

Amsterdam  
Movement  
Sciences



# Abstracts

**7<sup>th</sup> Annual Research Meeting**  
**March 14, 2024**

## Poster № 1

### ENGAGING PATIENTS IN DESIGNING A TRANSMURAL ALLIED HEALTH PATHWAY: A QUALITATIVE EXPLORATION OF HOSPITAL-TO-HOME TRANSITIONS

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#### Abstract

**Introduction:** The transition from hospital to home is often suboptimal, resulting in patients not receiving the necessary allied healthcare after discharge. This may lead to delayed recovery, a higher number of readmissions, more emergency department visits, and an increase in mortality and healthcare costs.

**Purpose:** This study aimed to gain insight into patients' experiences, perceptions, and needs regarding hospital-to-home transition, focusing on allied healthcare as a first step towards the development of a transitional integrated allied healthcare pathway for patients with complex care needs after hospital discharge.

**Method:** We conducted semi-structured interviews with patients. Participants were recruited from university and general hospitals in the Amsterdam region between May-July 2023. They were eligible if they: 1) were discharged from hospital minimally 3 and maximally 12 months after admission to an oncologic surgery department, internal medicine department, intensive care unit, or trauma center, 2) received hospital-based care from at least one allied healthcare provider, who visited the patient at least twice during hospital admission, 3) spoke Dutch or English, and 4) were 18 years or older. Interviews were audio-recorded and transcribed verbatim. We performed a thematic analysis of the interview data.

**Results:** 19 patients were interviewed. Three themes emerged from the analysis. "Allied healthcare support during transition" depicts patients' positive experiences when they felt supported by allied health professionals during the hospital-to-home transition. "Patient and family involvement" illustrates how much patients value involvement of their family members during discharge planning. "Information recall and processing" portrays the challenges of understanding and remembering overwhelming amounts of information, sometimes unclear and provided at the wrong moment. Overall, patients' experiences of transitional care were positive when they were involved in the discharge process. Negative experiences occurred when their preferences for post-discharge communication were ignored.

**Conclusions:** This study suggests that allied health professionals need to continuously collaborate and communicate with each other to provide patients and their families with the personalized support they need. To provide high-quality and person-centered care, it is essential to consider how, when, and what information to provide to patients and their families to allow them to contribute to their recovery actively.

## Poster № 2

### BEYOND THE HOSPITAL WALLS, TRANSITIONAL CARE FROM THE PERSPECTIVE OF HEALTHCARE PROFESSIONALS

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#### **Abstract**

**Introduction:** Patients hospital stay is becoming shorter, which implies that patients continue their recovery at home supported by healthcare professionals in primary care. Therefore, optimizing transitional care is needed. Gaining insight into the perspective of healthcare professionals responsible for the organization and guidance of patients during their hospital-to-home transitions and beyond, is essential for successfully developing and implementing transitional care interventions.

**Purpose:** To gain insight into healthcare professionals' experiences, perceptions and needs regarding hospital-to-home transitions.

**Method:** We conducted a qualitative descriptive study using focus groups and semi-structured interviews in a Dutch University hospital and among primary care professionals in Amsterdam. Data were analyzed using thematic analysis. Hospital professionals were recruited from a Dutch University hospital. Primary care professionals were recruited from our networks and snowball sampling. Recruitment took place between May and September 2023. Professionals were eligible if they 1) were working as healthcare professionals at the departments of oncologic surgery, internal medicine, trauma surgery, or intensive care unit of the participating hospital or 2) were working as healthcare professionals in primary care in the Amsterdam region.

**Results:** We conducted seven heterogeneous focus groups and twelve interviews, with a total of 53 professionals participating. Three themes emerged from the data: "Collaboration and information exchange between healthcare professionals", "Coordination and continuity of care", and "Interaction between professionals, patients, and families".

**Conclusions:** This study indicates that healthcare professionals need clear rules and arrangements for communicating with colleagues within and outside their settings to guarantee care coordination and continuity. All professionals should continuously collaborate and effectively exchange information to provide patient-centered care. Patients and families should be involved in making decisions regarding hospital-to-home transitions in a way that responds to their needs without being overwhelmed by healthcare professionals.

## Poster № 3

POWER2WALK STUDY PROTOCOL: THE IMPACT OF FUNCTIONAL POWER TRAINING ON PARTICIPATION AND ACTIVITY IN CHILDREN WITH CEREBRAL PALSY - A RANDOMIZED CONTROLLED TRIAL.

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**Introduction:** In children with cerebral palsy (CP), functional power training (FPT) has profound beneficial effects on gait speed and functional mobility. However, it remains unknown whether these physical improvements effectively translate into increased participation in social and/or physical activities.

**Purpose:** To investigate whether a 12-week high-intensity FPT program effectively accomplishes patient-tailored participation and activity goals in children with CP when compared to their usual care, and whether the effects of FPT are maintained at 12 and 24 weeks follow-up. Predictive factors for goal attainment will also be assessed.

**Methods:** A power-calculated fifty-eight ambulant children with CP or a related non-progressive disorder (age 4-12; GMFCS level I-III) will participate in a multicenter, randomized controlled trial. Half the children will undergo 12 weeks of high-intensity FPT (intervention group; 3x training per week; incorporating progressive overload), and the other half will receive usual care (control group). Follow-up assessments are conducted at 12 and 24 weeks post-trial to investigate long-lasting effects. During the first 12 weeks of follow-up, the control group will also receive 12 weeks of FPT. The primary outcome is goal attainment measured using Goal Attainment Scaling, with goals set at both activity and participation level. Secondary outcomes are i) self-perception of the child measured using Harter's Self-Perception Profile for Children on the domains of social competence, athletic competence, and global self-worth; ii) parent-reported mobility using the Gait Outcomes Assessment List and Mobility Questionnaire; iii) walking capacity using the 1-minute walk test, 10m shuttle run test, and muscle power sprint test; iv) body composition assessed through bioelectrical impedance analysis; v) baseline dietary intake logged in a 3-day food record, and vi) physical activity and sleep recorded for 7 days using a wrist-worn accelerometer. Randomized controlled trial data will be analyzed through Mann-Whitney U-tests and independent samples t-tests. Follow-up data will be analyzed using parametric and non-parametric one-way ANOVAs. A predictive model will be build using ordinal logistic regression with a maximum of six predefined secondary outcome measures as covariates. Additional exploratory analyses may also be conducted. Significance is set at  $\alpha = 0.05$  for all analyses.

## Poster № 4

### Imaging of intramuscular pathology by [<sup>18</sup>F]-FDG positron emission tomography in patients with rheumatic musculoskeletal diseases

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## Poster № 4

### Introduction:

This study explores the methodology of employing whole-body positron emission tomography (PET) with PET tracer F18-fluorodeoxyglucose ( $^{18}\text{F}$ -FDG) to assess muscle pathology in rheumatic musculoskeletal diseases (RMDs). In RMDs, muscle weakness is a common symptom associated with altered muscle glucose metabolism.  $^{18}\text{F}$ -FDG PET potentially allows for non-invasive investigation of these metabolic changes at skeletal muscle level, to better understand muscle pathology in RMDs. However, up until now, this potential of  $^{18}\text{F}$ -FDG is unexplored.

### Purpose:

The study objectives were to identify the most appropriate methodology for assessing  $^{18}\text{F}$ -FDG muscular uptake in RMDs and to compare uptake between patients with rheumatoid arthritis (RA), osteoarthritis (OA), inflammatory idiopathic myopathy (IIM), and controls.

### Methods:

The analysis involved retrospective examination of whole-body  $^{18}\text{F}$ -FDG PET scans in 31 RMD patients (11 RA, 10 OA, 10 IIM) and 8 controls, focusing on various muscle groups. For the qualitative assessment, regions with positive uptake and the uptake pattern were recorded. Two methods were compared to quantitatively assess  $^{18}\text{F}$ -FDG muscle uptake: fixed volume of interest (VOI) (fixed height position on bone) and hotspot VOI (visually highest uptake), whereafter standardized uptake values (SUVs) were compared for different muscle groups between the RMDs and controls.

### Results:

$^{18}\text{F}$ -FDG PET enables qualitative and quantitative differentiation of muscle glucose uptake in RA, OA and IIM patients. Qualitative assessment: a heterogenous uptake pattern of  $^{18}\text{F}$ -FDG was mostly seen in the quadriceps and the hamstring muscles while other muscles displayed either heterogenous or homogenous patterns. Quantitative assessment: the hotspot VOI method was preferred due to its higher sensitivity to detect differential  $^{18}\text{F}$ -FDG muscle uptake (mean=0.147, 95%CI [-0.411, 0.117]). In all muscle groups, the IIM patients had the highest SUVs followed by the OA and RA patients, respectively.

### Conclusion:

$^{18}\text{F}$ -FDG PET allows for both qualitative and quantitative assessment, of differential muscle glucose uptake in RA, OA, and IIM patients at both individual muscle and patient group levels. The increased FDG uptake indicates altered glucose metabolism in the muscles affected by the RMDs. This study provides the evidence for future exploration of  $^{18}\text{F}$ -FDG PET to study muscle pathology in RMDs in relation to muscle weakness.

## POLARIZATION-SENSITIVE OPTICAL COHERENCE TOMOGRAPHY AND SCLERAL COLLAGEN FIBER ORIENTATION IN OSTEOGENESIS IMPERFECTA

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### Introduction

Osteogenesis imperfecta (OI), a rare genetic disorder caused by collagen type I defects, is known for skeletal fragility. OI individuals often have blue sclerae and may face an increased risk of ophthalmic diseases. Collagen type I constitutes about 80% of the scleral dry weight and is believed essential for supporting the optic nerve head. The healthy sclera has multiple fiber layers, with a specific organizational pattern in the upper layer near the optic nerve head (Figure 1). Disruptions in this pattern may heighten the risk of ophthalmic diseases.

### Purpose

The aim was to examine the impact of collagen type I defects on the sclera by analyzing collagen fiber organization around the optic nerve head.

### Method

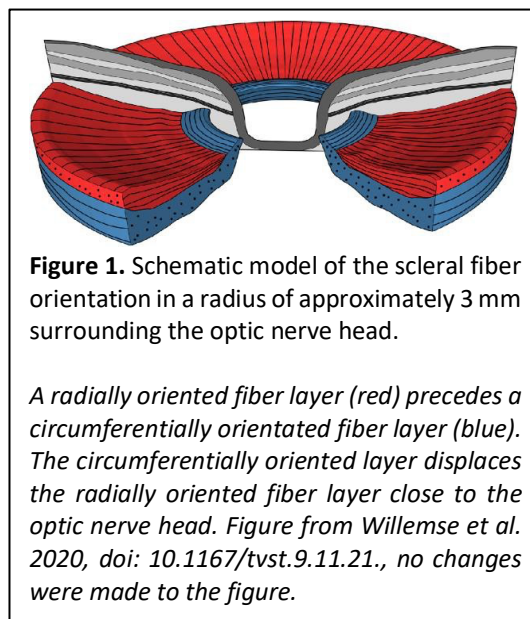
Polarization-sensitive optical coherence tomography (PS-OCT), an extension of conventional OCT, was used to visualize the fiber orientation within the upper layer of the sclera surrounding the optic nerve. The study involved three OI individuals and seventeen healthy participants. Birefringence, associated with light refraction, was measured, along with the thickness of the radially oriented collagen layer.

### Results

PS-OCT revealed comparable scleral collagen fiber orientation in OI participants and healthy controls. Two OI participants exhibited reduced birefringence of the radially oriented layer compared to the control group (OI participant 1 ODS: 0.34 °/μm, OI participant 2: ODS 0.26 °/μm, OI participant 3: OD: 0.29 °/μm, OS: 0.28 °/μm, healthy controls: ODS 0.38 ± 0.05 °/μm). The radially oriented layer was thinner although within ± standard deviations of the mean observed in healthy participants (OI participant 1 OD: 101 μm, OS 104 μm, OI participant 2: OD 97 μm, OS 98 μm, OI participant 3: OD: 94 μm, OS 120 μm, healthy controls: OD 122.8 ± 13.6 μm, OS 120.8 ± 15.1 μm).

### Conclusions

Comparable fiber orientations were observed around the optic nerve in OI individuals and healthy controls. However, differences in birefringence and thickness of the radially oriented scleral layer were noted, with two OI participants exhibiting reduced birefringence and thinner scleral layers. This implies abnormalities in collagen organization or composition, underscoring the necessity for additional research to comprehend the ocular phenotype in OI.



**Figure 1.** Schematic model of the scleral fiber orientation in a radius of approximately 3 mm surrounding the optic nerve head.

*A radially oriented fiber layer (red) precedes a circumferentially orientated fiber layer (blue). The circumferentially oriented layer displaces the radially oriented fiber layer close to the optic nerve head. Figure from Willemse et al. 2020, doi: 10.1167/tvst.9.11.21., no changes were made to the figure.*

## Poster № 6

### PRELIMINARY EFFECTIVENESS AND PRODUCTION TIME AND COSTS OF 3D-PRINTED ORTHOSES IN CHRONIC HAND CONDITIONS: A NON-RANDOMIZED FEASIBILITY STUDY

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#### ABSTRACT

**Introduction** Although three-dimensional (3D) printing is increasingly used to manufacture hand orthoses, the evidence on the effectiveness and costs in chronic hand conditions is scarce.

**Purpose** To assess the preliminary effectiveness of 3D-printed hand orthoses compared to conventionally custom-fabricated hand orthoses in persons with chronic hand conditions on performance of activities of daily living (ADL), hand function, quality of life, satisfaction, and production time and costs.

**Methods** In this interventional feasibility study, chronic hand orthotic users received a 3D-printed orthosis according to the same type as their current orthosis. The primary outcome, ADL performance, was assessed with a custom short form of the Dutch-Flemish Patient-Reported Outcomes Measurement Information System – Upper Extremity (DF-PROMIS-UE) and the Michigan Hand Questionnaire - Dutch language version (MHQ-DLV) ADL domain. Secondary outcomes were hand function (MHQ-DLV), quality of life (EuroQol 5-Dimension 5-Level (EQ-5D-5L)), and satisfaction (Dutch version of the Quebec User Evaluation of Satisfaction with Assistive Technology (D-QUEST); Dutch Client Satisfaction with Device (D-CSD)). Furthermore, production time and costs were recorded.

**Results** Twenty-one participants were included, and 19 completed the 4 months follow-up. No significant differences were found between 3D-printed orthoses and conventional orthoses on ADL performance (mean difference from baseline to 4 months follow-up: PROMIS: -1.46; 95%CI [-3.01;0.09], and MHQ ADL domain: -4.99; 95%CI [-12.36;2.23]), nor on hand function and quality of life. Satisfaction with the 3D-printed orthosis was significantly higher compared to the conventional orthoses (mean difference D-CSD: +5.11; 95%CI [0.62;9.59]). Production time and costs for 3D-printed orthoses (production time: median 129 min, IQR: 109-148 min, costs: median €187, IQR: €143-206) were significantly lower compared with the conventional orthoses (production time: median 269 min, IQR: 241-311 min; costs: median €398, IQR: €380-436). Fifteen participants (79%) preferred the 3D-printed orthosis over the conventional orthosis.

**Conclusions** This feasibility study in chronic hand orthotic users suggests that 3D-printed orthoses are similar to conventional orthoses in terms of ADL performance, hand function and quality of life. Satisfaction, production time and costs were in favor of the 3D-printed hand orthoses.



## **A Case of Melkersson-Rosenthal Syndrome with Temporomandibular Joint Osteoarthritis: Multidisciplinary Treatment and Autoimmune Etiological Hypothesis**

**Abstract:** Melkersson-Rosenthal syndrome (MRS) is a rare neuro-mucocutaneous disorder characterized by recurrent edema, facial palsies, and nerve dysfunctions often associated with the plicata tongue. Although the etiology of MRS is not well understood, there is growing evidence suggesting an autoimmune involvement. This paper presents a case report of a 25-year-old male with MRS as the initial symptom, followed by temporomandibular joint osteoarthritis (TMJ-OA). A comprehensive diagnosis and multidisciplinary treatment approach including surgery, local injections, and oral medication were implemented, resulting in a favorable prognosis. These findings support the hypothesis that MRS is a systemic granulomatous disease caused by autoimmunity, which may also influence the occurrence and development of TMJ-OA through immune-related mechanisms. This study emphasizes the significance of systemic immune regulation in the treatment of patients with MRS and TMJ-OA comorbid conditions.

**Keywords:** Melkersson-Rosenthal syndrome, Temporomandibular joint osteoarthritis, Systemic immune regulation

## Poster № 8

### **Accuracy assessment of pedicle screw insertion with patient specific 3D-printed guides through superimpose CT-analysis in thoracolumbar spinal deformity surgery**

**J. Cool. J. van Schuppen. M.A. de Boer. B.J. van Royen**

#### **Abstract**

**Purpose** In order to avoid pedicle screw misplacement in posterior spinal deformity surgery, patient specific 3D-printed guides can be used. An accuracy assessment of pedicle screw insertion can be obtained by superimposing CT-scan images from a preoperative plan over those of the postoperative result. The aim of this study is to report on the accuracy of drill guide assisted pedicle screw placement in thoracolumbar spinal deformity surgery by means of a superimpose CT-analysis.

**Methods** Concomitant with the clinical introduction of a new technique for drill guide assisted pedicle screw placement, the accuracy of pedicle screw insertion was analyzed in the first patients treated with this technique by using superimpose CT-analysis. Deviation from the planned ideal intrapedicular screw trajectory was classified according to the Gertzbein scale.

**Results** Superimpose CT-analysis of 99 pedicle screws in 5 patients was performed. The mean linear deviation was 0.92 mm, the mean angular deviation was 2.92° with respect to the preoperatively planned pedicle screw trajectories. According to the Gertzbein scale, 100% of screws were found to be positioned within the “safe zone”.

**Conclusion** The evaluated patient specific 3D-printed guide technology was demonstrated to constitute a safe and accurate tool for precise pedicle screw insertion in spinal deformity surgeries. Superimpose CT-analysis showed a 100% accuracy of pedicle screw placement without any violation of the pedicle wall or other relevant structures. We recommend a superimpose CT-analysis for the first consecutive patients when introducing new technologies into daily clinical practice, such as intraoperative imaging, navigation or robotics.

## Poster № 9

### ESTIMATED CUMULATIVE RADIATION EXPOSURE IN PATIENTS TREATED FOR ADOLESCENT IDIOPATHIC SCOLIOSIS

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#### Abstract

**Introduction:** Adolescent idiopathic scoliosis (AIS) is a progressive spinal deformity, most often observed in female patients of pubescent age. The deformity's severity, its progression through time, its treatment and subsequent follow-up are assessed with routine radiological evaluation of the patient's full spine.

**Purpose:** This study aimed to determine the cumulative radiation exposure in average patients with AIS treated by brace or surgery throughout their treatment.

