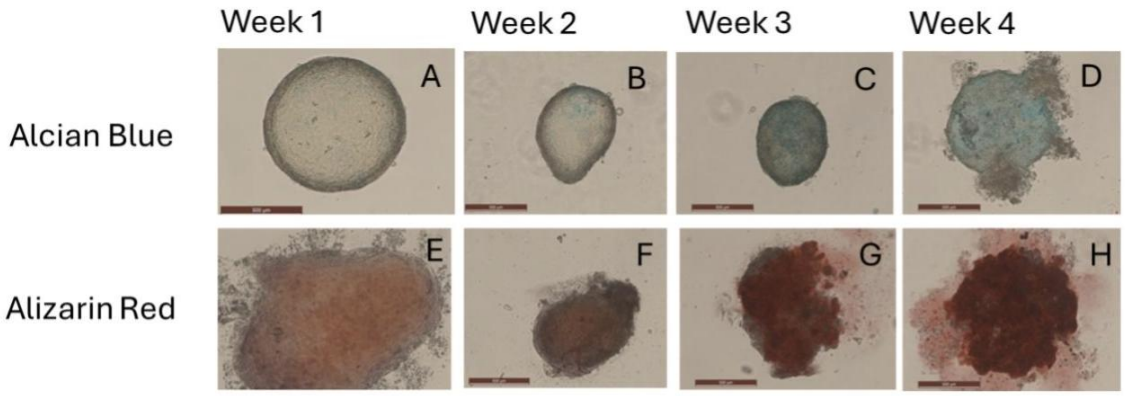
Background
Fibrodysplasia Ossificans Progressiva (FOP) is characterized by ectopic bone, which is formed via endochondral ossification. As yet, human disease models for FOP have focused on osteogenic differentiation, with limited focus on the preceding chondrogenic differentiation necessary for ectopic bone formation. To study both of these processes in vitro, a stable and reproducible micromass model is required. The aim of this study is to optimize a micromass culture model for chondro-osteogenic differentiation of periodontal ligament (PDL) cells.

Methods
Micromasses were generated using different cell concentrations and cultured under proliferation, chondrogenic, and osteogenic conditions, with and without the addition of Activin A. Agarose-coated 96-well plates were used to support micromass formation. Differentiation was assessed at time points; 7, 14, 21 and 28 days. Alcian Blue staining was used for cartilage matrix formation and Alizarin Red staining for mineralization. Technical aspects of medium replacement and staining procedures were also optimized.

Results
A cell concentration of 40,000 cells per micromass resulted in stable and well-formed structures. Transferring micromasses to microcentrifuge tubes before staining improved staining quality and reduced background signals. Alcian Blue staining was clearly visible from week 3 onward, indicating time-dependent matrix accumulation (Figure 1). Mineralization in osteogenic conditions was also visible from week 3 and was strongest at week 4, based on Alizarin Red staining (Figure 1).

Conclusion
This study shows that the optimized micromass model is suitable for studying chondro-osteogenic differentiation of PDL cells. The model provides a reliable basis for future experiments, including testing novel pharmacological treatment options for prevention of ectopic ossification in FOP.

Figure 1: Chondro-osteogenic differentiation of high-density micromasses, cultured in chondrogenic medium for the first two weeks and in osteogenic medium for the last two weeks. Weekly time points show increased staining intensity for alcian blue (A-D) and alizarin red (E-H) staining.



C13 – Brecht Haakma

WHEELCHAIRCHECK TOOL FOR EMPOWERING WHEELCHAIR USERS – PROJECT DESIGN FOR OPTIMIZATION, VALIDATION AND EVALUATION

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Introduction – The *WheelchairCheck* is an existing tool for wheelchair users, designed to promote health and well-being through better wheelchair fit. The tool consists of a questionnaire and feedback report that help users understand the functioning and suitability of their wheelchair. The tool aims to empower wheelchair users to feel confident and take initiative in care and services related to their wheelchair. The feedback report also supports health care professionals in identifying potential health risks and suboptimal fit more quickly and effectively.

WheelchairCheck is developed through practice and has been used for over 5 years, resulting in a database of over 1500 responses. During the *WheelchairCheck* PhD project we **aim** to optimize, validate and evaluate the Dutch version of the *WheelchairCheck* tool – *CheckJeZit* – and analyze the unique data that it generates.

Methods – We will optimize, validate and evaluate *WheelchairCheck* through systematically consulting existing literature and the experiences and opinions of wheelchair users as well as their health care professionals. This will entail the following steps:

Step 1: Set up an advisory group of wheelchair users. This group will be periodically consulted throughout the project and will act as a sounding board throughout the project to ensure the voice of people using a wheelchair is heard.

Step 2: Consult existing literature and write a review article to answer the research question: “What factors are associated with the suitability of a wheelchair?”. This review can indicate whether the *WheelchairCheck* tool covers all relevant domains.

Step 3: Content Validation of the Dutch questionnaire with a mixed-methods Delphi study design.

Step 4: Study the effects of the *WheelchairCheck* tool on wheelchair suitability.

Step 5: Analyze the epidemiological data collected in the *WheelchairCheck* tool. The focus of this research question will be determined later.

Results – With this project we hope to establish the *WheelchairCheck* tool as a robust means to inform and empower wheelchair users during the wheelchair-provisioning process, and the entire wheelchair-use lifespan, and to enable the answering of relevant research questions with the *WheelchairCheck* database.

Conclusion – This is the start of the *WheelchairCheck* PhD project where we’re evaluating the existing tool, building our plans, and developing our expertise. In the future we will be seen in various domains of the movement sciences and rehabilitation realm and AMS events, so we're excited to exchange ideas, knowledge and expertise and build meaningful relationships.

WHEELCHAIR CHECK CHECK JE ZIT

C14 – Braeden Charlton

AN INABILITY TO RECOVER: REDUCED REGENERATIVE MARKERS AND ALTERED METABOLISM IN PATIENTS WITH ME/CFS AND LONG COVID

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Aim: Patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and long COVID often experience worsening of symptoms with physical or mental exertion, known as post-exertional malaise (PEM), and frequently exhibit signs of muscular damage. Appropriate muscle regeneration is dependent on satellite cell and fibroadipogenic progenitor (FAP) cell presence and function, however it is unknown whether local inflammation associated with ME/CFS or long COVID impacts satellite cells. This study aimed to assess satellite cell and FAP cell abundance as markers of regeneration in ME/CFS and long COVID patients, and assess how metabolic alterations may relate to regenerative ability.

Methods: Biopsies from the vastus lateralis of 26 ME/CFS patients, 25 long COVID patients, and 30 healthy age- and sex-matched controls were obtained, and sections stained with Pax7 to visualize satellite cells and PGDFRα to visualize FAP cells, both of which were normalized to myonuclear count. Mitochondrial respiration was assessed using high resolution respirometry. Liquid chromatography mass spectrometry was used to assess metabolite concentrations in biopsies.

Results: There were no differences in myonuclear content between cohorts, and myonuclear content was proportional to fibre-cross sectional area in all groups (P<0.001, r=0.70). Both ME/CFS and long COVID patients exhibited fewer satellite cells than healthy controls, both prior to and 24-hours after exhaustive exercise (P<0.001). There was a tendency for both ME/CFS and long COVID patients to have reduced FAP cells (P=0.061) and for ME/CFS patients to have reduced FAP cells following exhaustive exercise (P=0.070). Satellite cell presence per myofiber was positively related to oxidative phosphorylation capacity across all groups at baseline (P=0.0035, r=0.43), suggesting a relationship between regeneration capacity and mitochondrial function. The metabolic profile of patients indicated a shift away from oxidative metabolism, which was corroborated by the impaired mitochondrial function and higher number of glycolytic fibres. Further, patients had lower levels of metabolites involved in antioxidation and hypertrophy.

Conclusion: The reduction in satellite cell abundance in both patient groups indicates a likely decreased ability to repair muscle following damage, while the reduction in FAP cell presence may indicate altered regenerative signalling. The shift away from oxidative metabolism and reduction in antioxidative metabolites suggests that ME/CFS and long COVID patient skeletal muscle is more susceptible to damage.