**Methods:** The average number of imaging procedures and corresponding radiation doses were retrospectively obtained from the medical charts of AIS patients treated conservatively and/or surgically at our institution. The median radiation exposure of all imaging modalities was stated in effective dose (mSv). The estimated cumulative effective radiation dose of the each treatment group was determined by multiplication of the average number of imaging conducted, and the median effective radiation dose per imaging modality.

**Results:** In total, 73 AIS patients were included (28 brace, 45 surgically). Patients treated with a brace were subjected to an average of 9.03 full spine radiographs, resulting in an estimated effective cumulative dose of 0.505 mSv over a median treatment period of 3.23 years. Patients treated surgically received an average of 14.29 full spine radiographs over a median treatment period of 2.76 years. The estimated effective cumulative dose amounted from 0.951 to 1.841 mSv, depending on the surgical technique.

**Conclusion:** The cumulative effective radiation doses rendered to AIS patients as part of their treatment and follow-up were relatively low. However, every exposure to ionising radiation for medical imaging purposes should be minimised.

## Poster № 10

### ACCURACY ASSESSMENT OF PEDICLE SCREW INSERTION WITH PATIENT SPECIFIC 3D-PRINTED GUIDES THROUGH SUPERIMPOSE CT-ANALYSIS IN THORACOLUMBAR SPINAL DEFORMITY SURGERY

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#### Abstract

**Introduction:** In order to avoid pedicle screw misplacement in posterior spinal deformity surgery, patient specific 3D-printed guides can be used. An accuracy assessment of pedicle screw insertion can be obtained by superimposing CT-scan images from a preoperative plan over those of the postoperative result.

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**Conclusion:** The evaluated patient specific 3D-printed guide technology was demonstrated to constitute a safe and accurate tool for precise pedicle screw insertion in spinal deformity surgeries. Superimpose CT-analysis showed a 100% accuracy of pedicle screw placement without any violation of the pedicle wall or other relevant structures. We recommend a superimpose CT-analysis for the first consecutive patients when introducing new technologies into daily clinical practice, such as intraoperative imaging, navigation or robotics.

## Poster № 11

### Collagen expression in cutaneous tissues of a new mouse model of haploinsufficient (mild) Osteogenesis Imperfecta

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Osteogenesis Imperfecta (OI) is one of the most common rare bone dysplasias. OI is characterized by congenital bone fragility, resulting in numerous fractures and skeletal deformities. In addition, patients develop a number of extraskeletal features: blue sclera, dentinogenesis imperfecta, hearing loss, cardiopulmonary complications, easy bruising, and joint and skin laxity. Around 85% of the OI patients harbor pathogenic variants in the *COL1A1* and *COL1A2* genes, coding for collagen type I. The vast majority (~80%) of dermis collagen is represented by collagen type I.

We developed a new mouse model for mild OI type 1 with a quantitative haploinsufficient defect in collagen type I. Haploinsufficient OI (hiOI) mice were genetically modified with CRISPR/Cas to knockout one *Col1a1* allele. Collagen gene expression was analysed in the total skin of 8-week-old mice by comparing 20 hiOI mice with 20 wild type (WT) littermates with RT-qPCR; second-harmonic generation (SHG) microscopy was used to detect collagen fibers.

Similarly to bone tissue, the ratio of *Col1a1/Col1a2* expression in total skin was significantly lower compared to WT littermates, supporting the haploinsufficient defect. Decreased *Col1a1/Col1a2* expression ratio was also noted in haploinsufficient OI patient skin fibroblast cultures, confirming a similar defective collagen type I expression pattern between hiOI mice and OI type 1 patients. SHG microscopy showed reduced number of collagen fibers in the dermis of hiOI mice, compared to WT animals.

Further histological analysis of the skin tissue in hiOI mice will shed more light on the skin phenotype of mild OI.

## Poster № 12

### PHYSICAL TRAINING FOR PEOPLE WITH PARKINSON'S DISEASE AND MULTIPLE SCLEROSIS: EFFECT ON MIND AND BODY – STUDY PROTOCOL

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#### **Abstract [Word Count: 296]**

##### **Introduction**

Next to motor deficits, people with Parkinson's disease (PD) and Multiple Sclerosis (MS) experience non-motor problems (e.g., depression, anxiety). Pharmacological treatment is available for symptom relief; however, various disease complaints respond insufficiently to medication and considering the gradual worsening of symptoms, there is an urgency for additional non-pharmacological interventions. Physical exercise is increasingly recognized as an assisting therapy but the optimal dose is not known.

##### **Purpose**

To investigate differences in response patterns of, primarily, depression and anxiety as well as motor and other non-motor symptoms, functional brain connectivity, and blood-based neuroplasticity (brain-derived neurotrophic factor (BDNF)) and neurodegeneration (neurofilament light (NfL)) biomarkers to high intensity interval training (HIIT), continuous aerobic exercise (CAE), and movement advice (MA) in people with PD and MS.

##### **Method**

People with PD [n=24] and MS [n=24] will be randomized to 8 weeks of HIIT [2x/week, 30min/session, ≥85% Wmax], CAE [2x/week, 50min/session, ~55% Wmax], or MA [+3000 daily steps for 5 days] with baseline and wash-out phases of 4 weeks. Frequently repeated assessment of the outcome measures [depression, anxiety, cognition, fatigue, sleep, well-being, motor capacity, quality of life, activities of daily living, level of physical activity, BDNF and NfL concentration, functional brain connectivity] will be conducted. Changes in outcome measures will be analyzed using visual inspection of trends in level, slope, and variability for each outcome intervention, confirmed by longitudinal regression analysis.

##### **Results**

We expect improvement in motor and non-motor symptoms as well as an increase and a decrease in biomarkers of neuroplasticity and neurodegeneration in blood, respectively, and enhanced functional brain connectivity in response to physical training; however, HIIT is expected to be significantly more effective in doing so.

##### **Conclusions**

The goal is to, ultimately, develop clinical guidelines and tangible training protocols for people with PD and MS to reduce disease burden.

## VALIDATION OF QUANTITATIVE [<sup>18</sup>F]NaF PET UPTAKE PARAMETERS IN BONE DISEASES: A SYSTEMATIC REVIEW

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**Introduction:** [<sup>18</sup>F]NaF PET has become an increasingly important tool in clinical practice towards understanding and evaluating diseases and conditions in which bone metabolism is disrupted. Full kinetic analysis using nonlinear regression with a two tissue compartment model to determine the net rate of influx ( $K_i$ ) of [<sup>18</sup>F]NaF is considered the gold standard for quantification of [<sup>18</sup>F]NaF uptake. However, dynamic scanning often is impractical in a clinical setting, leading to the development of simplified semi-quantitative parameters.

**Purpose:** This systematic review investigated which uptake parameters have been used to evaluate bone disorders and how they have been validated to measure disease activity.

**Methods:** A literature search (in PubMed, Embase.com and Clarivate Analytics/Web of Science Core Collection) was performed up to 28<sup>th</sup> November 2023, in collaboration with an information specialist. Each database was searched for relevant literature regarding the use of [<sup>18</sup>F]NaF PET/CT to measure disease activity in bone related disorders. The main aim was to explore whether the reported semi-quantitative uptake values were validated against full kinetic analysis. A second aim was to investigate whether the chosen uptake parameter correlated with a disease specific outcome or marker, validating its use as a clinical outcome or disease marker.

**Results:** The initial search included 1636 articles leading to 92 studies spanning 29 different bone related conditions in which [<sup>18</sup>F]NaF PET was used to quantify [<sup>18</sup>F]NaF uptake. In 12 bone related disorders, kinetic analysis was performed and compared with simplified uptake parameters.  $SUV_{mean}$  (standardised uptake value) and  $SUV_{max}$  were used most frequently, though normalization of these values varied greatly between studies. In some disorders, various studies were performed evaluating [<sup>18</sup>F]NaF uptake as a marker of bone metabolism, but unfortunately, not all studies used this same approach, making it difficult to compare results between those studies.

**Conclusions:** When using [<sup>18</sup>F]NaF PET to evaluate disease activity or treatment response in various bone related disorders, it is essential to standardize scanning protocols and analytical procedures. The most accurate outcome parameter can only be obtained through kinetic analysis, but where possible simplified uptake parameters may be used.

## Poster № 14

### TAILORED INJURY PREVENTION IN ADAPTED SPORTS; A ONE-SEASON RANDOMIZED CONTROLLED TRIAL

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#### **Introduction:**

Sporting activities can increase the risk of sport-related health problems. Within the domain of adapted sport, preventing sports-related health problems and reducing their severity and impact is of great importance, as such health problems can further burden daily activities. Effective prevention strategies can reduce the number of sports-related health problems and/or reduce their severity.

#### **Purpose:**

This randomised controlled trial evaluated the effectiveness of the 'Tailored Injury Prevention in Adapted Sports' (TIPAS) intervention over a one-season period.

#### **Method:**

107 athletes with a physical impairment started the 40-week trial period. After randomisation, 59 athletes were in the intervention group and 48 in the control group. Both groups completed the Dutch translation of the Oslo Sports Trauma Research Center (OSTRC) Questionnaire on Health Problems every week. Direct automatic preventive measures corresponding to the weekly reported health problems, the physical impairment and the type of sports were given to the intervention group. The control group only received an overview of preventive strategies before study start. Injury and illness prevalence, incidence, weekly cumulative severity score, weekly time loss, and total burden are calculated based on the reported data. A multinomial mixed methods analysis was performed to identify an intervention effect over time.

#### **Results:**

The athletes (53 women - 54 men; age  $\pm$  45) reported 450 health problems, of which 163 were illnesses and 287 injuries. The overall prevalence of health problems was 25% in the intervention group and 20% in the control group. Over time, there is a significant positive interaction effect between the intervention group and the prevalence of illnesses, but not for injuries. Furthermore, there is a significant positive intervention effect regarding the severity of all health complaints, injuries and illnesses over time.

#### **Conclusion:**

The TIPAS intervention has a positive effect regarding the decrease in the prevalence of illnesses and the severity of health problems (injuries and illnesses) over time. This tailored online preventive approach allows athletes to receive conveniently accessible care that is suited to their physical impairment, their sports participation and the health status of that moment in time.



## Poster № 15

### EFFECTS OF TRAINING FOR AN ATHLETIC CHALLENGE ON ILLNESS COGNITION IN INDIVIDUALS WITH CHRONIC DISABILITY: A PROSPECTIVE COHORT STUDY

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**Introduction:** Illness cognition (IC) describes a patient's thoughts and beliefs about their condition. These thoughts and beliefs influence how a patient adapts to a chronic disease. It is important to know more about illness cognitions and how to possibly influence illness cognitions as research in individuals with spinal cord injury (SCI) showed strong negative associations between helplessness and well-being and strong positive associations between acceptance and well-being. Cognitive interventions targeting illness cognition have improved health behaviors and outcomes in diverse populations. Unfortunately, there is a lack of research into physical activity-types of interventions to improve illness cognition.

**Purpose:** The aim was (1) to determine if training for a handcycling mountain time trial (HandbikeBattle) improves IC and (2) to identify factors associated with IC change scores.

**Method:** Persons with a chronic disability (N = 220; including N = 151 with SCI) trained five months and participated in the time trial. The IC Questionnaire measured helplessness, acceptance, perceived benefits and was assessed before training (T1), after training (T2), and four months after the event (T3). Age, sex, body mass index (BMI), time since injury (TSI), disability characteristics, self-efficacy, mental health (MH) and musculoskeletal pain were obtained at T1.

**Results:** Multilevel regression analyses showed that helplessness decreased (from 11.96 to 11.28,  $p < 0.01$ ) and perceived benefits increased (from 16.91 to 17.58,  $p < 0.01$ ) from T1 to T2. For helplessness this decrease persisted during follow-up (11.16 at T3). Changes in helplessness were associated with self-efficacy ( $p = 0.02$ ), MH ( $p = 0.02$ ) and lesion completeness ( $p = 0.02$ ), and were independent of disability type ( $p = 0.66$ ), lesion level ( $p = 0.30$ ) and demographics such as sex ( $p = 0.29$ ) and age ( $p = 0.67$ ).

**Conclusions:** Training with peers may improve helplessness and perceived benefits in individuals with a chronic disability. Especially individuals with MH problems might benefit from training for an athletic challenge with peers to improve illness cognitions, and ultimately, quality of life.

**A NOVEL X-LINK OSTEOPOROSIS MICE MODEL WITH PLS3 KNOCKOUT**

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**Introduction**

PLS3 encodes the protein T-plastin, which is an actin-bundling protein mediating the formation of actin filaments in cells. Loss-of-function mutations in *PLS3* have been reported to cause X-linked osteoporosis and fractures. However, there is no conclusive evidence for the molecular mechanism of *PLS3* mutation-mediated effects in the etiology of osteoporosis.

**Purpose**

This study aims to set up a novel ubiquitous *Pls3* knockout (*Pls3* KO) mouse model to simulate PLS3 X-linked osteoporosis, which helps us to better understand the molecular mechanism of the disease.

**Method**

Global *Pls3*<sup>em1cyagen</sup> mouse model was generated in C57BL/6J mice, using the CRISPR/Cas 9 system at Cyagen Biosciences Inc (Suzhou, China). Breedings, primers, allele names, and PCR conditions were applied as suggested by the manufacturer. Body length and weight of the mice were measured twice a week from 2 to 12 weeks old and sacrificed at 12 weeks by CO<sub>2</sub>-induced hypoxia. Bone tissues from ten hemizygous *Pls3* KO and ten wild-type littermates (WT) were analyzed with 3-point bending test, microcomputed tomography (micro-CT) and bone histomorphometry.

**Results**

The genotype of *Pls3* KO mouse was confirmed by PCR. *Pls3* gene expression in *Pls3* KO mouse was all lower than in WT mice. The body weight was significantly different between *Pls3* KO and WT mice, only at 4 weeks old age. *Pls3* KO mice tibiae presented a significantly lower breaking load and stiffness compared to their WT littermates. MicroCT scanning of the distal trabecular femoral bone and midshaft cortical femoral bone indicated significant lower trabecular bone volume fraction, trabecular thickness and trabecular connectivity density and a significantly higher trabecular separation were detected in *Pls3* KO mouse. In addition, *Pls3* KO mouse presented a significantly lower cortical bone volume fraction, cortical bone area, cortical area fraction (Ct.Ar/Tt.Ar), cortical thickness and medullary cavity area. The histomorphometric parameters cortical width, trabecular width and Ct.Ar/Tt.Ar presented significantly lower between in *Pls3* KO mouse, but the number of osteocytes and osteoclasts were not different within normal range.

**Conclusions**

Impaired bone microstructure and bone strength were significant characteristics of the *Pls3* KO mouse model. The exact mechanism of this phenotype still needs further exploration.

RADIAL PEDAL FORCES IN CYCLING: DUE TO SUB-OPTIMAL CYCLING OR UNAVOIDABLE BY-PRODUCTS?

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**Introduction:** A cyclist’s performance crucially depends on the average mechanical power output (*AMPO*) generated. The instantaneous mechanical power output of a cyclist equals the product of crank angular velocity, crank length and the tangential pedal force ( $F_{tan}$ ). Radial pedal forces ( $F_{rad}$ ) do not contribute to mechanical power. In the literature, but also in the “cycling field” [e.g., by trainers and coaches], it is suggested that  $F_{rad}$  arise from sub-optimal pedalling technique, and that limiting them increases *AMPO* and efficiency.

**Purpose:** First, we set out to understand if radial pedal forces are indeed a consequence of sub-optimal pedalling technique or an unavoidable by-product of optimal cycling. Second, we want to understand the relationship between limiting radial pedal forces and maximal attainable *AMPO*.

**Method:** We used an optimal control musculoskeletal model of a cyclist (5 segments driven by 9 Hill-type muscles; see Fig.1). We simulated optimal sprint cycling while limiting  $F_{rad}$  to various levels. We calculated the *Index of Effectiveness* (*IE*)<sup>[1]</sup>: ratio of  $F_{tan}$  and  $F_p$ , typically used as a measure of “pedalling technique”.

**Results:** *AMPO* dropped from 1115 W without a limit on  $F_{rad}$  to 528 W when not allowing  $F_{rad}$  ( $F_{rad\_max} = 0$ ; Fig.2). Highest *IE* does not coincide with highest attainable *AMPO* (Fig.2). This shows that  $F_{rad}$  is an unavoidable “by-product”. We calculated the power delivered and work done by all individual muscles in one full cycle. When limiting radial forces, muscles not only clearly deliver less positive power, but also deliver more negative power (and thus dissipate energy; see Fig.3).

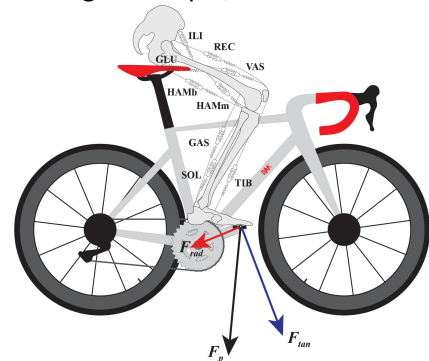


Fig.1 Musculoskeletal model and pedal force.

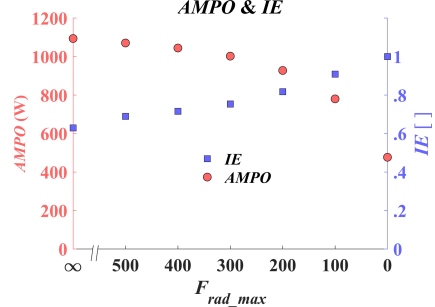


Fig.1. *AMPO* and *IE* as a function of allowed radial pedal force ( $F_{rad\_max}$ )<sup>[2]</sup>.

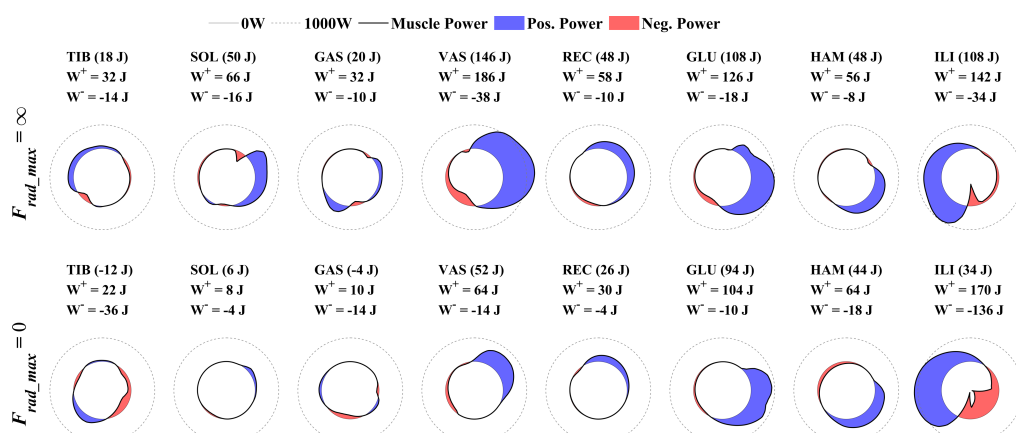


Fig. 2. Instantaneous mechanical power and work delivered by each of the modelled muscles in one full cycle<sup>[2]</sup>.