C15 – Maarten Steinz

SYSTEMICALLY ELEVATED INFLAMMATORY CYTOKINE IL-6 IN ESTABLISHED RHEUMATOID ARTHRITIS AFFECTS MUSCLE MITOCHONDRIAL RESPIRATION

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Patients with established rheumatoid arthritis (RA) often experience muscle fatigue even in clinical remission due to anti-inflammatory treatment. It affects up to 60% of the patients and contributes to functional decline. Muscle fatigue is not solely due to reduced muscle size but also involves intramuscular impairments. Impaired muscle mitochondrial oxidative phosphorylation (OXPHOS), normally crucial for ATP production and muscle fatigue resistance, may play a role. Elevated systemic inflammatory cytokine interleukin-6 (IL-6) in RA has been implicated in impaired mitochondrial OXPHOS, but its exact effect remains unclear. The aim of this study was to investigate the effect of IL-6, at systemic concentrations relevant in established RA, on muscle mitochondrial respiration, ROS production and OXPHOS gene expression *in vitro*.

For this study, human primary muscle cells were cultured *in vitro*, differentiated into myotubes, and exposed for 72 hours to IL-6 (0, 10, 20, 40, or 160 pg/mL). Mitochondrial respiration was assessed with Seahorse respirometry, measuring basal, maximal, leak and ATP-linked respiration. Myotube mitochondrial ROS production was measured by MitoSox immuno-fluorescent imaging. OXPHOS gene expression was quantified with qPCR after incubation of myotubes with IL-6 and RA serum (N= 6 patients). The cytokine concentrations were based on multiplex measurements of RA serum and previous literature. Results are presented as mean ± SEM.

IL-6 increased myotube maximal respiration by 40.9% (± 8.8%) and 37.7% (± 7.5%) at 10 and 20 pg/ml ($p<0.05$). 40 pg/ml did not alter maximal respiration and a tendency of decrease by 28.9% (± 5.8%) was observed at 160 pg/ml ($p= 0.09$). IL-6 increased leak respiration by 21.1% (± 5.4%) at 10, 25.5% (± 6.0%) at 20 and 23.0% (± 4.4%) at 40 pg/ml. 160 pg/ml did not change leak respiration. Basal and ATP-linked respiration were not affected by IL-6 incubation for 72h at any concentration. Since 20 pg/mL produced the most significant changes, this concentration was selected for subsequent experiments. Myotubes incubated for 72h with 20pg/ml IL-6 showed significant increased mitochondrial ROS production by 14.4% (± 2.0%). IL-6 also affected the expression of mitochondrial OXPHOS genes NDUFA4 and COX4I1, which were decreased by 22.5% (± 5.5%) and 31.7% (± 1.9%) ($p<0.05$). RA serum also decreased the expression of mitochondrial OXPHOS genes NDUFA4 and COX4i1 by 45.2% (± 7.0%) and 43.0% (± 2.9%) in myotubes after 24h of serum incubation ($p<0.05$). The IL-6 concentration in the serum was on average 50.3 (± 16) with a minimum of 6.1 and maximum of 109.5 pg/ml. Furthermore, RA Serum decreased the expression of other complexes: NDUFA2, SDHB, CYC1 and ATP5A1 by 52.9% (± 2.7%); 28.2% (± 2.5%); 32.2% (± 5.0%); and 18.5% (± 4.6%) ($p<0.05$).

Systemically elevated IL-6, at concentrations found in serum of established RA patients, impact mitochondrial respiration, ROS production and OXPHOS gene expression in human myotubes *in vitro*. These findings highlight IL-6-mediated impaired mitochondrial OXPHOS as a potential contributor to impaired muscle function in RA. It remains to be elucidated how these findings translate *in vivo*.

C16 – En Deng

Biomarkers that predict the onset or progression of osteoarthritis: A systematic review

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Abstract

Objective: To identify the biomarkers that predict the onset or progression of osteoarthritis (OA) in humans.

Methods: A systematic review was performed in accordance with PRISMA and registered with PROSPERO (CRD420251052912). PubMed, Embase and Cochrane Library for clinical trials were searched from inception through February 2025. Papers were included if baseline biomarkers were related to the onset or progression of osteoarthritis in humans at follow-up.