**Conclusions:** We showed that radial pedal forces are an unavoidable by-product of (*AMPO*) optimal cycling. We explained that avoiding radial pedal forces leads to ineffective muscle use, resulting in less positive power delivery and a lower efficiency. Cyclists should not try to limit radial forces.

References

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MICROVASCULAR IMPAIRMENTS IN SKELETAL MUSCLE CONTRIBUTE TO EXERCISE CAPACITY IN PATIENTS WITH LONG COVID AND ME/CFS

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**Introduction:** Post-viral diseases, like Long COVID- and ME/CFS, are characterized by excessive fatigue, brainfog and post-exertional malaise, which is the worsening of symptoms after exertion. We previously observed reduced muscle oxygen extraction in Long COVID patients during exercise, where patients also presented with worsening of skeletal muscle abnormalities after exertion. This suggests a potential role for reduced muscle oxygenation or endothelial dysfunction in the disease progression.

**Purpose:** This study aimed to study vascular responses using near-infrared spectroscopy (NIRS), and endothelial markers using immunofluorescence microscopy and proteomics, before and one day after maximal cycling exercise that induce post-exertional malaise.

**Method:** NIRS were monitored during a maximal exercise test in patients with Long COVID (n=25), ME/CFS (n=25), and healthy controls (n=25). Venous blood was taken at different timepoints for proteomics. Vastus lateralis biopsies were obtained before- and 1 day after the exercise test, and markers for microvascular architecture (lectin) and vascular permeability (CD31) were assessed.

**Results:** Following exercise, the muscle HHb and O<sub>2</sub>Hb recovery was significantly faster in controls compared to PASC and ME patients ( $p < 0.0001$ ), indicating reduced oxygen utilization and delivery responses after acute exercise. The recovery slopes correlated with capillary density in both Long COVID and ME/CFS ( $p < 0.05$ ). Long COVID patients tended to have lower CD31 expression levels at rest, with a subsequent higher foldchange 1 day after exercise. The increase in CD31 expression strongly correlated to patient VO<sub>2max</sub> ( $p < 0.001$ ). Lastly, proteomics analysis revealed increased markers of endothelial activation and thromboinflammation.

**Conclusions:** Our findings suggest distinct vascular impairments in Long COVID and ME/CFS. The increased (de)oxygenated recovery time in patients may relate to differences in blood perfusion and/or oxygen extraction. Our proteomics data, coupled with decreased CD31 expression, point towards underlying events of endothelial inflammation and damage, affecting permeability. These factors, in turn, have significant implications for skeletal muscle tissue, and contribute to the pathophysiology of post-exertional malaise.

# OPTIMIZING AND IMPLEMENTING A COMMUNITY-BASED GROUP FALL PREVENTION PROGRAM: A MIXED METHODS STUDY

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## Abstract

### Introduction

Falls and fall-related injuries among older adults are associated with decreased health. Therefore, fall prevention programs (FPPs) are increasingly important. However, the implementation of such complex interventions is often difficult and results in an adaptation of the program. Insight into the implementation process provides context to research findings and may identify barriers and facilitators for the further implementation of the FPP and similar programs.

### Purpose

Therefore, this study aimed to identify how to optimize and further implement the In Balance program, which is a widely used group-based FPP in the Netherlands among participants, therapists and stakeholders using a mixed methods study.

### Method

FPP participants and therapists filled out a questionnaire about their experiences with the FPP. Moreover, three focus groups were conducted with older adults who followed the FPP, one with therapists and one with other stakeholders. The older adults and therapists are participating in the randomized controlled trial investigating the (cost-)effectiveness of the In Balance FPP. For the stakeholders, we searched for a varied group in our network. Data were analysed according to the thematic analysis approach of Braun and Clarke.

### Results

Overall, 93% of the 104 FPP participants were satisfied with the FPP and 86% (n = 12) of the therapists would recommend the FPP to older adults with balance or mobility difficulties. Moreover, six themes were identified regarding optimisation and further implementation: (1) recruiting and motivating older adults to participate; (2) structure and content of the program; (3) awareness, confidence and physical effects; (4) training with peers; (5) funding and costs; and (6) long-term continuation.

### Conclusions

This study resulted in practical recommendations for optimizing and further implementing FPPs in practice. For example, the combination of theory and practice and the tailor-made approach was experienced as positive. A crucial factor for adherence is that FPP participants perceive some degree of training effects, such as more awareness. Moreover, sharing experiences with peers and learning from each other were perceived as helpful for adherence and wellbeing. Last, there is a need for the continuation of exercising after the FPP, preferably with the same group as in the FPP.

# THE SHORT PHYSICAL PERFORMANCE BATTERY IS NOT ASSOCIATED WITH DAILY-LIFE GAIT QUALITY AND QUANTITY IN COMMUNITY-DWELLING OLDER ADULTS

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## Abstract

### Introduction

The Short Physical Performance Battery (SPPB) consists of performance measures of lower extremity function and is frequently used in a clinical setting to determine and monitor functional status in older adults. Besides, objective daily life performance can be measured by wearable inertial sensors. For both the SPPB and daily-life gait quality and quantity variables are indications that they are measures for functional status. It is generally assumed that they are interrelated and exchangeable, but this has not yet been established.

### Purpose

The purpose of this study was to determine the correlations between the SPPB and wearable sensor-based gait quality and quantity variables in community-dwelling older adults. This knowledge can help to explore whether functional status could not only be determined in a clinical setting, but also can be remotely monitored by quality and quantity variables.

### Method

This cross-sectional study included 229 community-dwelling adults of 65 years or older. The SPPB is combined score of the Three Stage Balance test, Four Meter Walk test and Five Times Sit to Stand test and ranges from 0-12. To determine gait quality and quantity variables, participants received a tri-axial inertial sensor measuring gait quality (e.g. number of strides and ambulation bouts) and quantity (e.g. gait stability and smoothness) variables. These assumed independent gait quality and quantity variables were correlated with the SPPB scores using Spearman correlations.

### Results

The median age of the study population was 76 years (IQR 72.6-81.0), and 76% were women (n=175). The median SPPB score was 10 (IQR 8-11). Spearman's rho values of the correlation between the SPPB and gait quality and quantity variables were all below 0.3.

### Conclusions

We found that there are only low correlations between the SPPB and gait quality and quantity variables. This implicates that SPPB scores appear to have little correlation with the performance of daily activities in older people. A possible explanation for finding weak correlations is that the SPPB showed little variation in our study population. Another potential explanation is that the SPPB is a measure for capacity, while gait quality and quantity variables are a measure for performance in daily life.

## Poster № 21

### Title:

EXPLORING PHYSICAL INACTIVITY-INDUCED MUSCLE FIBER-TYPE SPECIFIC ATROPHY THROUGH PROTEOMICS-COUPLED LASER MICRODISSECTION

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**Introduction:** Skeletal muscles undergo atrophy after physical inactivity, in a muscle fibre-type specific manner. Physical inactivity has been shown to induce muscle atrophy in primarily type I fibres. Anabolic resistance is one of the mechanisms underlying atrophy. However, it is unknown if this is also fibre-type specific. Laser microdissection can isolate single fibre-types, which can then be used to investigate the proteome of the different fibre-types under conditions of physical inactivity.

**Purpose:** This pilot study aims to investigate the feasibility of utilizing laser microdissection coupled with mass spectrometry-based proteomics in skeletal muscle tissue. We will use various amount of tissue to understand the possible proteome depth. Ultimately, this study seeks to assess the viability of laser microdissection for comprehensive proteome analysis of muscle fibre-types under conditions of physical inactivity, specifically in anabolic resistance.

**Method:** Mice underwent hindlimb suspension to induce physical inactivity. In the first part of this study anabolic resistance was determined using the surface sensing of translation assay to measure protein synthesis rates after an anabolic stimulus. In the second part of the study, laser microdissection will be employed to establish a calibration curve between amount tissue dissected and proteome depth. The gastrocnemius medialis of the mice will be cut into sections. These sections will be stained for oxidative activity by succinate dehydrogenase staining, thus allowing for distinguishment between high- and low-oxidative fibres. When the optimal proteome depth is determined these specific fibres will be isolated. They are then subjected to mass spectrometry analysis for protein profiling.

**Results:** Muscle atrophy was determined in all hindlimb muscles undergoing hindlimb suspension. Gastrocnemius medialis & lateralis underwent the largest amount of atrophy. Additionally, anabolic resistance was higher after inactivity. Preliminary data about laser microdissection or mass spectrometry is not available yet.

**Conclusions:** The findings of this pilot study will underscore the feasibility of utilizing mass spectrometry data for comprehensive analysis of muscle fibre-types. Future research into atrophy from other conditions, like ageing, could also benefit from this fibre-type targeted proteomic approach. Furthermore, laser microdissection could be employed to dissect other targeted parts of muscles, like satellite cells, myonuclei, and neuromuscular junctions.

## Poster № 22

### BALANCING ACT: THE DYNAMIC NATURE OF BEING A HEALTHY DANCER

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#### **Introduction**

Professional ballet dancers are artistic athletes who are highly exposed to pain and injuries. Maintaining physical and mental health is essential to achieve a high level of performance. However, it can prove challenging given the context in which they evolve. A deeper understanding of these contextual factors would allow us to help dancers preserve their health.

#### **Purpose**

This study explored the perceptions of dancers and their entourage regarding dancers' health and how to be a healthy dancer in a professional ballet company.

#### **Method**

In this qualitative study, we conducted twenty-two semi-structured interviews with dancers, health professionals, artistic staff, and administrators. All participants were employed with the Dutch National Ballet. Interviews were audio-recorded, transcribed, and analysed with reflexive thematic analysis.

#### **Results**

According to dancers and their entourage, being a healthy dancer is not a static state. They need to have a dynamic balance, react, and adapt to their environment. Three main themes emerged during analysis: dancers must adopt (1) **behaviours** supported by the (2) **team** surrounding them within the (3) **context** of a professional ballet company. Each theme can be a challenge or an opportunity to maintain dancers' health.

To be healthy, the participants mentioned that dancers need to manage their physical and mental health, as well as keep a balance between their professional and personal life. Participants supported that pain was expected in ballet but that knowing themselves and knowing when to push through or speak up about their pain was a good way to manage injury risk.

These behaviours were influenced by the support or lack thereof, that their entourage provided. Finally, contextual elements such as ballet culture, monetary and time resources, and organizational factors influenced the support that could be provided to the dancers and, after that, their behaviours.

#### **Conclusions**

Dancers and their entourage mentioned a constant and dynamic process balancing the physical and mental load, as well as contextual factors inherent to professional ballet. They emphasized that support, trust, and communication with the artistic and health teams was essential, ultimately promoting attainment of the high-performance standards expected.



### EXERCISE-INDUCED MUSCLE FATIGUE LEADS TO CHANGES IN GAIT-RELATED PARAMETERS AMONG OLDER ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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#### **Abstract**

##### **Introduction**

Muscle fatigue is a common phenomenon as a result of physical activity. This exercise-induced fatigue, is shown to affect certain spatiotemporal parameters, gait stability, and/or gait variability parameters in community-dwelling older adults. Due to a wide variety in fatiguing protocols and gait-related outcomes used in experimental settings, overall effects are not yet clear. Furthermore, specific characteristics of fatiguing protocols (i.e., intensity, duration or type of activity) may lead to different changes in gait-related outcomes.

##### **Purpose**

A systematic review and meta-analysis to obtain insight in (the extent of) changes in gait-related outcomes and to identify specific characteristics of fatiguing protocols in older adults.

##### **Method**

In September 2022 and April 2023, we searched in PubMed, Web of Science, Scopus, Cochrane and CINAHL databases. Two independent researchers screened and assessed articles using ASReview and Rayyan. We extracted data related to spatiotemporal, gait-stability or gait-variability parameters of healthy older adults (55+) before and after a fatiguing protocol or prolonged activity. Random-effects meta-analyses were performed on both absolute and non-absolute values in R-Studio. Moderator analyses were performed on six predefined clusters of gait-related outcomes: "Walking capacity", "Regularity", "Coordination", "Dynamic balance", "Symmetry" and "Foot movement".

##### **Results**

We included 573 effect sizes on gait parameters from 31 studies. The included studies were conducted on a total population of 761 older adults (on average 25 individuals per study), with a mean age of 71 ( $\pm 2.8$ ) years and 57% of all participants were female. Meta-analyses indicated that exercise-induced fatigue affected gait with a standardized mean change of 0.31 ( $p < 0.001$ ). Moderator analysis showed no statistical differences between clusters. Within clusters, the effects of exercise-induced fatigue were non-uniform, resulting in an overall effect that was indistinguishable from zero. The fatiguing protocol, in terms of duration, intensity, or type of activity, showed no moderator effects.

##### **Conclusions**

Exercise-induced fatigue results in small to moderate changes in gait-related outcomes, but these changes cannot be attributed to specific clusters of gait-related parameters. Besides, due to the heterogeneity between studies, no hard conclusions can be drawn on whether and how specific characteristics of fatiguing protocols moderate the extent and direction of changes in gait-related outcomes.

## Poster № 24

### BONE PHENOTYPE IN A NOVEL ESSENTIAL MOUSE MODEL FOR MILD HAPLOINSUFFICIENT OSTEOGENESIS IMPERFECTA

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#### Introduction

Osteogenesis Imperfecta (OI) is a genetic bone fragility disorder and one of the most common rare skeletal dysplasias. The mildest OI form, known as OI type 1, is caused by collagen type I haploinsufficiency due to pathogenic variants in the *COL1A1* gene leading to quantitative collagen deficiency. Although OI type 1 is the most common OI type and composes 1/3 of total OI patient population, to date there is no broadly available and reliable mouse model, slowing down progress in research and therapy development for this disorder type.

#### Purpose

We have developed a genetically modified mouse model with collagen type I haploinsufficiency.

#### Method

The haploinsufficient OI (hiOI) mice were developed with the C57BL/6J strain by performing a heterozygous deletion of the *Col1a1*. The bone phenotype was characterized comparing 20 hiOI mice with 20 wild-type (WT) littermates, with 10 male and 10 female animals per group. Analysis of collagen type I expression and bone markers was performed with RT-qPCR for 8 week and 24 week old mice. Bone volume and microarchitecture was analyzed using microCT in 8 week old mice. Bone RNAseq in 8 week old mice (5 OI and WT males) was performed to investigate dysregulated gene expression pathways in this new model.

#### Results

The *Col1a1/Col1a2* expression ratio was significantly lower in the hiOI compared to WT mice in bone of 8 and 24week old mice, in agreement with the expected collagen deficiency in mild OI. Increased expression of bone markers in hiOI animals highlighted the presence of a metabolic bone disorder. MicroCT analysis confirmed lower trabecular and cortical bone volume in hiOI mice, and it correlated with the reduced expression ratio of collagen type I chains. Bone RNAseq of hiOI mice showed upregulation of 51 genes, altering extracellular matrix structure, collagen trimer formation and bone cells function.

#### Conclusions

In conclusion, we have developed a new mouse model for mild haploinsufficient OI with reduced bone mass and altered collagen type I expression.

## DOES BED REST REDUCE BIOLOGICAL AGE IN HUMANS?

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**Introduction:** Epigenetic “clocks” are used to quantify human biological age using trained algorithms based on DNA methylation patterns. The use of biological age is therefore thought to be a better indicator of a person’s health than chronological age. Recent evidence suggests that hypermetabolism accelerates biological ageing, but does the reverse also hold true? The epigenetic clock ‘PhenoAge’ [1] is based on circulating biomarkers related to the hallmarks of ageing.

**Purpose:** Here we utilized PhenoAge to test whether bed rest-associated hypometabolism reduces biological age in humans.

**Methods:** We measured the nine biomarkers required for the Horvath-Levine PhenoAge calculation (albumin, creatinine, glucose, C-reactive protein, lymphocytes, mean corpuscular volume, red blood cell distribution width, alkaline phosphatase and white blood cell count), and determined biological age in 24 healthy individuals (age 33±9 years, 8 females) before and after 60 days of bed rest at the German Aerospace Center in collaboration with ESA and NASA, as part of the AGBRESA study.

**Results:** PhenoAge-assessed biological age highly correlated with chronological age ( $R^2=0.82$ ). Biological age was not affected by bed rest (from 30.91 to 30.87 years), despite a two-months increase in chronological age. Lower creatinine and mean corpuscular volume decreased biological age, while glucose, alkaline phosphatase and white blood cell count increased biological age.

**Conclusion:** PhenoAge biomarkers have varying impact on a person’s biological age, with some accelerating ageing and others showing a rejuvenation effect. It remains questionable whether the use of blood biomarkers as surrogate measures for the hallmarks of ageing is specific enough to detect the real underlying molecular mechanisms associated with ageing.

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## Poster № 26

### BALANCING ENERGY EXPENDITURE AND ENERGY INTAKE IN PEOPLE WITH NEUROMUSCULAR DISEASES; NEXT STEPS TOWARDS INDIVIDUALIZED NUTRITIONAL ADVICE

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**Introduction:** Many people with neuromuscular diseases (NMD) are overweight and have difficulties to lose their excessive weight, which may result in co-morbidities and risk on metabolic syndrome that negatively impact daily functioning and quality of life. Nutritional advice, specifically for NMD, is lacking.

**Purpose:** To describe the energy balance and body composition in people with NMD.

**Methods:** We analyzed data of the first 15 participants of an ongoing study (aim 30 adults with NMD, BMI: 18-40 kg/m<sup>2</sup>). Resting energy expenditure (REE) was measured using indirect calorimetry with a ventilated hood system; total energy expenditure (TEE) was, for the purpose of this abstract, calculated as the REE plus a 30% addition for physical activity energy expenditure. Energy intake was recorded with a 3-day weighed food diary, cross checked by an experienced dietitian. Body composition was measured by air displacement plethysmography (BODPOD). We defined a difference of  $\geq 10\%$  between TEE and energy intake as higher/lower and excess or high fat mass as 21-30% or higher of their total body mass, respectively in males, and 31-40% or higher, respectively in females.

**Results:** 15 participants (7 females, mean  $\pm$  SD age:  $64.0 \pm 14.0$  years), diagnosed with Charcot-Marie-Tooth disease (n=7), post-polio syndrome (n=6), and inclusion body myositis (n=2) with a mean body mass index of  $26.4 \pm 4.4$  were included. The mean  $\pm$  SD measured REE was  $1412 \pm 294$  kcal/day, estimated TEE was  $1835 \pm 382$  kcal/day and the mean daily energy intake was  $1896 \pm 465$  kcal/day. In 8 participants (53%) the energy intake was higher than their TEE. The mean  $\pm$  SD percentage fat mass of total body mass was  $38.5 \pm 10.1$  % and percentage fat free mass was  $61.5 \pm 10.1$  %. All participants had excess or high fat mass rating.