Results: After screening, 71 studies fulfilled the inclusion criteria. A total of 96 biomarkers have been reported to correlate to the onset or progression of OA in our review. Most biomarkers were obtained from blood or synovial fluid, while most biomarkers would predict worsening of pain and joint space width (JSW) progression. 12 biomarkers (Interleukin-6 (IL-6), Monocyte Chemoattractant Protein-1 (MCP-1), Tumor Necrosis Factor-α (TNF-α), Interleukin-1β (IL-1β), C-reactive protein (CRP), Interleukin-1Ra (IL-1Ra), Interleukin-8 (IL-8), C-telopeptide of type II collagen (CTX-II), Matrix Metalloproteinase-3 (MMP-3), Tissue Inhibitor of Metalloproteinases-1 (TIMP-1), Hyaluronic Acid (HA), Cartilage Oligomeric Matrix Protein (COMP)) were reported to be a predictor by at least 3 studies. Base on comprehensive assessment of effect size, source, follow-up time range, prediction outcome and focused joint, IL-6 was identified as the biomarker with the strongest evidence that it can predict the onset or progression of OA.

Conclusions: A variety of markers was investigated, of which most biomarkers were obtained from blood or synovial fluid, and were tested for prediction of worsening pain and JSW progression. IL-6 would be the most commonly reported biomarker able to predict the onset or progression of OA.

C17 – Joep Suskens

CREATING SPACE IN SMALL JOINTS FOR VISUAL EVALUATION AND SURGICAL TREATMENT OF OSTEOARTHRITIS

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Introduction. Investigating cartilaginous joints for visual evaluation of cartilage or for surgical treatment is often challenging due to limited joint space. Small joint size and strict containment make the insertion of arthroscopic or surgical devices challenging. The ankle and first metatarsophalangeal (MTP1) joints are of particular orthopedic interest, as osteoarthritis frequently affects these joints and surgical treatment is sometimes required.

Manual distraction of the distal part of the joint is common practice in orthopedic surgery. This noninvasive method allows the surgeon to apply traction subjectively of unknown force until satisfactory joint space is achieved. However, the relationship between the applied distraction force and the resulting joint space is unknown. Furthermore, it remains unclear to what extent the passive structural tissues surrounding the joint can stretch, resist, or fail in response to increasing distraction forces. The aim of this cadaveric study was to investigate the relationship between applied distraction force and the resulting joint space distance in the ankle and MTP1 joints.

Methods. Eight unique fresh-frozen cadaveric lower-leg specimens were thawed for more than 48h and used to investigate both the ankle and MTP1 joints. Joint space distance was assessed using computed tomography (CT) scans and analyzed with in-house medical imaging software (Articulus). A custom-made device was developed to fixate the specimen horizontally at the tibia and to apply static distraction forces of 100, 150, and 200 N to the ankle using a commercially available ankle distractor belt. Distraction forces of 50, 100, and 150 N were applied to the MTP1 joint via a pen placed perpendicularly through the first proximal phalanx (for traction). A first baseline CT scan without distraction force was obtained, followed by CT scans under each distraction force, finalized by a second baseline CT scan without distraction force.

Results. The median age of the specimens at time of death was 85.5 years (25^{th}-75^{th} percentile: 83.5-89.5), and two specimens were female (four left and four right sides). The median ankle joint space distance increased from 1.4mm (1.2-1.8 mm) at 100N to 2.1 mm (1.8-2.7 mm) at 200N (Figure 1). For the MTP1 joint, the median joint space distance increased from 1.3 mm (1.0-1.9 mm) at 50 N to 2.5 mm (1.9-3.2 mm) at 150N (Figure 2).

Discussion. No stagnation in joint space widening was observed up to the highest applied distraction forces, suggesting that the applied distraction forces remained within the elastic range of the passive tissue surrounding the ankle and MTP1 joints. Distraction forces up to 200 N for the ankle and 150 N for the MTP1 joint are therefore considered safe for achieving joint space widening greater than 2 mm.

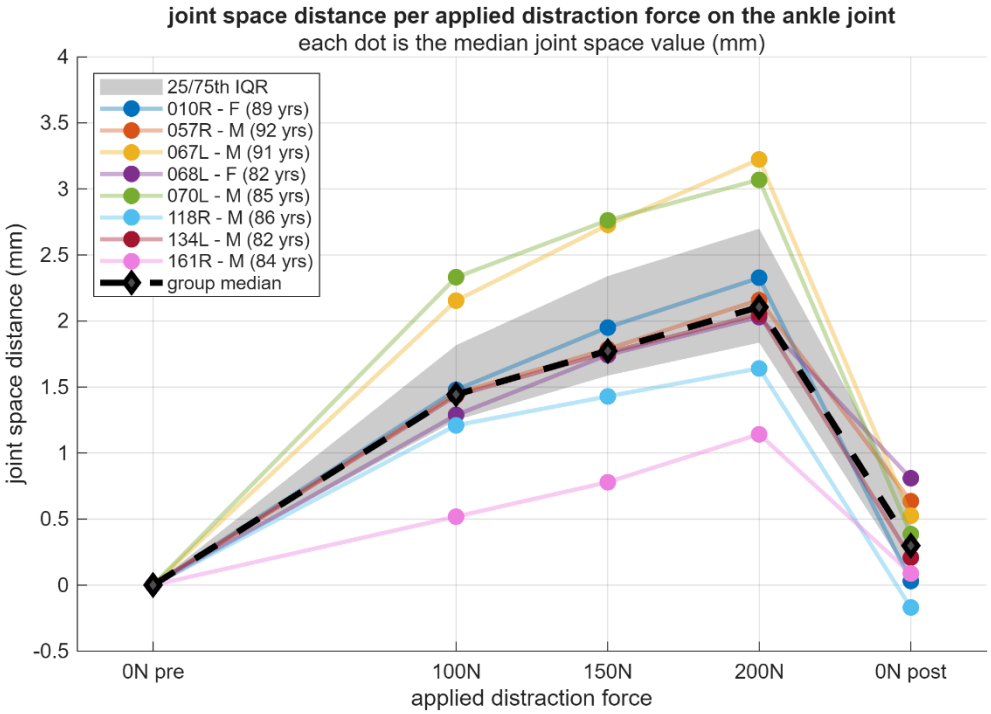

Figure 1. *Ankle joint space distance (mm; millimeters) versus applied distraction force (N; Newton). Individual data points and group median with interquartile range (25th–75th percentile) are shown.*

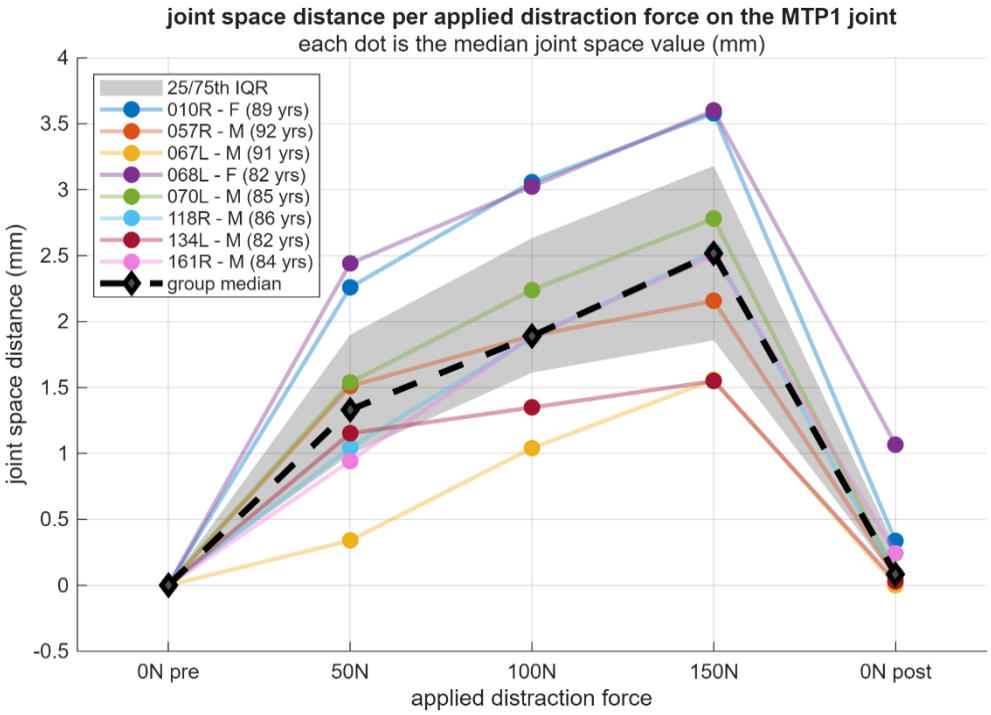

Figure 2. *First metatarsophalangeal joint space distance (mm; millimeters) versus applied distraction force (N; Newton). Individual data points and group median with interquartile range (25th–75th percentile) are shown.*