**Conclusion:** In most participants there seems to be a disbalance in energy metabolism, with a higher energy intake than energy expenditure and all participants had excess or high fat mass. The results of this study will provide directions towards individualized nutritional advice in this population.

**INTEGRATED ANALYSIS OF TRANSCRIPTOME AND PROTEOME REVEALS A CORE SET OF GENES INVOLVED IN OSTEOBLAST UNDER OXIDATIVE STRESS**

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**Introduction:** Osteoporosis figures as high incidence, great harm and complex etiology. Oxidative stress (OS) induced osteoblast injury and osteogenic differentiation disorder is the pathological basis of osteoporosis, the mechanism of which remains to be deciphered.

**Purpose:** This study aims to reveal a core set of genes involved in osteoblast under oxidative stress by transcriptome and proteome analysis.

**Method:** In this study, we investigated the cellular behavior of osteoblast after H<sub>2</sub>O<sub>2</sub>-induced oxidative stress, based on the result of which, we performed the transcriptome and proteome analysis of osteoblast in response to oxidative stress. Cell viability experiment, flow cytometry, and TUNEL assays were performed to determine the effects of H<sub>2</sub>O<sub>2</sub> on the proliferation and apoptosis of osteoblasts. We used immunofluorescence to detect the mitochondrial reactive oxygen species (ROS) level and mitochondrial membrane potential (MMP) in H<sub>2</sub>O<sub>2</sub> treated osteoblasts. Adenosine triphosphate (ATP) level was measured using the ATP assay kit. Mineralization assay was also performed. The mRNA expression was determined by RT-qPCR, and protein levels were measured by Western blot.

**Results:** A total of 164 and 186 differentially expressed genes (DEGs) and proteins (DEPs) were identified, respectively. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) functional analysis showed that they were enriched in pathways associated with apoptosis and osteoblast differentiation. A protein-protein interactions (PPIs) network of DEPs was detected. Furthermore, seven important positive correlated DEGs and DEPs (cor-DEGs-DEPs genes) were characterized based on the integrated analysis of mRNA-protein expression, the interactions of which was revealed using PPIs analysis.

**Conclusions:** Our results provide important candidates for uncovering the mechanism of pathogenesis of osteoporosis, and will provide new clues for understanding the effects of oxidative stress on bone formation.

## Poster № 28

### FOOT AND ANKLE BIOMECHANICS DURING GAIT OF PATIENTS WITH AN OSTEOCHONDRAL LESION OF THE TALUS

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**Introduction:** An osteochondral lesion of the talus (OLT) is a defect of talar cartilage and subchondral bone, primarily linked to a history of ankle trauma. Alterations in ankle biomechanics are listed among potential reasons for OLT development. The clinical assessment of various ankle conditions frequently involves the examination of ankle biomechanics through three-dimensional gait analysis. However, the specific gait biomechanics within the OLT population have not yet been quantified.

**Purpose:** The primary aim of the study was to compare the foot and ankle biomechanics during gait between individuals with OLT and healthy controls. The secondary purpose was to compare those parameters between individuals with a medial and lateral OLT.

**Method:** 10 patients diagnosed with symptomatic OLT (5 medial and 5 lateral lesions (MOLT, LOLT)) underwent a gait analysis. 3D skin-marker data according to the Amsterdam Foot Model, ground reaction force and plantar pressure data were collected during walking to quantify the motions (i.e., kinematics) and forces (i.e. kinetics) of the foot and ankle joints. OLT data were compared to a reference dataset of healthy controls (HC) (n=13) using a one-way ANOVA SPM. When significant, adequate post-hoc tests were applied to identify specific between group differences.

**Results:** The hindfoot-shank joint demonstrated more valgus in both MOLT and LOLT groups compared to the HC group. Moreover, the MOLT group showed decreased plantarflexion in the Lisfranc joint, and the LOLT group showed higher peak pressures in the midfoot zone compared to the HC group.

**Conclusions:** The OLT population shows gait alterations that can potentially be associated with osteochondral damage in the ankle joint and which align with clinical description in current literature. The excessive ankle valgus may influence impact forces acting between the talus and tibia, leading to increased load on ankle cartilage and potentially resulting in osteochondral damage. This study demonstrates that 3D gait analysis can be a valuable tool to assess potential biomechanical mechanisms of OLT development. Further investigation of foot and ankle biomechanics deserves attention for advancing the understanding of the etiology of OLTs.

## Poster № 29

### PREOPERATIVE GAIT PATTERNS AS PREDICTORS OF GAIT CHANGES FOLLOWING SELECTIVE DORSAL RHIZOTOMY IN CHILDREN WITH SPASTIC DIPLEGIA

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**Introduction:** Selective Dorsal Rhizotomy (SDR), a neurosurgical procedure, can improve gait in children with bilateral spastic paresis, but outcomes are variable between children. Therefore, selecting individuals eligible for SDR remains challenging, while the effect of pre-SDR gait pattern on post-SDR gait has not yet been investigated.

**Purpose:** Do distinguishable pre-SDR gait patterns lead to different kinematic and kinetic responses after SDR?

**Methods:** Kinematic and kinetic data of nineteen children with 3D gait analysis before and two years after SDR, were extracted from an in-hospital database. A cluster analysis was performed to distinguish different gait patterns based on sagittal hip, knee and ankle angles pre-SDR. Deviations from typical gait per leg pre- and post-SDR were quantified by the gait profile score (GPS) calculated for joint angles, moment, and powers. GPS scores were compared pre- and post-SDR per cluster, and the pre-post difference was compared between clusters. Pre- and post-SDR curves were compared using Statistical parametric mapping to evaluate in which gait phases changes had occurred.

**Results:** Three pre-SDR gait patterns emerged, with (GP1) increased knee flexion (18 legs), (GP2) increased ankle plantarflexion (14 legs), and (GP3) increased knee flexion and increased ankle plantarflexion (6 legs). GPS-kinematics improved significantly for GP1 (-3.1°) and GP3 (-6.6°), but not for GP2 (no change). GPS-kinematics improved more in GP3 than in GP2. GPS-moments improved equally in all groups, while. GPS-powers improved more for GP1 and GP2 (0.07W/kg and 0.24W/kg respectively) than for GP3 (no change).

**Conclusions:** Our results indicate that different pre-SDR gait patterns have different outcomes post-SDR in children with spastic diplegia and, therefore, could guide the expectation management and selection process for SDR. Future studies should confirm these results in a larger cohort.

## Poster № 30

### ASSOCIATING SCALAR AND MULTIDIMENSIONAL PLANTAR PRESSURE PARAMETERS FOR ASSESSING OFFLOADING EFFECTIVENESS IN CUSTOM-MADE FOOTWEAR FOR PEOPLE WITH DIABETES

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**Introduction:** The effectiveness of custom-made footwear in providing adequate offloading for people with diabetes is assessed using plantar pressure measurements. While data from these measurements is multidimensional, it is often only analyzed using a scalar - mostly maximum peak plantar pressure (PMax). Analyzing plantar pressure as a multidimensional parameter might enhance in-shoe pressure and offloading assessment of footwear.

**Purpose:** The aim of this study was to investigate the associations between multiple peak plantar pressure parameters for footwear offloading assessment and if the assessment of offloading capabilities depends on the chosen parameter.

**Method:** In-shoe plantar pressure was measured in 77 participants with diabetes, peripheral neuropathy and a recent ulcer or amputation history, while walking in their own custom-made footwear. Six peak plantar pressure parameters, ranging from scalar to multidimensional parameters, were extracted to quantify footwear offloading effectiveness (Fig.1). Three parameters were scalars, i.e. PMax, PTI and PGrad. The other parameters included temporal (PTC), spatial (PMap) and spatiotemporal dimensions (PTM). Footwear was ranked from highest to lowest pressure according to each of the parameters and the associations between these six rankings were compared using Spearman's rank correlation coefficient.

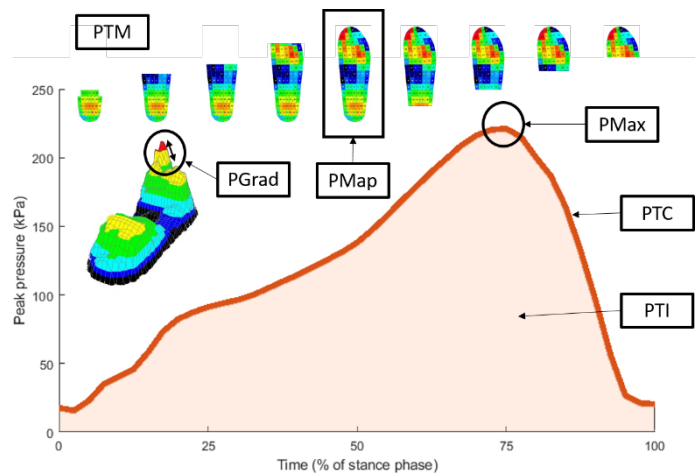


Figure 1: Visual representation of the six peak plantar pressure parameters. PMax = Maximum peak plantar pressure; PTI = Peak pressure Time Integral; PGrad: Maximum Gradient change surrounding PMax; PTC = Pressure Time Curve: maximum peak plantar pressure for each timeframe; PMap = Pressure Map: maximum peak plantar pressure for each sensor; PTM = Pressure Time Map: maximum peak plantar pressure for each sensor and each timeframe.

**Results:** The rank correlation coefficient was moderate between PMax and the scalar parameters PTI ( $\rho_{152}=0.59$ ) and PGrad ( $\rho_{152}=0.46$ ), and negligible to weak between PMax and the multidimensional parameters, i.e. PTC, PMap and PTM ( $\rho_{152}=0.03-0.25$ ).

**Conclusions:** The association between scalar and multidimensional plantar pressure parameters in footwear offloading assessment is low. This indicates that the assessment of in-shoe plantar pressure for offloading effectiveness depends on the chosen parameter. We need to unlock the potential of the multidimensionality of plantar pressure measurements for use in footwear evaluation by focusing future studies on the association with clinical outcomes.



**VARUS FOOT DEFORMITIES LEAD TO MORE INVERTED MUSCLE MOMENT ARMS IN CHILDREN WITH CEREBRAL PALSY****Gaia van den Heuvel<sup>123</sup>, Wouter Schallig<sup>12</sup>, Ruud Wellenberg<sup>4</sup>, Mario Maas<sup>4</sup>, Annemieke Buizer<sup>125</sup>, Ajay Seth<sup>3</sup>, Marjolein van der Krogt<sup>12</sup>****Affiliations:**

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**Introduction**

Cerebral palsy (CP) is one of the most frequent causes of motor disability among children. Secondary to the neurological disorder, children with CP often develop musculoskeletal problems. More than 90% develops a foot deformity, which can lead to pain and gait impairments. One of the causes of such deformities is an imbalance in muscle forces around the foot. In turn, these deformities can also alter muscle function due to altered muscle moment arms.

**Purpose**

The aim of this study was to quantify the change in moment arm lengths of the tibialis and peroneal muscles around the subtalar joint using musculoskeletal modeling in children with CP demonstrating cavovarus and equinovarus foot deformities.

**Method**

Six children with CP and a hindfoot varus deformity and four typically developed (TD) adults were included. Personalized musculoskeletal foot models were created in OpenSim Creator using weight-bearing computed tomography scans. Muscle moment arms were calculated using OpenSim and normalized to tibia length. Groups were compared using Mann-Whitney U tests.

**Results**

The tibialis anterior muscle had an inversion moment arm (median [range]: -0.032 [-0.064,-0.025]) in deformed CP feet, in contrast to an eversion moment arm in TD (0.0052 [0.00083,0.024]),  $p < 0.01$ . For the tibialis posterior, the range in moment arms was larger in CP (-0.041 [-0.051,-0.032]) versus TD (-0.041 [-0.045,-0.041]). The eversion moment arm of the peroneal muscles was smaller in most CP children (longus: 0.054 [0.033,0.067] versus 0.064 [0.062,0.069], and brevis: 0.057 [0.037,0.070] versus 0.066 [0.063,0.069]).

**Conclusions**

The shift of moment arms towards either more inversion or less eversion leads to larger varus moments in the subtalar joint with similar muscle forces, thereby pulling the foot even more towards varus, which could contribute to the progression of the foot deformity. This study highlights the importance of proper foot alignment, to prevent the progression of foot deformity in children with CP once it is present.

## INTEGRATIVE TRANSCRIPTOMIC-PROTEOMIC ANALYSIS OF PRIMARY HUMAN FETAL, ADULT DERMAL AND ESCHAR MESENCHYMAL CELLS AND THEIR SECRETED EXTRACELLULAR MATRICES

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**Introduction:** During wound healing, mesenchymal cells (MC) rebuild tissue through extracellular matrix (ECM) secretion. While early fetal skin regenerates, adult skin forms scars in full-thickness wounds.

**Purpose:** We aim to identify the underlying differences by comparing MC populations and their ECMs: fetal vs adult (regeneration vs repair), and adult dermal vs eschar (healthy vs wounded).

**Method:** MC isolated from healthy fetal skin, adult dermis, and tissue from burn wound patients (eschar) were cultured either without stimulation or under conditions promoting ECM production. We assessed differences between cell populations by: 1) analyzing the expression profile of the cells using transcriptome sequencing; and 2) analyzing the ECM produced by the cells by proteomics analysis.

**Results:** Fetal and adult samples revealed remarkable differences in their transcriptomic and proteomic profiles, including ECM related targets, showing a significant difference in ECM composition and its regulation between MC types. Protein differences between fetal vs adult noticeably fade at gestational week 22, when skin regeneration ability ceases. Only fetal samples showed simultaneous upregulation at the RNA and protein level of 9 ECM core proteins and 13 ECM-associated proteins. Adult MC, particularly eschar MCs, have a higher contractile profile and state of activation, upregulated focal adhesion, adherens junctions and LIM domain proteins compared to fetal MC. Fetal MC showed downregulated proteins associated with platelet aggregation, contrary to adult MC, where genes/proteins associated with platelet activation and aggregation were upregulated, particularly in eschar MC. Additionally, our research revealed differences in gene ontology and pathways related to the innate immune system between MC types.

**Conclusion:** Our findings emphasize differences in both cell and ECM characteristics between fetal and adult stages, showing their differential contribution to the wound microenvironment. These differences are remarkable up to the ontogenic transition from scarless healing to scarring, emphasizing their potential impact on the wound healing outcome. Our findings identify 22 ECM-related targets upregulated at both the RNA and protein levels exclusively in fetal MC. These targets may serve as potential regenerative candidates for novel skin regeneration therapies.

## Poster № 33

### STREPTOMYCIN INHIBITS MYOTUBE CELL DIFFERENTIATION BY IMPACTING MITOCHONDRIA AND PROTEIN SYNTHESIS

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**Introduction:** Streptomycin is an aminoglycoside antibiotic which forms an integral part of cell culture medium to avoid bacterial infections. Because streptomycin inhibits bacterial protein synthesis, streptomycin can also have off-target effects on cell function. These off-target effects might complicate interpretation of experiments with cultured skeletal muscle when studying muscle hypertrophy and metabolism. Here, we studied the effect of streptomycin on C2C12 myoblasts and myofiber growth and metabolism.

**Purpose:** Study the effect of streptomycin on C2C12 myoblasts and myofiber function.

**Methods:** C2C12 cells were cultured in a medium with or without streptomycin. The control condition consisted of carbenicillin and ampicillin treatment to avoid contamination of the medium with bacteria. Proliferation rate was assessed by the EdU assay, and myofiber diameter, differentiation and fusion index were measured after 6 days exposure of differentiated myotubes to streptomycin. Gene and protein expression of key markers of contractile and mitochondrial function, protein synthesis and degradation were assessed by qPCR and western blotting. The SUnSET assay was used to determine overall protein synthesis rates. Mitochondrial respiration was performed to measure mitochondrial respiration. Mitochondrial networks were visualized by MitoTracker.

**Results:** Streptomycin did not impair proliferation rate. Differentiated myotubes were thinner and had a lower differentiation and fusion index upon streptomycin exposure, due to a reduced global protein synthesis rate. Mitochondrial respiration was not affected upon streptomycin exposure, but gene and protein content of some mitochondrial complex subunits were lower. Fragmentation of the mitochondrial network was induced by streptomycin.

**Conclusions:** Streptomycin does not alter C2C12 myoblast proliferation, but reduced global synthesis rates made cells grow less rapidly. Streptomycin modestly affected mitochondrial gene expression and protein content, but caused mitochondrial fragmentation. The use of streptomycin should be carefully considered with regards to the side effects on muscle cell function. Other antibiotics such as carbenicillin and ampicillin are recommended for cell culture, provided that bacteria are responsive to these.

## Poster № 34

### **SIMVASTATIN AND METFORMIN NEGATIVELY AFFECT SKELETAL MUSCLE STRUCTURE AND FUNCTION**

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**Introduction:** Polypharmacy is common among elderly individuals but this is associated with adverse health outcomes. Statins, for the preventive treatment of hypercholesterolemia, and metformin, to treat type 2 diabetes mellitus (T2DM), are often combined. While the side effects of statin use on skeletal muscle function is anecdotally known, the effects of the combination on skeletal muscle have never been studied.

**Purpose:** This study aims to investigate the combined effects of statins and metformin in an isolated microenvironment with C2C12 skeletal muscle cells, and to elucidate the molecular mechanisms through which these effects are achieved.

**Methods:** C2C12 myoblasts were cultured and differentiated into myotubes. Cells were treated with simvastatin (10  $\mu$ M), metformin (50  $\mu$ M or 1000  $\mu$ M) or with the combination for 24-72h. Proliferation rate was assessed by the EdU assay, and myofiber diameter were measured. The gene and protein expression of key markers of atrophy, glucose metabolism, mitochondrial homeostasis, and differentiation were assessed by qPCR and western blotting. Mitochondrial respiration was performed to measure mitochondrial respiration.

**Results:** Simvastatin treatment leads to atrophy in myotubes, which is mitigated by metformin treatment. The observed mitigation of the cytotoxic effects of simvastatin by metformin in myotubes, was not seen in myoblasts. GLUT4 and HKII expression were increased with metformin and simvastatin, and GLUT4 expression doubled with metformin and simvastatin compared to simvastatin alone. Simvastatin increased gene expression of markers for atrophy (MuRF-1 and MAFbx), and reduced gene expression of the differentiation marker MyoD, which was not prevented by metformin. Increased extracellular acidification rate and decreased routine respiration with metformin and the combination of metformin and simvastatin suggests a shift from aerobic to anaerobic metabolism.

**Conclusions:** Simvastatin and metformin have different effects on skeletal muscle size and mitochondrial function. This research provides a mechanism of the microenvironmental effects of two inexpensive, preventative, commonly used medications, and could contribute to a better understanding in combining these drugs in patients.