C18 – Mackenna Schouw

CENTRAL NERVOUS SYSTEM ANOMALIES IN OSTEOGENESIS IMPERFECTA: A HISTOPATHOLOGICAL CASE-CONTROL STUDY

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Osteogenesis Imperfecta (OI) is a rare genetic skeletal dysplasia, characterized by frequent bone fractures, bone deformities, and short stature caused by pathogenic variants in genes involved in the production or processing of collagen type I. The disease shows a broad phenotypic spectrum, with the most severe form (OI type 2) resulting in perinatal death. In addition to skeletal symptoms, OI presents extraskeletal manifestations, such as pulmonary and cardiovascular complications, blue sclerae, and dentinogenesis imperfecta. Neurological manifestations, however, remain understudied. Only two small neurohistological case series from the previous century have assessed central nervous system (CNS) abnormalities in OI brain autopsies. They report structural changes in 78-100% of cases, including neuronal lamination defects, haemorrhage, and gliosis. Collagen type I is a main extracellular matrix component of the meninges, the protective layers surrounding the brain, and is present in intra- and extracerebral vessels.

This study investigates the impact of collagen type I abnormalities on the CNS using a case-control study of four genetically confirmed OI type 2 fetuses harboring mutations in *COL1A1*, *COL1A2* or *PPIB*. Histopathological and immunohistochemical techniques (Picrosirius Red staining, Elastic van Gieson staining, and *COL1A1* immunostaining) are applied to fetal brain tissue at gestational stages from 21 to 34 weeks and compared with age-matched controls. Collagen type I localization and quantification is performed, as well as neuropathological examination.

We found that collagen type I localized in the leptomeninges of control and OI fetuses throughout development. In the choroid plexus, collagen type I was found in the stroma, epithelial membranes and vascular basement membranes. Additionally, COL1A1 is expressed in extraparenchymal and intraparenchymal vessels of the arterial and venous system, in both OI fetuses and controls.

Due to its localization, collagen type I may therefore play a role in neuronal development, the blood-brain barrier and production of cerebrospinal fluid. Consequently, pathogenic variants may affect the development of the CNS and cerebrovasculature in OI. We currently aim to elucidate the consequences of collagen type I impairment on cerebrovascular integrity, meningeal architecture, and neuronal development and migration. This investigation can potentially advance understanding of the collagen type I dysfunction on neurodevelopment in OI and its broader implications of bone-brain interplay.

C19 – Aske Larsen

Outcome Measures in Gait Rehabilitation of Neurological Patients: A Meta-analysis

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Background: Gait impairment is a hallmark of many neurological conditions, including stroke, Parkinson's disease, cerebral palsy, and multiple sclerosis, and is a major contributor to reduced mobility and independence. Although numerous outcome measures are used to evaluate gait rehabilitation, their ability to sensitively detect meaningful change remains limited. The heterogeneity of outcome measures across studies complicates interpretation and comparison of rehabilitation effects.

Objective: The aim of this meta-analysis was to investigate the sensitivity to change of commonly used outcome measures in neurological gait rehabilitation.

Methods: A systematic literature search was conducted in PubMed, Medline, and Google Scholar in accordance with PRISMA 2020 guidelines. Studies on gait rehabilitation in neurological populations were screened by two independent reviewers. Outcome measures were extracted by two independent reviewers for pre-, post-, and retention tests where available (ICC = 0.91 for methodological data and 0.99 for outcome measures). Standardized effect sizes were calculated using bias-corrected Hedges' g with 95% confidence intervals and grouped into outcome domains. Effect sizes were evaluated relative to the Timed Up and Go test (TUG), gait speed, and Berg Balance Scale (BBS) as reference standards to minimize bias related to pathology and intervention characteristics.

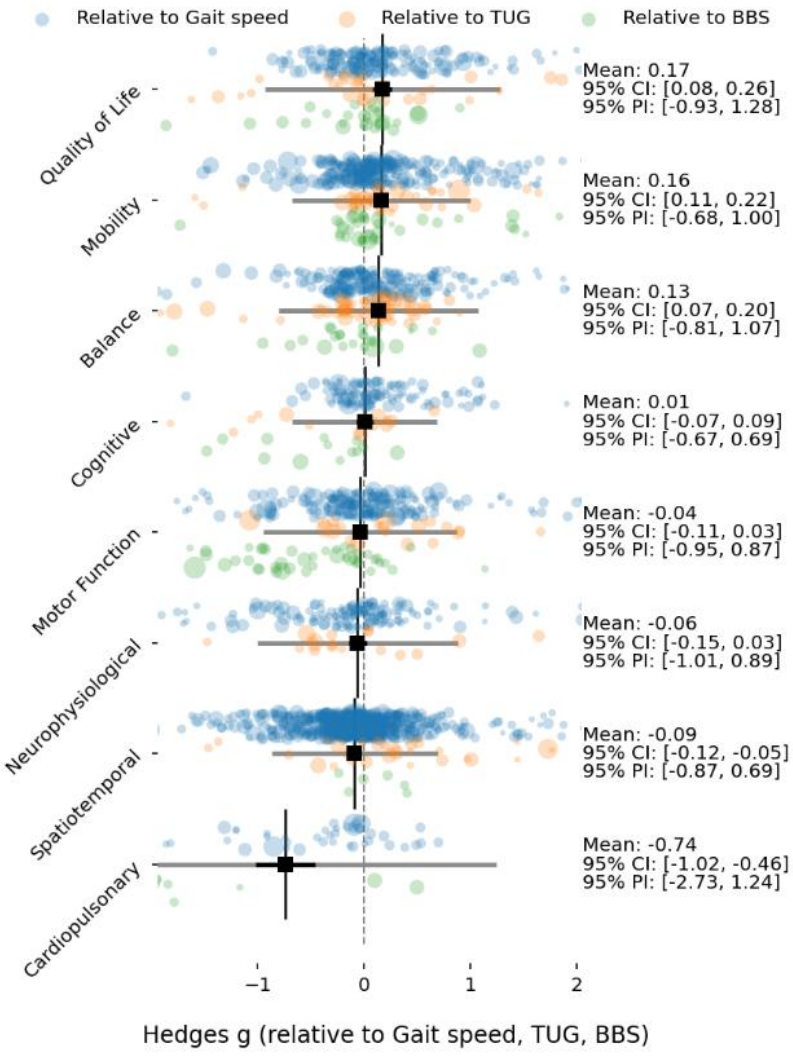

Figure 1. *Orchard plot showing standardized effect sizes relative to the most commonly used reference outcome available per study (gait speed, TUG and BBS). Points represent individual effect sizes; black squares indicate pooled means, black horizontal lines indicate 95% confidence intervals (95% CI) and grey horizontal lines indicate 95% prediction intervals (95% PI).*

Results: A total of 312 unique studies were included, comprising 11,420 participants and yielding 3,720 effect sizes across a range of 8 summarized outcome domains (Figure 1). Spatiotemporal gait measures

were most frequently reported, followed by balance, functional mobility, and gait speed outcomes. Kinematic measures demonstrated the highest average relative effect sizes, but were accompanied by substantial variability, indicating inconsistent sensitivity to change. In contrast, activities of daily living (ADL) and functional mobility measures showed both high relative effect sizes and low variability, suggesting robust and consistent responsiveness to gait rehabilitation. Cardiorespiratory outcome measures showed consistently low relative effect sizes, indicating limited sensitivity for detecting changes related to gait rehabilitation.

Conclusion

Quality of Life and functional mobility measures showed consistent sensitivity to change, whereas cardiorespiratory and cognitive outcomes demonstrated limited responsiveness and should be used with caution in monitoring rehabilitation effects.