## Poster № 35

### SKELETAL MUSCLE MITOCHONDRIAL FRAGMENTATION AND FUNCTION IN TYPE I DIABETES

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**Introduction:** Otherwise healthy individuals with type I diabetes (T1D) have been reported to display signs of skeletal muscle mitochondrial dysfunction. This finding is of high clinical relevance given that a reduction in skeletal muscle mitochondrial function would be predicted to impair the ability to mitigate dysglycaemic burdens and accelerate the progression of diabetic complications. However, studies reporting differences in mitochondrial respiration between individuals with T1D and healthy controls typically have not measured whole-body aerobic capacity, which potentially confounds these findings. **Purpose:** To compare mitochondrial respiratory function and morphology between individuals with T1D and healthy controls (CON) matched for maximal oxygen uptake ( $\dot{V}O_{2max}$ ). **Methods:** 16 individuals with T1D and 16 CON performed a maximal incremental exercise test on a cycle ergometer for determination of  $\dot{V}O_{2max}$ . A skeletal muscle biopsy was obtained from the vastus lateralis on a separate day. Mitochondrial respiration was measured via high-resolution respirometry, mitochondrial content and morphology were determined via transmission electron microscopy, and succinate dehydrogenase (SDH) activity was determined via quantitative histochemistry. **Results:** Both groups did not differ with respect to  $\dot{V}O_{2max}$  (T1D:  $41 \pm 11$  mL.kg<sup>-1</sup>.min<sup>-1</sup>, CON:  $42 \pm 8$  mL.kg<sup>-1</sup>.min<sup>-1</sup>,  $P = 0.71$ ). Skeletal muscle SDH activity did not differ between the two groups (T1D:  $1.19 \pm 0.46$   $\Delta A_{660} \cdot \mu M^{-1} \cdot s^{-1} \cdot 10^{-5}$ , CON:  $1.10 \pm 0.23$   $\Delta A_{660} \cdot \mu M^{-1} \cdot s^{-1} \cdot 10^{-5}$ ,  $P = 0.49$ ). Oxidative phosphorylation capacity did not differ between groups (T1D:  $101.3 \pm 34.9$  pmol.s<sup>-1</sup>.mg<sup>-1</sup>, CON:  $98.8 \pm 23.3$  pmol.s<sup>-1</sup>.mg<sup>-1</sup>,  $P = 0.81$ ), however, leak respiration was increased in individuals with type I diabetes (T1D:  $13.5 \pm 5.1$  pmol.s<sup>-1</sup>.mg<sup>-1</sup>, CON:  $10.4 \pm 2.5$  pmol.s<sup>-1</sup>.mg<sup>-1</sup>,  $P = 0.047$ ). Electron microscopy revealed that, despite similar overall mitochondrial content, the skeletal muscle of individuals with type I diabetes were characterized by more fragmented mitochondria, reduced cristae density, and lipid accumulation. **Conclusions:** These data demonstrate that previous reports of mitochondrial dysfunction in individuals with T1D are exaggerated when comparisons are made with controls possessing a similar aerobic training status. However, that more subtle alterations in mitochondrial function and morphology in individuals with T1D persisted when the control group was matched for  $\dot{V}O_{2max}$  suggests that maintaining a normal aerobic capacity does not completely offset the deleterious consequences of diabetes on muscle mitochondria.

## Physical inactivity does not explain exercise intolerance and skeletal muscle adaptations in long COVID

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**Introduction:** Patients with long COVID (or post-acute sequelae of COVID) present a unique set of symptoms, marked by a reduced exercise capacity and post-exertional malaise, which is the worsening of symptoms following mental or physical exertion. The combination of these symptoms renders many patients unable to perform daily physical tasks, which limits their movement and ultimately leads to a severely inactive lifestyle. Physical inactivity *per se* causes physiological alterations in skeletal muscle that can underly the reduced exercise capacity and increased feeling of fatigue. It is unknown to what extent the changes in exercise capacity are a consequence of long COVID, or due to physical inactivity. The current study aims to compare the exercise capacity and skeletal muscle alterations in patients with long COVID with those occurring after long term bed rest, which is used as a model for extreme physical inactivity.

**Methods:** Exercise capacity (by means of a cardiopulmonary exercise test) was assessed in 25 patients with long COVID, in 21 healthy participants, and in 24 participants before and after 60 days of bed rest. For each condition, vastus lateralis muscle biopsies were stained for fibre cross-sectional area, muscle fibre type distribution, oxidative enzyme activity, and capillarization.

**Results:** Peak power output was 23% lower in patients with long COVID and 26% lower after bed rest. Long COVID patients had a 20% lower  $\dot{V} O_{2peak}$  which was similar after bed rest (-23%). However, the skeletal muscle adaptations underlying the reduction in exercise tolerance were different: whereas long COVID patients showed no signs of a lower fiber cross-sectional area relative to age-matched controls, fiber cross-sectional area decreased markedly across all muscle fiber types after 60 days of bed rest. Muscle fiber type did not change after bed rest, but long COVID patients had a lower percentage of type I and a higher percentage of type IIx muscle fibers, compared to healthy controls. Succinate dehydrogenase (SDH) activity was lower after bed rest, but not different between long COVID patients and healthy controls. Similarly, capillary-to-fiber ratio did not differ between long COVID patients and controls, while 60 days of bed rest resulted in a decreased capillary-to-fiber ratio.

**Conclusions:** While both extended bed rest and long COVID result in decreased exercise tolerance, the accompanying skeletal muscle adaptations in both conditions diverge. As such, we conclude that the decreased exercise capacity observed in long COVID patients is not simply a matter of physical inactivity, and that further research is needed to resolve the underlying adaptations in patients with long COVID.

**INTEGRATED ANALYSIS OF TRANSCRIPTOME AND PROTEOME REVEALS A CORE SET OF GENES INVOLVED IN OSTEOBLAST UNDER OXIDATIVE STRESS**

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**Introduction:** Osteoporosis is a prevalent disease characterized by high incidence rate, increased fracture risk, and complex etiology. Oxidative stress (OS)-induced osteoblast injury and impaired osteogenic differentiation are considered the pathological basis of osteoporosis, although the underlying mechanisms remain to be fully elucidated.

**Purpose:** To reveal a core set of genes involved in osteoblast function under oxidative stress by transcriptome and proteome analysis.

**Method:** In this study, cell viability experiments, flow cytometry, and TUNEL assays were performed to determine the effects of H<sub>2</sub>O<sub>2</sub> on the proliferation and apoptosis of osteoblasts. We used immunofluorescence to detect the mitochondrial reactive oxygen species (ROS) level and mitochondrial membrane potential (MMP) in H<sub>2</sub>O<sub>2</sub> treated osteoblasts. Adenosine triphosphate (ATP) level was measured using the ATP assay kit. Alkaline phosphatase (ALP) Activity Assay, ALP Staining and Alizarin red staining (ARS) were also performed to examine cellular capability of differentiation and mineralization. Based on the result of oxidative stress on cellular behavior, we performed the transcriptome and proteome analyses of osteoblast in response to oxidative stress. At last, the mRNA expression levels were determined by RT-qPCR, and protein levels were assessed using Western blot.

**Results:** H<sub>2</sub>O<sub>2</sub> significantly promoted osteoblast apoptosis and inhibited cell differentiation. In addition, suppression of cell cycle and decrease of mitochondrial membrane potential were also observed. A total of 164 and 186 differentially expressed genes (DEGs) and proteins (DEPs) were identified, respectively. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) functional analysis showed that they were enriched in pathways associated with apoptosis and osteoblast differentiation. A protein-protein interactions (PPIs) network of DEPs was detected. Furthermore, seven important positive correlated DEGs and DEPs (cor-DEGs-DEPs genes) were identified based on the integrated analysis of mRNA-protein expression, and their interactions were revealed using PPIs analysis.

**Conclusions:** Our results provide seven candidate genes which are likely to play an important role in the pathogenesis of osteoporosis, and these provide novel insight in the mechanisms underlying detrimental effects of oxidative stress on bone formation.

**A Case of Melkersson-Rosenthal Syndrome with Temporomandibular Joint Osteoarthritis: Multidisciplinary Treatment and Autoimmune Etiological Hypothesis**

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**ABSTRACT:**

**Introduction:** Melkersson-Rosenthal syndrome (MRS) is a rare neuro-mucocutaneous disorder characterized by recurrent edema, facial palsies, and nerve dysfunctions often associated with the plicata tongue. Although the etiology of MRS is not well understood, there is growing evidence suggesting an autoimmune involvement.

**Purpose:** This paper presents a case report of a 25-year-old male with MRS as the initial symptom, followed by temporomandibular joint osteoarthritis (TMJ-OA).

**Methods & Results:** A comprehensive diagnosis and multidisciplinary treatment approach including surgery, local injections, and oral medication were implemented, resulting in a favorable prognosis.

**Conclusion:** These findings support the hypothesis that MRS is a systemic granulomatous disease caused by autoimmunity, which may also influence the occurrence and development of TMJ-OA through immune-related mechanisms. This study emphasizes the significance of systemic immune regulation in the treatment of patients with MRS and TMJ-OA comorbid conditions.



## Poster № 39

# Does Hypertrophying Skeletal Muscle Benefit from Cancer Cell Metabolic Reprogramming? A Pyruvate Kinase M2 Focused Perspective

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### Abstract:

#### Introduction

In the Warburg effect, a hallmark of cancer cells, intermediates of the glycolysis process are used for synthesis of nucleotides and amino-acids, favoring proliferation and growth. One of its key regulators is Pyruvate Kinase M2 (PKM2). PKM2 can be found as a tetramer in the cytoplasm, with high kinase activity, or as a dimer in the nucleus, for transcription of genes favoring glycolysis and proliferation, such as the oncogene *Myc*. In hypertrophying skeletal muscle a similar “Warburg effect” has been suggested and associated in part with PKM2. Interestingly, different myopathies also share high PKM2 expression such as myotonic dystrophy, dermatomyositis and polymyositis. However, the mechanisms of PKM2 in differentiated muscle cells are poorly understood.

#### Purpose

This study aims to investigate how PKM2 is regulated and if it affects other “Warburg effect genes” expression in skeletal muscle cell hypertrophy.

#### Methods

To explore the conditions by which PKM2 is expressed in differentiated muscle cells, C2C12 myotubes were treated with Insulin Growth Factor-1 (IGF-1; to stimulate hypertrophy), Compound 3k (C3k; PKM2 dimer stabilizer) or DASA-58 (PKM2 tetramer stabilizer) for 24h and cultured in either Low or High Glucose. In a second experiment, myotubes underwent 12h of serum free media starvation and were reintroduced to serum and serum with IGF-1 for 12h. In both experiments, it was measured myotube diameters and “Warburg effect genes” expression: *PKM2*, *PHGDH* and *Myc*.

#### Results

In the first experiment, IGF-1 had a significant main effect in myotube size and for all genes, except for *Myc*. Compound treatment showed a main effect in myotube size but not in gene expression, suggesting neither tetrameric or dimeric PKM2 are regulating other oncogenes. DASA-58 treatment trended for less *PKM2* expression compared to C3k and no compound, suggesting PKM2 might autoregulate itself. Glucose levels had no main effects. In the second experiment, the expression of all three genes were increased progressively with the added serum and serum with IGF-1, respectively.

#### Conclusion

Collectively, the results suggest the “Warburg effect-like” in hypertrophying myotubes is regulated by growth factors availability and not by glucose levels as IGF-1 induced PKM2 expression as well as other oncogenes.

## Poster № 40

### TYPE 1 DIABETES MELITUS ALTERS GLUT4 SIGNALING IN SKELETAL MUSCLE AFTER ACUTE EXERCISE

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**Introduction:** Patients with type 1 diabetes mellitus (T1DM) experience exercise-induced hypoglycemia, but differences in exercise-induced translocation of glucose transporter 4 (GLUT4) has not been studied in T1DM.

**Purpose:** The aim of this study was to assess GLUT4 translocation in skeletal muscle of patients with T1DM and healthy controls before and after a bout of aerobic exercise.

**Methods:** We studied GLUT4 by staining muscle biopsy sections of T1DM (n=9) and control (n=9) participants taken before and immediately after moderate exercise. Deconvoluted images were analyzed for spread (as a surrogate measure of GLUT4 vesicles number), colocalization and co-occurrence between GLUT4 and the cell membrane.

**Results:** Skeletal muscle from T1DM patients had a 7% higher ( $p<0.001$ ) spread of GLUT4 than controls. Higher GLUT4 spread was positively correlated with adipose tissue thickness ( $r^2=0.32$ ,  $p=0.029$ ), indicating a positive association between tissue adipose thickness and GLUT4 content. A smaller fraction of GLUT4 resided within the membrane in T1DM patients at rest and during exercise ( $p=0.014$ ) compared to healthy controls. GLUT4 translocation to the cell membrane increased after exercise ( $p=0.028$ ), but similarly in both groups. GLUT4 showed exercise-induced patch forming in both groups, as a larger fraction of GLUT4 was divided over a smaller part of the cell membrane following acute exercise ( $p<0.001$ ).

**Conclusion:** The higher intracellular GLUT4 vesicles in T1DM provides possible new insights in the cause of exercise-induced hypoglycemia, but also development of insulin resistance in T1DM. Aerobic exercise-induced patch formation in the membrane in both T1DM patients and controls, but the intracellular mechanisms are unknown.

## Poster № 41

### THE EFFECT OF THE SCAN PROTOCOL ON THE METHODOLOGICAL ERROR OF MEASURING KNEE IMPLANT DISPLACEMENT FROM 3D CT-IMAGES

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#### Introduction

3D-CT image analysis technology can be used to detect loosening of the tibial component of a total knee arthroplasty under external valgus and varus loading conditions. However, measurements of relative displacement between the implant and the bone are hampered by metal artefacts in the images.

#### Purpose

The objective is to determine if the increase in tube voltage, charge, and using metal artefact reduction (MAR) for image reconstruction, reduces the error of quantifying implant displacement.

#### Method

The methodological error and the severity of metal artefacts were determined in 40 CT images (10 repetitive scans per setting) of a cadaver leg with a total knee implant. No loading was applied so the apparent displacement, quantified as the magnitude of the translation ( $\sqrt{x^2 + y^2 + z^2}$ ), between the implant and bone can be attributed to methodological error. The tested settings were 120 kVp/160 mAs and 140 kVp/320 mAs, with and without MAR, using a Siemens Somatom Force CT scanner (isotropic voxel spacing 0.45 mm). Custom software for segmentation and registration was used for image analysis.

Intensity variation around the implant in the axial plane is a measure for metal artefacts severity. The discrete Fourier transform of the angle-dependent intensity profile drawn at a contour around the implant was used to compute a histogram of spatial frequencies. The low bins ( $<16 \text{ deg}^{-1}$ ), which characterize metal streak artefacts, were cumulated over all axial slices (Cumulative Metal Artefacts, CMA) to quantify metal artefact severity.

#### Results

The CMA reduced by increasing the kVp/mAs and using MAR. The methodological error (mean $\pm$ sd) from 120kVp/160mAs and 140 kVp/320 mAs changed from (no MAR: 0.08 $\pm$ 0.04 mm, MAR: 0.10 $\pm$ 0.05 mm) to (no MAR: 0.07 $\pm$ 0.03 mm, MAR: 0.07 $\pm$ 0.03 mm).

#### Conclusions

CT images with increased kVp/mAS and MAR reconstruction show less severe metal artefacts, yet do not reduce the methodological error of quantifying relative displacement between knee implant and bone.

## SPECIALIZED ORTHOTIC CARE TO IMPROVE FUNCTIONING IN ADULTS WITH NEUROMUSCULAR DISORDERS: RESULTS OF AN OPEN LABEL BLINDED END-POINT RANDOMIZED CONTROLLED TRIAL

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### Introduction

People with leg muscle weakness due to neuromuscular disorders (NMD) are often provided with lower limb orthoses to improve walking. A multidisciplinary guideline for provision of lower limb orthoses in NMD was published to enhance standardization of care.

### Purpose

We assessed (cost-)effectiveness of guideline-based provision of lower limb orthoses, including ankle-foot orthoses and knee-ankle-foot orthoses, in an expert setting (i.e. specialized orthotic care) compared to usual orthotic care on functioning in adults with NMD.

### Methods

We performed a randomized controlled trial with measurements at baseline, 12 and 24 weeks follow-up, and an economic evaluation alongside. Sixty-one adults with plantarflexor and/or quadriceps weakness due to NMD, who experience walking problems and are indicated for a lower limb orthosis, were randomly assigned to specialized orthotic care (n=31), or usual orthotic care (n=30) at the participants' regular centers. Primary endpoints were attainment of personal goals (24 weeks follow-up), and energy cost of walking at comfortable speed (change from baseline to 24 weeks follow-up). Secondary endpoints included comfortable walking speed, gait biomechanics, stability, physical functioning, (fear of) falling, fatigue and satisfaction.

### Results

Personal goal attainment was significantly higher for specialized orthotic care compared to usual orthotic care ( $p=0.011$ ). Although reduction in energy cost of walking did not significantly differ between groups ( $p=0.140$ ), it decreased significantly with -11.8% (-0.55 J/kg/m; 95% CI -0.99 to -0.11) following specialized care, but not following usual care. Secondly, we found significant effects on step length, walking speed, physical functioning, and orthosis satisfaction in favor of specialized orthotic care ( $p\leq 0.042$ ). Despite higher healthcare costs, societal costs were lower in the intervention group. Specialized orthotic care was cost-effective from a societal perspective and presumably also from a healthcare perspective.

### Conclusions

Specialized orthotic care was demonstrated to be beneficial in terms of attaining personal goals, and presumably cost-effective compared to usual orthotic care. This suggests that guideline-based provision of lower limb orthoses in expert settings could benefit the daily functioning of adults with NMD and it could generate cost savings from a societal perspective.

**EFFECTS OF GAIT VARIABILITY TRAINING FOLLOWING ANKLE-FOOT ORTHOSIS PROVISION IN THREE INDIVIDUALS WITH BILATERAL CALF MUSCLE WEAKNESS DUE TO NEUROMUSCULAR DISORDERS**

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**Introduction**

In many neuromuscular disorders (NMD), calf muscle strength deteriorates, which limits walking ability. To improve walking, ankle-foot orthoses (AFOs) are provided. However, effects on walking ability and perceived stability are sometimes suboptimal. This may be explained by insufficient exploration of gait patterns when adapting to the AFO, leading to suboptimal adaptation. If exploratory variability indeed facilitates learning, providing variability training might improve walking ability of AFO users.

**Purpose**

To investigate the effects of gait variability training in adults with calf muscle weakness due to NMD following AFO provision.

**Method**

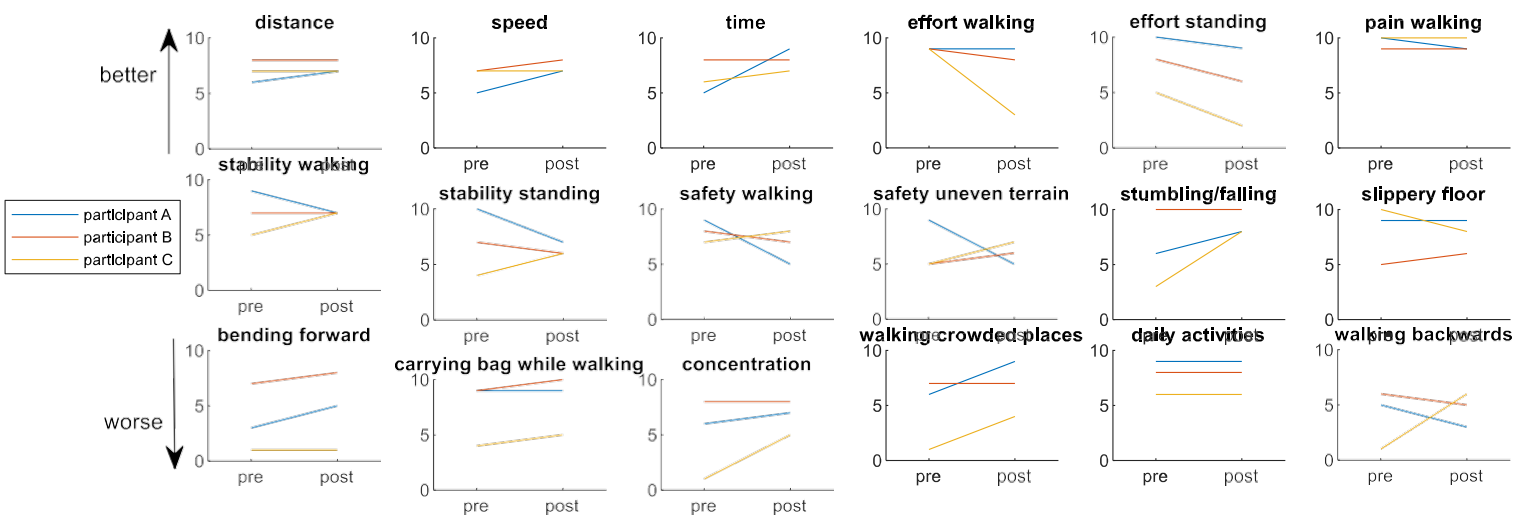
Three users of stiffness-optimized dorsal leaf AFOs (mean 72 years) received three gait variability training sessions on an interactive treadmill (C-Mill). Directly before the first training, and one week after the last training, we evaluated the functional gait assessment (FGA) (range 0-24), and perceived walking ability, fear of falling (Fall Efficacy Scale (FES)) (range 0-28), balance confidence (activities-specific balance confidence (ABC) scale (range 0-100)) through questionnaires. Further, target-stepping accuracy, and variability (SD) of step time, step length, and step width during walking on the C-Mill were evaluated.

**Results**

At individual level, participant B increased scores on FGA (+3) and FES (+4), participant C on ABC (+9.4). Participant A did not show improvements. In all participants, perceived walking ability improved on some aspects (figure). Target-stepping accuracy improved in all participants in terms of an on average smaller mean error (-29% [-23% to -35%]) and variability of the error (-24% [-17% to -31%]) in anteroposterior direction, while the mean error and variability in mediolateral direction decreased -5% [-19% to +8%] and -3% [-1% to -5%]. All participants appreciated the gait variability training. Variability of step time, step length, and step width decreased with an average of -29% [range -50% to +2%] after training.

**Conclusions**

In this pilot study, we found improvements on perceived walking ability, target-stepping accuracy and gait variability after three sessions of gait variability training in AFO users. These findings seem promising, and highlight the relevance of designing a larger study to investigate the effectiveness of gait variability training following AFO provision to improve walking ability in adults with NMD.



# An open-source, externally validated neural network algorithm to detect real-world gait episodes from inertial sensor data

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## Abstract

### Background:

Digital mobility outcomes (DMO), especially from gait monitoring, provide an opportunity to assist rehabilitation in the clinic and evaluate fall risk in the community for impaired or healthy older adults (OA). Although there are few open-source algorithms for detecting real-world gait for impaired and healthy OA, external validation is still required.

**Objective:** Our study aims to comparatively develop and externally validate an open-source algorithm (convolutional neural network (CNN)) to detect real-world gait episodes based on inertial sensor data.

**Methods:** The data for training the model consisted of data from a lower back-mounted inertial measurement unit (uSense, including 3-axis accelerometers and 3-axis gyroscopes, 100Hz) and ground truth activity labels from video footage (25fps) from the ADAPT dataset (n= 20, age 76.4±5.6, female 75%) containing walking, and other 10 activities episodes. Before training the model, the ADAPT data was split by subjects into test, training-train, and training-validation datasets, and then further separated into windows. The training and training-validation datasets were task-balanced before training the model. Then the model was validated with external IMU data of stroke patients (n=47, age 72.3±12.2, female 37%), approved by the medical ethical review committee of Utrecht (METC number: 20-462/C) consisting of labeled walking and balance episodes. To improve generalizability, we augmented the external dataset by rotating each axis 90°.

**Results:** The proposed CNN performed excellently on the testing, training-train, training-validation, and external validation datasets. In particular, the average model performance on external validation (containing rotation) reached an accuracy of 99.4%, precision of 98.9%, sensitivity of 95.9%, f1-score of 97.4%, and specificity of 99.9%. The best model performance on the external dataset resulted in an accuracy of 99.7%, precision of 99.1%, sensitivity of 98.4%, f1-score of 98.8%, and specificity of 99.9%.

**Conclusions:** Our model provides a reliable and externally validated approach to detect real-world gait episodes from healthy and impaired OA and is openly available allowing and stimulating others to update, add, or refer to models for other activities or other proposes.

**Keywords:** Walking, deep learning, IMU, field data, free-living, elderly

**GENDER DISPARITIES IN FUNCTIONAL OUTCOME AND QUALITY OF LIFE FOLLOWING SURGICAL MANAGEMENT OF DISPLACED INTRA-ARTICULAR CALCANEAL FRACTURES: A COMPREHENSIVE ANALYSIS**

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**Introduction.** Displaced intra-articular calcaneal fractures (DIACFs) represent a complex orthopedic challenge often requiring surgical intervention for optimal functional recovery. While numerous studies have investigated the outcome post-surgery, knowledge about the potential gender disparities remains limited.

**Purpose.** This study aims to elucidate potential differences between men and women in their postoperative recovery trajectories after surgical treatment of DIACFs by analyzing a prospective database.

**Methods.** In this prospective cohort study, all consecutive patients who underwent surgical treatment for DIACFs at a level 1 trauma center between January 2012 and December 2022 were included. The primary outcome measures consisted of differences between men and women in functionality and quality of life as assessed by the Foot Function Index (FFI), AOFAS Ankle-Hindfoot Scale (AOFAS), and the EuroQol 5-dimension questionnaire (EQ5D). Secondary outcomes were differences in surgical site infections (SSIs) and re-interventions such as implant removal (IR) and a secondary subtalar arthrodesis (SSA).

**Results.** In total 310 patients (227 men and 83 women) were included, of which 195 (140 men and 55 women) filled in the questionnaires. The median FU was 46 (21-74) months for men and 43 (19-77) months for women ( $p=0.641$ ). In our cohort, women were older (median 45 (35-57) yrs vs. 56 (42-66) yrs,  $p<0.001$ ), had a lower BMI (median 24.8 (22.4-27.2) vs. 22.7 (19.7-25.5),  $p<0.001$ ) and were less often smokers (44.5% vs. 19.3%,  $p<0.001$ ). The fracture characteristics, as expressed in Sanders and Essex-Lopresti classifications, Böhler's Angle and amount of open/bilateral fractures, were similar between the two groups ( $p=0.690$ ,  $p=0.807$ ,  $p=0.353$ ,  $p=0.354$  and  $p=0.847$ ). AOFAS, FFI and EQ5D-index/VAS scores were also similar between the two groups (median 82 (66-90) vs. 85 (64-90),  $p=0.817$ ; 14 (12-33) vs. 17 (6-33),  $p=0.826$ ; 0.852 (0.775-1.000) vs. 0.881 (0.807-0.887),  $p=0.720$  and 85 (70-92) vs. 81 (70-92)  $p=0.784$ ). Except for the IR rate (14.5% vs. 25%,  $p=0.033$ ), the SSI rate and amount of performed SSAs were equal between the two groups (6.7% vs. 7.5%,  $p=0.800$  and 6.6% vs. 10.8%,  $p=0.138$ ).

**Conclusions.** In conclusion, our study revealed that except for the demographic characteristics, the fracture characteristics, functional outcome and quality of life are largely similar between men and women.

**BASELINE CLINICAL AND MRI FINDINGS AS PREDICTOR OF HAMSTRING REINJURY:  
AN INTERNATIONAL MULTICENTRE, PROSPECTIVE MERGED COHORT STUDY**

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**Introduction** Studies on clinical and MRI hamstring reinjury risk factors are hampered by relatively small sample sizes. This study aimed to use a dataset with larger sample size and more predictor findings.

**Purpose** To examine the association between baseline clinical and MRI findings with the incidence of hamstring reinjuries.

**Method** We merged the data from four prospective studies (three randomized controlled trials and one ongoing prospective case series) from Qatar and the Netherlands. Inclusion criteria included patients with MRI-confirmed acute hamstring injuries ( $\leq 7$  days). We performed a modified Poisson regression analysis to assess the association of baseline clinical and MRI data and hamstring reinjury incidence within two- and 12 months of follow-up.

**Results** Three hundred thirty and 302 patients were included in the two-month (31 reinjuries) and 12-month (52 reinjuries) analyses, respectively. In the two-months analysis, the presence of discomfort during the active knee extension test was associated with reinjury risk (adjusted risk ratio (ARR) 3.38 ; 95% CI 1.19 to 9.64). In the 12 months analysis, straight leg raise test on the injured leg (ARR 0.98; 95% CI 0.96 to 1.00), presence of discomfort during active knee extension test (ARR 2.52; 95% CI 1.10 to 5.78), time to return to play (ARR 0.99; 95% CI 0.97 to 1.00), the extent of oedema anteroposterior (ARR 0.74; 95% CI 0.57 to 0.96) and hamstring injury with myotendinous junction (MTJ) involvement (ARR 3.10; 95% CI 1.39 to 6.93) were independently associated with hamstring reinjury.

**Conclusions** This study represents the world's largest analysis of reinjury risk factors including over 300 hamstring injuries. Three clinical findings (straight leg raise test on the injured leg, presence of discomfort during active knee extension test, and time to return to play) and two MRI findings (extent of oedema anteroposterior and injury with MTJ involvement) were associated with hamstring reinjury risk. These findings provide valuable information to the clinician for identifying patients at increased reinjury risk (risk profiling), and they can assist in reinjury risk management following an acute hamstring injury.



## REQUIRED CAPABILITIES FOR USING TELEMONITORING IN PHYSIOTHERAPY: A QUALITATIVE STUDY AMONG PHYSIOTHERAPY TEACHERS

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### Abstract

**Background:** The use of telehealth in healthcare develops rapidly. Telemonitoring (TM), as part of telehealth, allows physiotherapists to monitor and coach their patients using remotely collected data. The use of TM requires a different approach than face-to-face treatment, since healthcare professionals will not always see the patient in practise. The availability of the technology, financial resources, and limited experience and competencies of healthcare professionals are known as barriers for implementation of TM. In addition, although a telehealth capability framework exists for healthcare professionals, it remains unclear what specific capabilities are required to use TM during physiotherapy treatments.

**Purpose:** This study aims to identify the capabilities required to use TM in physiotherapy treatment.

**Methods:** An exploratory qualitative study was conducted using a constructivist semi-structured grounded theory approach. Three heterogeneous focus group discussions were conducted with 15 lecturers of the School of Physiotherapy (BSc.) from the Amsterdam University of Applied Sciences. Focus group discussions were audiotaped and transcribed verbatim. Capabilities for using TM in physiotherapy treatment were identified during an iterative process of data collection and analysis, based on an existing eHealth capability framework for graduates and health professionals. This framework consists of four different domains; digital health technologies; systems, and policies, clinical practice and application; data analysis and knowledge creation; and system and technology implementation. Team discussions supported further conceptualization of the findings.

**Results:** Seventeen capabilities for the use of TM in physiotherapy treatment were identified related to in the domains 'digital health technologies, systems, and policies', 'clinical practice and application' and 'data analysis and knowledge creation'. No capabilities were identified in the domain 'system and technology implementation'.

**Conclusion:** The use of TM in physiotherapy treatment requires different capabilities than those used in regular treatment. To make the best use of TM in physiotherapy treatment, it is important to integrate these capabilities into the education of current and future physiotherapists.

## Patients' and healthcare professionals' experiences with the Optimal Physical Recovery After Hospitalization (OPRAH) intervention

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### Abstract

**Background:** The Optimal Physical Recovery After Hospitalization (OPRAH) intervention was developed to improve physical recovery in patients after gastrointestinal or lung cancer surgery. The OPRAH intervention consists of a smartphone app enabling self-monitoring of physical activity and protein intake in combination with remote coaching by a healthcare professional after hospitalization. In addition to the evaluation of effectiveness, we investigated the experiences of patients and healthcare professionals with this intervention.

**Purpose:** This study aimed to evaluate the experiences of patients and healthcare professionals using the OPRAH intervention.

**Methods:** A mixed-methods approach was used, consisted of semi-structured interviews and online survey. The online survey for patients included the System Usability Scale (SUS). Topics of the interviews were: the influence of nutrition and physical activity on recovery and experiences of the Atris app, the activity tracker, and coaching on distance. For interviews with healthcare professionals additional questions about collaboration and knowledge were asked. Interviews were analysed qualitative using inductive thematic strategy.

**Results:** 55 surveys, 10 interviews with patients, 4 physiotherapists interviews, and 6 dieticians interviews. Participants rated the app highly usable (SUS 86.1) and mentioned that the OPRAH intervention was stimulating and motivating. They appreciated the opportunity to be actively involved in their recovery. The use of an activity tracker and protein diary, along with personalised goals, was perceived as a significant help in staying on the right track. Patients mentioned that they felt seen and supported. 96% of the patients would recommend this intervention to other patients, based on the survey. However, patients reported technical issues that need to be solved. In addition, some patients do not like the appearance of the activity tracker. Healthcare professionals stated that the availability of continuous data on activity and dietary intake facilitates the provision of personalised care. However, they mentioned that accurate interpretation of the collected data requires additional knowledge in order to make it valuable to the intervention.

**Conclusions:** The feasibility of the OPRAH intervention is supported by positive user experiences from patients and healthcare professionals, as well as good system usability. Improvements to the activity tracker's technical issues and design could aid in its implementation in regular healthcare.

HOW TO GENERATE MAXIMAL MUSCLE POWER?

Edwin D.H.M. Reuvers<sup>1</sup>, A.J. ‘Knoek’ van Soest<sup>1</sup> & Dinant A. Kistemaker<sup>1</sup>

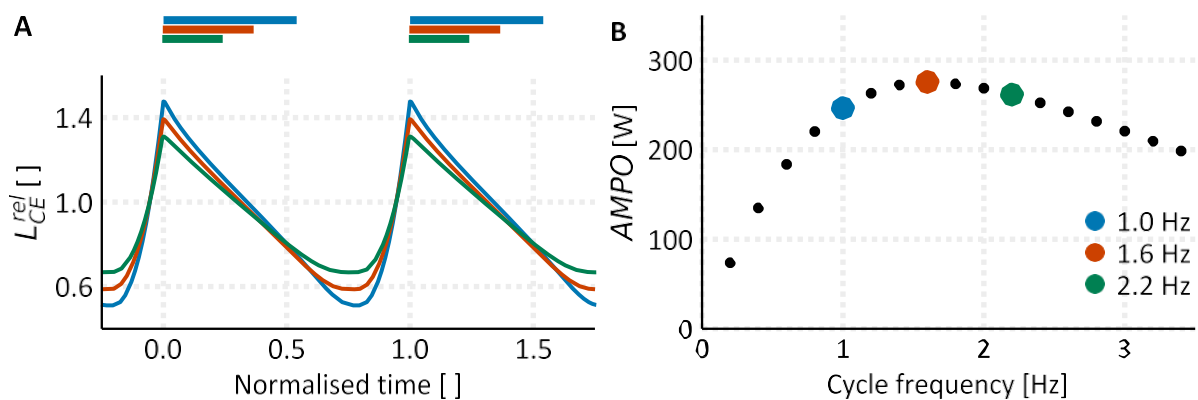
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**Introduction:** The average mechanical power output (*AMPO*) of an athlete is a performance determining factor in many sports disciplines. Remarkably, little is known about the relation between muscle contractions and resulting *AMPO*. At what frequency should muscles contract for maximal *AMPO*? With which amplitude? Do these factors interact, and if so, how? What other aspects of muscle contraction substantially affect *AMPO*? What is the maximal *AMPO* that a muscle can deliver?

**Purpose:** To understand the relationship between periodic muscle contraction, muscle stimulation and the resulting maximal *AMPO* during a short-duration all-out task.

**Method:** The behaviour of muscle fibres was modelled using a Hill-type muscle model in which muscle fibre (contractile element; *CE*) force depends on active state, *CE* length and *CE* velocity. The optimization problem was to find periodic *CE* length and muscle stimulation over time that maximised *AMPO* at imposed cycle frequencies ranging from 0.2 to 4.0 Hz.

**Results:** We predicted that the shortening time of the contractile element (*CE*) should exceed the lengthening time for maximal *AMPO*, with an optimal ratio of ~3:1 (Fig. 1A). This ratio is almost independent of cycle frequency. As expected, for maximal *AMPO*, the average *CE* length should be close to the *CE* optimum length for all cycle frequencies (Fig. 1A). The *CE* length-amplitude is ~40% of *CE* optimum length at *AMPO*-optimal cycle frequency (1.6 Hz) and decreases with cycle frequency. We predicted maximal *AMPO* for m. gluteus maximus and mm. vastii, to be ~275 W and ~250 W. As a reference, during sprint cycling, *AMPO* of both muscles is ‘only’ 100 W and 150 W. The difference is mainly due to a shortening:lengthening ratio of ~1:1 for both muscles in sprint cycling, while the *CE* length-amplitude of m. gluteus maximus is also small (~15%). Interestingly, maximal *AMPO* of the m. gluteus maximus and mm. vastii combined equals *AMPO* of all(!) leg muscles combined during sprint cycling. This suggests that the cycling motion does not allow muscles to maximise *AMPO*; far from it.