C20 – Elza van Duijnhoven

ADVANCING EVIDENCE GENERATION WITH HIPHOP: Hybrid reglster-based evaluation Platform in a Hip Osteoarthritis Population

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Introduction
Hip osteoarthritis is a common cause of pain and reduced mobility in adults worldwide, often leading to total hip replacement (THA) at the end stage of the disease. While outcomes after surgery are generally good, around 3-5% of patients require a revision within ten years, usually due to infection, loosening, or ongoing pain. Optimal choices around the type of implant and perioperative care remain uncertain, highlighting the need for stronger evidence to guide treatment decisions.

Traditional clinical trials can take many years, are expensive, and usually focus on a single intervention with strict patient eligibility. This limits how quickly findings can influence routine care and reduces their applicability to everyday practice. Platform trials offer a more flexible and efficient approach. They allow multiple interventions to be evaluated at the same time within a single overarching framework and can use interim analyses to make earlier decisions about effectiveness. We are designing HIPHOP, *Hybrid reglster-based evaluation Platform in a Hip Osteoarthritis Population*, to provide a framework to continuously study and improve treatment choices for patients indicated for THA.

Methods
HIPHOP is an adaptive platform trial embedded within the Dutch arthroplasty registry (LROI). Patients with end-stage hip osteoarthritis indicated for THR will be included. New interventions can be added over time and evaluated against standard care within randomised comparisons. Data are collected prospectively through the registry, including surgical details, revision rates, and patient-reported outcomes (PROMs). The primary outcome is the win-ratio, a patient-prioritized composite outcome measure that combines mortality, revision surgery, and PROMs. Analyses are conducted using a Bayesian framework, with predefined interim analyses that allow trial arms to continue, be adjusted, or be stopped based on emerging effectiveness estimates.

Results
No results are available yet.

Discussion
HIPHOP applies innovative platform trial methods to accelerate the generation of meaningful clinical evidence. By linking the trial to a national registry, results will be directly relevant to everyday clinical practice. This adaptive approach aims to guide both national and international strategies for managing hip osteoarthritis and, ultimately, to improve outcomes for patients.

C21 – Yu-Xuan Chuang

NOT FOR COMPETITION

CAN WE STOP THE CASCADE OF POST-TRAUMATIC ANKLE OSTEOARTHRITIS AFTER A SIMPLE ANKLE SPRAIN BY EARLY DETECTION?

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Introduction: Traumatic events contribute substantially to ankle osteoarthritis, and early cartilage alterations after an ankle sprain can be difficult to detect with conventional clinical tools. Timely identification of cartilage damage could support earlier decision-making and potentially reduce progression toward post-traumatic osteoarthritis. This four-year PhD project aims to develop a minimally invasive method that provides objective, quantitative assessment of cartilage integrity by integrating optical spectroscopy into a needle arthroscope.

Methods: We developed a first version of a spectroscopy-enhanced needle arthroscopy prototype that combines arthroscopic visualization with optical reflectance measurements. During inspection, incident light is delivered to cartilage and wavelength-dependent reflectance R(λ) is recorded. As an initial feasibility evaluation, we performed a preliminary cadaver impact study in which reflectance spectra (visible to near-infrared) were acquired before and after controlled impacts with different energy levels, including a no-impact control. Spectra were summarized using a power-law model, $R(\lambda)=A*\lambda^{-b}$ and the exponent b as explored as a quantitative indicator sensitive to cartilage changes. In parallel, the first prototype is currently under technical testing to evaluate measurement stability and usability.

Results: Preliminary data indicate that spectral features, summarized by the exponent b differ between pre-impact and post-impact measurements. Importantly, b lso showed separable trends across cartilage exposed to different impact energy levels compared with the no-impact control, suggesting that spectroscopy-based reflectance may capture impact-related changes. Prototype testing is ongoing to assess repeatability, robustness to measurement conditions, and integration into an arthroscopic workflow.

Conclusion: These early findings support the feasibility of spectroscopy-enhanced needle arthroscopy to provide quantitative, objective information related to cartilage condition and to discriminate cartilage subjected to different impact energies in a controlled setting. Ongoing work will focus on systematic validation, reliability testing, and refinement of the prototype toward in vivo applicability for early post-traumatic cartilage assessment.