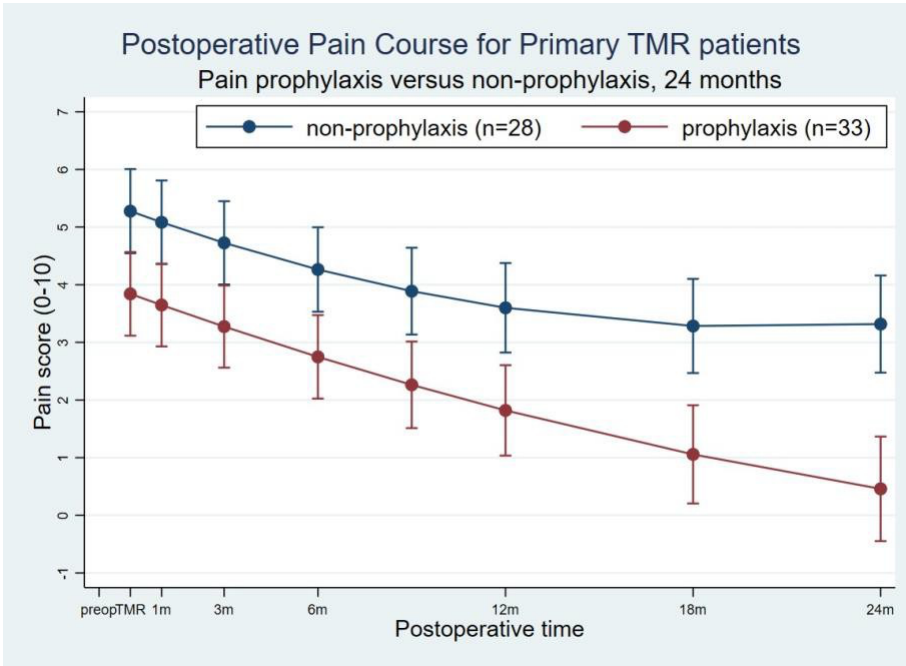


**Figure 1:** A) *AMPO*-optimal *CE* length normalised to *CE* optimum length ( $L_{CE}^{rel}$ ) as a function of normalised time (i.e. time divided by the cycle time). *CE* stimulation was maximal during the period indicated by the coloured bars and zero elsewhere. B) Average mechanical power output (*AMPO*) of m. gluteus maximus as a function of cycle frequency. The colours of the dots in B correspond to those of the *CE* length trajectories in A.

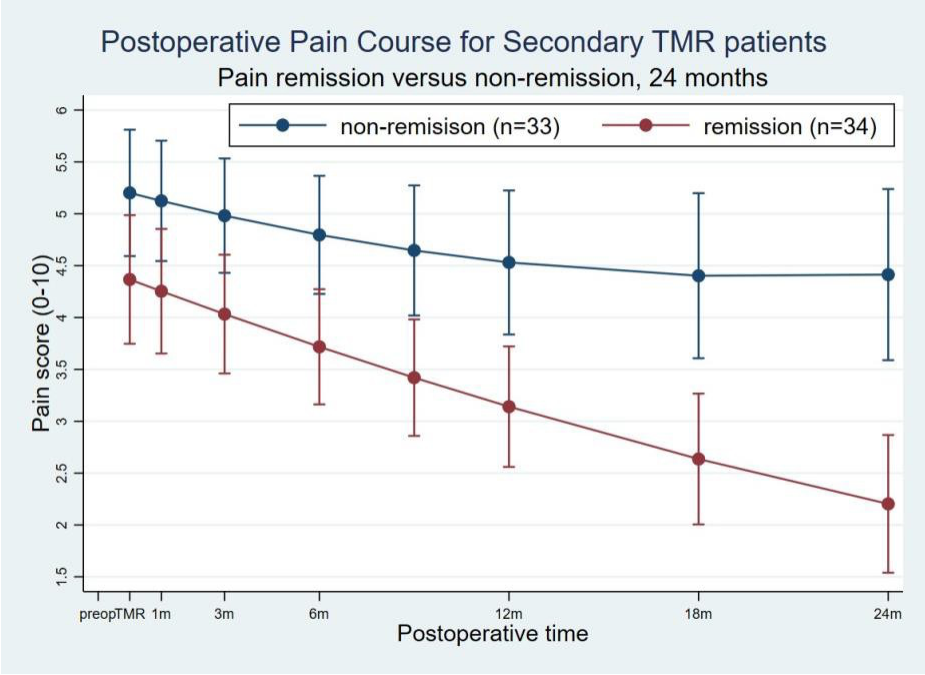
**Conclusion:** We gained fundamental insight in the relationship between periodic muscle contraction, muscle stimulation and the resulting maximal *AMPO*. These results suggest that muscles do not contract optimally in many movement tasks. Thus, we predict that sports/rehabilitation performance can be greatly improved by tuning equipment such that muscles can contract closer to their optimum.

## Poster № 50

<b>Submission:</b>	AAPS - Presentation or poster
<b>Category:</b>	Peripheral nerve
<b>Subcategory:</b>	Amputation of the extremities
<b>Keywords:</b>	Targeted muscle reinnervation, pain outcomes, associated factors
<b>Title:</b>	Factors Associated with Successful Pain Mitigation Following Primary and Secondary Targeted Muscle Reinnervation in Amputees
<b>Authors:</b>	Maximilian Mayrhofer-Schmid Floris V. Raasveld, MD Barbara Gomez-Eslava, MD Yannick Albert J. Hoftiezer, MD Kyle R. Eberlin, MD Ian L. Valerio, MD, MS, MBA
<b>Words:</b>	<i>250/250 words including 2 figures</i>
<b>Introduction:</b>	Targeted Muscle Reinnervation (TMR) is an effective modality in the surgical management of neuropathic pain for in amputees. TMR can be performed primarily (within 14 days of amputation) for prevention, or secondarily (>14 days post-op) for treatment of neuropathic pain. However, the specific patient cohort for whom this technique is most effective is not known.
<b>Methods:</b>	Prospectively enrolled amputees who underwent TMR between 2018 through 2023, (minimum follow-up: 6 months). Demographic, surgery-related and pain data (NRS, 0-10) were analyzed. Sustainable pain remission and pain prophylaxis was defined as NRS of $\leq 3/10$ for $\geq 3$ months until last follow-up. Multi-level mixed-effects models were utilized to analyze and visualize postoperative pain courses.
<b>Results:</b>	One hundred twenty-eight amputees were included (1.9 years follow-up (IQR: 1.0-2.8)), of which 61 patients (47.7%) underwent Primary TMR Following primary TMR, 54.1% of patients achieved sustainable pain prophylaxis and demonstrated significantly lower pain scores ( $p < 0.001$ ), compared to other patients (Fig. 1). Following Secondary TMR, 50.1% of patients achieved sustainable pain remission and demonstrated significantly lower pain levels at 12-24 months postoperative ( $p < 0.05$ ) compared to other patients (Fig. 2). In primary TMR patients, pain prophylaxis was associated with an absent history of depression, absent post-traumatic stress disorder, and absent smoking ( $p < 0.05$ ). In secondary TMR patients, higher BMI, absence of psychiatric diseases and peripheral vascular disease were associated with pain remission ( $p < 0.5$ ).
<b>Conclusions:</b>	Following TMR, pain improvement was observed for both primary and secondary TMR patients. Psychiatric comorbidities appear to be a risk factor for worse outcomes in both groups.



**Figure 1:** Primary TMR patients who achieve successful pain prophylaxis (red), versus patients who do not achieve this (blue). Adjusted linear prediction of the average post-operative pain with 95% confidence intervals. Abbreviation: TMR = Targeted Muscle Reinnervation

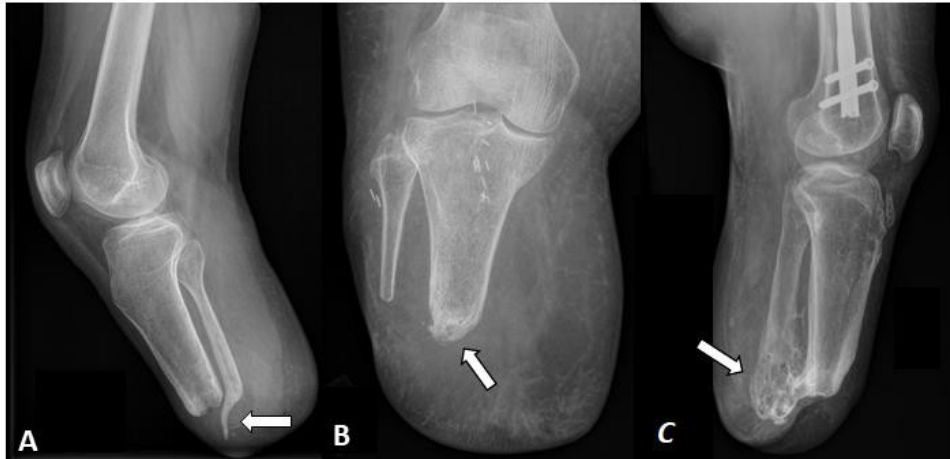


**Figure 2:** Secondary TMR patients who achieve successful pain remission (red), versus patients who do not achieve this (blue). Adjusted linear prediction of the average post-operative pain with 95% confidence intervals. Abbreviation: TMR = Targeted Muscle Reinnervation

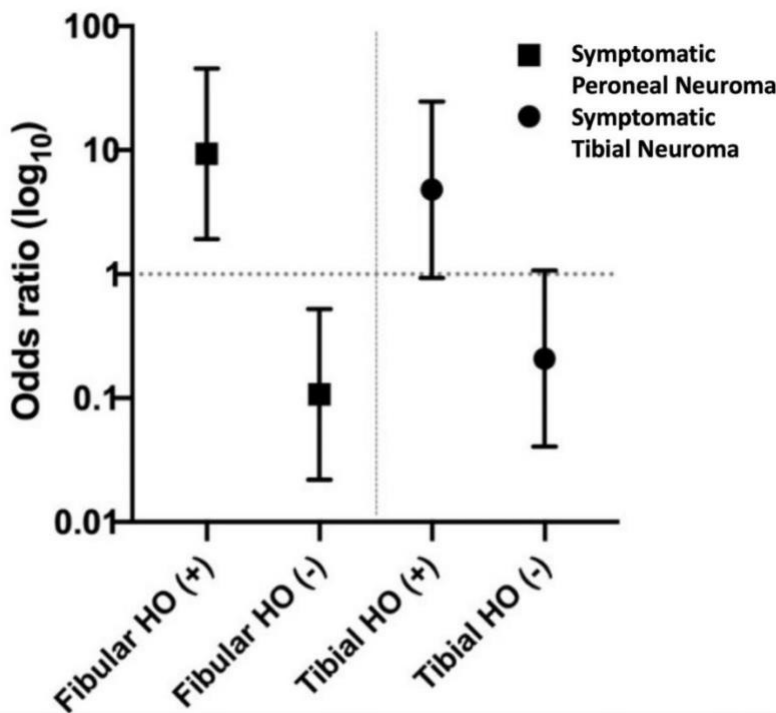
## Poster № 51

- Submission:** PSRC - Presentation or poster
- Category:** Peripheral nerve
- Keywords:** Neuroma, Pain outcomes, heterotopic ossification, transtibial amputees
- Title:** Heterotopic Ossification Is Associated with Painful Neuromas in Transtibial Amputees Undergoing Surgical Treatment of Symptomatic Neuromas
- Authors:** Floris V. Raasveld, MD  
Wen-Chih Liu, MD  
William Renthal, MD, PhD  
Mark Fleming, DO, FAAOS  
Ian L. Valerio, MD, MS, MBA, FACS  
Kyle R. Eberlin, MD
- Words:** *300/400 words including 3 figures*
- Introduction:** The relationship between nerve regeneration and osseous growth has been described. During surgical treatment of neuroma in below-knee amputees, we have noticed that heterotopic ossification (HO) depicted on preoperative X-ray appears to be predictive of the location of symptomatic neuromas in both the peroneal (fibula) and tibial (tibia) nerve distributions.
- Methods:** Data were collected for transtibial amputees who underwent surgical management of symptomatic neuroma and who were registered in a prospective data repository from 2017 through 2023. Preoperative X-rays were assessed for the presence of HO located at the distal fibula and tibia (Fig. 1). Presence of a peroneal and/or tibial neuroma was based on findings contained within the operative reports. Pain levels were measured on a numeric rating scale from 0 to 10.
- Results:** Sixty-five limbs of 62 amputees were included in this study. Peroneal neuroma and presence of fibular HO ( $P=0.001$ ), and tibial neuroma and presence of tibial HO ( $P=0.038$ ) demonstrated an association. The odds of having a symptomatic peroneal neuroma with fibular HO present are greater than the odds of a symptomatic peroneal neuroma when fibular HO is absent (OR 9.3; 95% CI [1.9-45.6],  $P=0.006$ ). No significantly higher odds were demonstrated for tibial neuroma and tibial HO (OR, 4.8; 95% CI [0.9-24.7],  $P=0.061$ ) (Fig. 2). Pre-operative pain scores were significantly higher for all patients with HO ( $P<0.001$ ), those with fibular HO ( $P<0.001$ ) and those with tibial HO ( $P<0.001$ ), compared to patients without distal stump HO (Fig. 3).
- Conclusion:** Distal HO in transtibial amputees is associated with increased pre-operative pain as well as the presence of a symptomatic neuroma,

specifically a peroneal neuroma with fibular distal stump HO and a tibial neuroma with tibial distal stump HO. These findings may assist in decision-making about which nerves to address in neuroma surgery, and provide information about the biology of neuroma formation and development.



**Figure 1.** Distal heterotopic ossification of the residuals bones in transtibial amputees. Different types HO with different severity are shown, based on the Walter Reed classification, which categorizes based on the proportion of the soft tissue envelope involved.  
 A) Distal fibular HO, Walter Reed grade 1 (arrow)  
 B) Distal tibial HO, Walter Reed grade 1 (arrow)  
 C) Distal tibiofibular synostosis HO, Walter Reed grade 2 (arrow).  
 Abbreviation: HO = Heterotopic ossification



**Figure 2:** The odds of neuroma presence for the presence of HO. If distal fibular HO is present, the odds of having a peroneal neuroma are 9.3 times higher, compared to distal fibular HO absence. If distal tibial HO is present, the odds of having a tibial are not significantly higher. Abbreviations: HO = Heterotopic ossification



Poster № 51

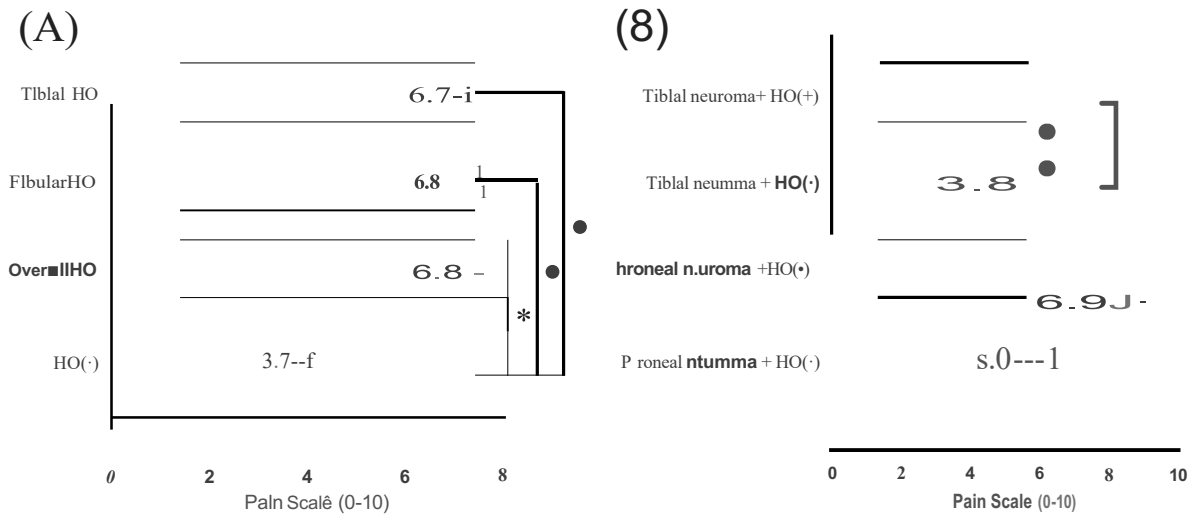


Figure 3: Pre-operative pain for HO presence and HO absence

A} for absence of HO versus HO presence overall, distal fibular HO presence and distal tibial HO presence.

B} Pain for the presence of a peroneal neuroma with the presence of distal fibular HO versus absence of distal fibular HO, and pain for the presence of a tibial neuroma with the presence of tibial HO versus absence of tibial HO.

Abbreviations: HO= Heterotopic ossification

**PHYSICAL CONTACT MODULATION OF MACROPHAGE-MEDIATED ANTI-INFLAMMATORY RESPONSE IN OSTEOIMMUNE MICROENVIRONMENT BY POLLEN-LIKE NANOPARTICLES**

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## Poster № 54

### Introduction

Nanomaterial-based bone regeneration is greatly influenced by the immune microenvironment. Tissue-engineered nanomaterials mediate the inflammatory response of macrophages to regulate bone regeneration. Silica nanoparticles have been widely used in tissue engineering-related preclinical studies. However, the effect of topological features on the surface of silica nanoparticles on the immune response of macrophages remains unknown.

### Purpose

To investigate the influence of silica nano-surface topography on macrophage immune responses and revealed the potential regulatory mechanisms.

### Method

Macrophages (RAW 264.7 cells) were exposed to silica nanoparticles with normal morphology (MSNs) and pollen-like morphology (PMSNs). RNA-seq, RT-qPCR, and LSCM were used to test the immune response-related genes and proteins. SEM and TEM were executed to evaluate the contact and phagocytosis situation of macrophages with silica nanoparticles treated.

For the immunomodulation-mediated osteogenic potential study, BMSCs were cultured with conditioned medium (CM) from LPS pre-stimulated macrophage culture treated with MSNs or PMSNs. Osteoimmunomodulatory potential of MSNs and PMSNs in vivo was tested in an osteolysis model in a mouse cranial bone.

### Results

PMSNs inhibited the expression of pro-inflammatory genes and proteins in macrophages via RNA-seq, RT-qPCR, and LSCM assays. SEM images showed distinct cell membrane-material surface binding behaviors on macrophages between MSNs and PMSNs. MSNs were more evenly dispersed across the macrophage cell membrane, while PMSNs were aggregated. PMSNs-induced macrophage anti-inflammatory response was associated with up-regulation of the cell surface receptor CD28 and inhibition of ERK phosphorylation. TEM images showed that both MSNs and PMSNs could be phagocytosed by macrophages, and inhibiting nanoparticle phagocytosis exerted no effect on the expression of anti-inflammatory genes and proteins. Interestingly, PMSNs-induced conditioned medium from macrophages enhanced BMP-2 expression and osteogenic differentiation of mBMSCs. Similarly, PMSNs could prevent LPS-induced bone resorption via downregulation of inflammatory reaction.

### Conclusions

PMSNs can promote bone regeneration by modulating osteoimmunology through surface topography. The study offers insights into how surface physical contact cues can tune the regulation of osteoimmunology and provides a basis for tissue engineering particles with immunomodulation.

**Keywords:** Physical contact, Osteoimmunology, Macrophages, Silica nanoparticles, Surface morphology, Membrane receptor, Osteogenesis, Inflammation.

# Understanding the Dynamics of the Proliferative Phase in Local Burn Wound Healing: A Computational Model

## **Abstract**

Understanding the dynamic processes that underlie burn wound healing is a complex endeavor that requires advanced computational approaches. The proliferative phase in burn wounds is critical for the closure of the burn wound. We present a novel model that uses a set of coupled ordinary differential Equations that predict intricate interactions between different cell types, cytokines, growth factors, and proteins during the proliferative phase of wound healing after burn injury. We simulated the model for 30 weeks and were able to predict cell and molecular dynamics in this intricate phase of burn wound healing. We achieved biologically sensible results and were able to identify fibroblasts, myofibroblasts, and collagen types III and I as crucial parameters that drive the proliferative phase in burn wounds.

**Keywords:** Burn , Burn injury, Computational Modeling, Mechanistic Approach

**PHYSICAL CONTACT MODULATION OF MACROPHAGE-MEDIATED ANTI-INFLAMMATORY RESPONSE IN OSTEOIMMUNE MICROENVIRONMENT BY POLLEN-LIKE NANOPARTICLES**

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### Introduction

Nanomaterial-based bone regeneration is greatly influenced by the immune microenvironment. Tissue-engineered nanomaterials mediate the inflammatory response of macrophages to regulate bone regeneration. Silica nanoparticles have been widely used in tissue engineering-related preclinical studies. However, the effect of topological features on the surface of silica nanoparticles on the immune response of macrophages remains unknown.

### Purposes

To compare the influences of normal and pollen-like silica nano-surface topography on macrophage immune responses, and to obtain insight in their potential regulatory mechanisms.

### Method

Macrophages (RAW 264.7 cells) were exposed to mesoporous silica nanoparticles with normal morphology (MSNs) and pollen-like morphology (PMSNs). RNA-seq, RT-qPCR, and LSCM were used to assess the changes in expression levels of immune response-related genes and proteins. SEM and TEM were executed to evaluate the contact and adherence of silica nanoparticles by macrophages. For the assessment of the immunomodulation-mediated osteogenic potential, BMSCs were cultured with conditioned medium (CM) from LPS pre-stimulated macrophage cultures treated with MSNs or PMSNs. Osteoimmunomodulatory potential of MSNs and PMSNs *in vivo* was tested in a mouse cranial bone osteolysis model.

### Results

The results of the RNA-seq, RT-qPCR, and LSCM assays showed that PMSNs inhibited the expression of pro-inflammatory genes and proteins in macrophages. SEM images showed distinct macrophage membrane surface binding patterns of MSNs and PMSNs. MSNs were more evenly dispersed across the macrophage cell membrane, while PMSNs were aggregated. PMSNs-induced macrophage anti-inflammatory response was associated with upregulation of the cell surface receptor CD28 and inhibition of ERK phosphorylation. TEM images showed that both MSNs and PMSNs could be phagocytosed by macrophages, and inhibiting nanoparticle phagocytosis did not affect expression of anti-inflammatory genes and proteins. Moreover, PMSNs-induced conditioned medium from macrophages enhanced BMP-2 expression and osteogenic differentiation mBMSCs. Similarly, PMSNs prevented LPS-induced bone resorption via downregulation of inflammatory reaction.

### Conclusions

PMSNs can promote bone regeneration by modulating osteoimmunological processes through surface topography. The study offers insights into how surface physical contact cues can modulate the regulation of osteoimmunology and provides a basis for the application of nanoparticles with pollen-like morphology to affect immunomodulation in bone tissue engineering and regeneration.

**Keywords:** Physical contact, Osteoimmunology, Macrophages, Silica nanoparticles, Surface morphology, Membrane receptor, Osteogenesis, Inflammation.

ASSESSING THE IMPACT OF ANKLE FOOT ORTHOSIS STIFFNESS ON TRIPPING RESPONSE: A PREDICTIVE SIMULATION STUDY

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**Introduction:** In individuals with neuromuscular diseases, calf muscle weakness leads to an elevated risk of tripping and consequent falling. Ankle foot orthoses (AFOs) can be prescribed to reduce fall risk. Although AFOs reduce the number of trips, concerns have arisen regarding the influence of AFOs on balance recovery after tripping, in other words the tripping response.

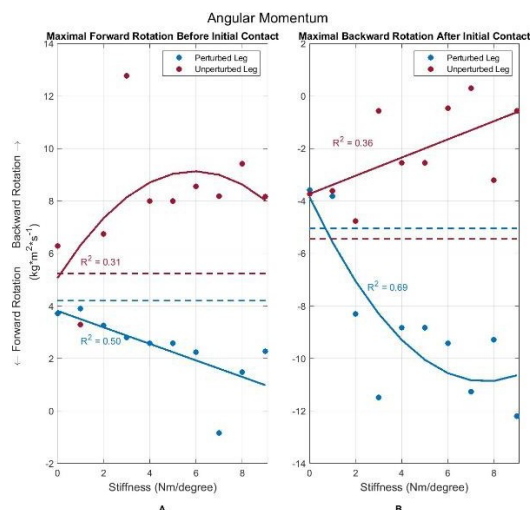
**Purpose:** How does AFO stiffness affect tripping response in individuals with calf muscle weakness?

**Method:** A two-dimensional simulation assessed tripping responses across eleven conditions: a healthy baseline, a condition with 80% reduced calf muscle strength, and nine with varying AFO stiffness (1-9 Nm/degree). The AFO was modelled as a massless rotational spring. Tripping response was quantified by step length of both the first (perturbed) step and second step, margin of stability (MoS) at initial contact of the first (perturbed) step and angular momentum between perturbation and first initial contact (IC) of both legs. Regression analysis was applied to assess the relationship between AFO stiffness and step length, margin of stability (MoS) and angular momentum during the tripping response.

**Results:** Increased AFO stiffness strongly correlated with decreased first step length after perturbation, observed with a quadratic relationship in both the perturbed leg ( $R^2 = 0.81$ ) and the unperturbed leg ( $R^2 = 0.63$ ). Additionally, a strong quadratic correlation between AFO stiffness and MoS was found ( $R^2 = 0.84$ ), where with higher AFO stiffness, the MoS shifted further forward towards the toes (e.g., positioned outside the base of support). Regarding angular momentum, higher stiffness levels were moderately associated with increased forward angular momentum before Initial Contact of the perturbed leg (IC), following a linear trend ( $R^2 = 0.50$ ) and a strong quadratic relationship between increased backward angular momentum after IC of the perturbed leg ( $R^2 = 0.69$ ). The unperturbed leg showed a fair positive quadratic relationship between stiffness and backward momentum before IC ( $R^2 = 0.31$ ) and a moderate linear fit after IC ( $R^2 = 0.36$ ).

**Conclusions:** The findings indicate that AFOs, particularly those with higher stiffness levels, substantially hinder the balance recovery after tripping. Future research should focus on optimizing AFO design and stiffness to support better balance recovery mechanisms in the context of tripping events.

Video simulation results: <https://youtu.be/4i0VxnUuP9A>



**A NOVEL TGF- $\beta$ 3-DERIVED PEPTIDE PROMOTES CHONDROGENESIS *IN VITRO* AND *IN VIVO***

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**Introduction:**

The repair of critical size cartilage defects remains highly challenging in the fields of orthopedics and oral and maxillofacial surgery. One viable approach is to apply chondro-inductive growth factors, such as bone morphogenetic protein-2 (BMP-2) and transforming growth factor- $\beta$ 3 (TGF- $\beta$ 3), but their use is associated with low production yield, high cost, and potential immunogenicity. To provide an alternative, in comparison with recombinant proteinaceous growth factors, peptides can be chemically synthesized, thus can be produced in a higher yield, lower cost, and show lower immunogenic risk.

**Purpose:**

We aimed to develop a novel chondro-inductive peptide and functionalized hydrogel, and hypothesized that as a chondro-inductive peptide derived from TGF- $\beta$ 3, this peptide would induce chondrogenic differentiation of mouse bone marrow stem cells (BMSCs) more effectively than TGF- $\beta$ 3.

**Method:**

We analyzed the crystallographic data of the critical binding domain of TGF- $\beta$ 3 with its type II receptor and designed 10 TGF- $\beta$ 3-derived peptides (TPs). We tested the ability to form cartilage of all 10 TPs adsorbed onto collagen sponges transplanted intramuscular in rats. Based on the results, we analyzed the efficacy of TP number 8 (TP8) in inducing *in-vitro* chondrogenesis of mouse BMSCs in a micromass. We also explored the molecular mechanisms for the chondro-inductivity of TP8 using western blot. All data are presented as mean  $\pm$  SD. Comparisons between groups were made by one-way ANOVA (Post hoc; Bonferroni).

**Results:**

We found that TP8, adsorbed onto absorbable collagen sponge, potently induced *de novo* cartilage formation. TP4 stimulated bone formation, while the other TPs were ineffective. TP8 (500 ng/ml) induced a significantly higher area of glycosaminoglycans (GAGs) in the micromass than every other TP, comparable to BMP-2 (500 ng/ml) and TGF- $\beta$ 3 (10 ng/ml). Interestingly, in comparison with TGF- $\beta$ 3, TP8 induced a much higher expression of *Sox9* gene (chondrogenic gene) while a much lower level of *Col10* gene (endochondral ossification-related gene). Furthermore, TP8 significantly upregulated the amount of phosphorylated Smad1/5 over total Smad 1/5 in mouse BMSCs by 1.5-fold.

**Conclusions:**

We developed a novel, bioactive, TGF- $\beta$ 3-derived chondro-inductive peptide, TP8, which induces chondrogenic differentiation of BMSCs *in vitro* superior to that induced by TGF- $\beta$ 3.



## Poster № 59

### SHORT-TERM EFFECT OF PULSATING FLUID SHEAR STRESS ON THE ACTIVATION OF MACROPHAGES IN VITRO

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**Introduction** The muscle stem cell niche plays a pivotal role in the regeneration and repair of the skeletal muscle after traumatic injuries or diseases that cause damage to the muscle fiber. As the most dynamic system in the human body, the contraction and elongation of muscles give rise to multiple mechanical loadings including shear stress that influence satellite cells as well as neighboring cells within the niche. Among which, macrophages draw much attention for governing the early inflammatory response after muscle damage and also participating in the remission of inflammation and long-term repair and remodeling of the tissue. However, the exact mechanism underlying the interaction between mechanical loadings and macrophages still needs to be elucidated. **Purpose** To assess the activation and function states of macrophages after pulsating shear stress. **Methods** Pulsating fluid shear stress (PFSS, Peak stress: 6.5 Pa/s, 1Hz, 1h), RT-qPCR, Western blot, nano-indentation, multiplex assay, Griess and phagocytosis assay were used in the research. **Results** Expression of NO, IL1 $\beta$ , IL6, and TNFa was elevated in the PFSS group; whereas IL10, TGF $\beta$ , Arg1, iNOS, MMPs, Caspase1, and NLRP3 showed no difference to the control group. The phagocytosis rate increased whereas the young's modulus decreased in the PFSS group. **Conclusions** PFSS polarized macrophages to a pro-inflammatory state with less stiffness and higher phagocytosis function. The research can provide a better understanding of the interaction between mechanical loadings and macrophage activation within the muscle stem cell niche, thus giving us insights into promoting the regeneration process after damage by focusing on the muscle stem cell niche.

## FES-ASSISTED GAIT TRAINING INTERVENTION TO IMPROVE GAIT IN INDIVIDUALS WITH AN INCOMPLETE SPINAL CORD INJURY – PRELIMINARY RESULTS

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**Introduction:** A spinal cord injury (SCI) disrupts nervous system communication, leading to limitations in sensorimotor activities like walking. These limitations are associated with muscle weakness, reflex activity disturbance, and the inability or difficulty to recruit muscles below the lesion. Functional electrical stimulation (FES) can result in recovery of voluntary muscle control and muscle strength. Studies that investigated the effects of treadmill-based locomotor training with FES show improved function of the lower limbs, suggesting that FES-assisted gait training may be a promising method for improving gait function in incomplete SCI individuals.

**Purpose:** This study aims to evaluate the feasibility and safety of FES-assisted gait training in incomplete SCI individuals. Additionally, this study investigates potential improvements in gait function and if these improvements persist over time.

**Method:** Four individuals with chronic incomplete SCI ( $\geq 12$  months post-injury, ASIA C or D) participated in a 10-week FES-assisted gait training intervention, walking twice weekly for 30 minutes. The quadriceps, gluteal, hamstring, tibialis anterior and gastrocnemius muscles were stimulated in a gait-like sequence.

Outcomes were assessed pre- and post-intervention, and at 10-week follow-up, with a 10-meter walk test. During the 10-meter walk test, spatiotemporal parameters (i.e., walking speed, step length, step width) were measured. Feasibility and safety were evaluated via self-administered questionnaires, missed training sessions, and number of (serious) adverse events.

**Results:** All participants completed the intervention, with only an average of 1.5 missed session due to other commitments or illnesses. Participants experienced temporary skin redness, which disappeared within half an hour after the training session. No other (serious) adverse events were reported.

While overall improvements in walking speed, step length and width were not statistically significant across pre-, post- and follow-up measurements, three participants demonstrated increased walking speeds post-intervention. Follow-up measurement revealed that, although two participants had slightly reduced speeds compared to post-intervention, they still maintained faster walking speeds than baseline.

**Conclusions:** The FES-assisted gait training intervention demonstrated feasibility and safety. While significant improvements in walking speed, step length, and width were not observed, the findings emphasize considerable individual variability in response to the intervention. Further randomized controlled trials with larger cohorts are needed.



## AMS abstract version 1.0 TEAMS

### BLENDED COUNSELING AND PROTEIN SUPPLEMENTATION INCREASE PROTEIN INTAKE IN COMMUNITY DWELLING OLDER ADULTS DURING A RESISTANCE EXERCISE PROGRAM: PRELIMINARY RESULTS OF THE TEAMS RCT

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**Introduction:** In order to optimize training effects for prevention of sarcopenia and frailty in community dwelling older adults a higher daily protein intake is required. To increase total daily protein intake to optimal levels (minimal 1.2 g/kgBW/d, optimal 1.5 g/kgBW/d) during a resistance exercise training of 12 weeks we use blended dietary counseling and protein supplementation with protein enriched food products.

**Purpose:** This study focusses on 1) first effects on protein intake; 2) the adherence to this protein intervention.

**Method:** Preliminary data of the TEAMS RCT is available for 148 community dwelling older adults with physical limitations or receiving home-care (age  $\geq 65$ y): 80 in exercise only (EX) and 68 in exercise+protein (EXpro) group. Dietary intake was measured by a 3d dietary record at baseline and after 12 weeks of intervention. A two-way mixed ANOVA with time, group, and group\*time interaction was performed. Adherence data was logged by a dietician coach.

**Results:** The mean age of the subjects was  $73.8 \pm 5$ y, of which 74% were females. SPPB score was  $10.0 \pm 1.7$ , 1-RM leg press  $101 \pm 24$  kg, BMI  $26.7 \pm 6.1$  and protein intake  $1.07 \pm 0.3$  g/kgBW/d. ANOVA revealed significant effect of time ( $P < 0.001$ ), and group\*time ( $p < 0.001$ ) (See Table 1). Adherence to the blended coaching sessions was high (91%), with the face-to-face sessions (85%) and tele-coaching (94%). In the EXpro group 68% of the subjects increased protein intake above the minimum intake level of 1.2 g/kgBW/d and 42% above optimal level of 1.5 g/kgBW/d, compared to 29% and 12% in the EX group.

**Table 1. Protein intake (g/kgBW/d)**

Group	Baseline (Mean $\pm$ SEM)	12 weeks (Mean $\pm$ SEM)
EX	$1.05 \pm 0.04$	$1.04 \pm 0.05$
EXpro	$1.06 \pm 0.04$	$1.45 \pm 0.05^\dagger$

$^\dagger$  ANOVA revealed group\*time effect ( $p < 0.001$ )

**Conclusion:** This study shows that blended dietary counseling with use of protein supplementation improves protein intake sufficiently in exercising community dwelling older adults. Blended counseling and the use of protein enriched food products is a promising strategy for dieticians in the prevention of sarcopenia and frailty.

**Disclosure of Interest:** M. Benali on behalf of TEAMS project: The study is funded by NWO grant. Fonterra and Carezzo take part in research consortium as a sponsor. These sponsors have no scientific influence on the presented data in this study

**Keywords:** aging, frailty, nutrition, sarcopenia, telehealth

## AMS abstract version 1.0 ProMIO2.0

### THE EFFECTS OF A MULTICOMPONENT EXERCISE AND NUTRITION PROGRAM ON PHYSICAL FUNCTIONING AND SARCOPENIA RELATED OUTCOME IN SURINAMESE OLDER MIGRANTS (55+YEARS): RESULTS OF THE PROMIO2.0 RCT

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**Introduction:** The number of older adults from non-Western ethnic minority populations is rising in society. In comparison to the Dutch majority population, these ethnic minority populations have higher prevalence on chronic diseases, including higher prevalence on sarcopenia. The ProMIO2.0 lifestyle intervention was developed to counteract and prevent sarcopenia among older adults from ethnic minorities. However, it is still unknown whether this new lifestyle intervention is effective on sarcopenia related outcomes.

**Purpose:** We aim to determine the effect of a culturally sensitive multicomponent exercise (MCE) and nutrition program on physical performance, sarcopenia related outcome, and protein intake in Surinamese older adults.

**Method:** This randomized controlled trial consisted of an intervention (INT) and control (CON) group. INT received a MCE and nutrition program divided into an intensive support phase (months 1-3) and a moderate support phase (months 3-6). CON received no intervention. The primary outcome physical functioning (PF) was assessed by 6-minute walking test (6 MWT), Secondary outcomes were Appendicular Skeletal Muscle Mass (ASM), the cross-sectional area (CSA) of the Vastus Lateralus (VL), Rectus Femoris (RF) and the corrected CSA of the VL\*RF (2DUS imaging), knee-extension strength [(KES) MicroFET], and protein intake (48-hour recall). Linear Mixed Model analysis was used for analysis at 3 and 6 months.

**Results:** The population included 65 older adults (mean age  $65 \pm 7$  (SD) years), 91% female. Improvements in the INT group compared to CON were found for Physical functioning (6 MWT; +23.48 m,  $P=0.014$ ) muscle CSA (RF; +0.70 cm<sup>2</sup>,  $P=0.035$ . VL\*RF; +0.12 cm<sup>2</sup>,  $P=0.01$ ), and protein intake (+0.20 g/kg BW/d,  $P=0.014$ ) for the intensive support phase. A positive change was observed in physical functioning (after 6-months)(6 MWT;  $P=0.048$ ). No significant difference for the moderate support phase and muscle strength (KES) were found.

**Conclusion:** The intervention effectively improved physical performance, muscle CSA and protein intake in this population of Surinamese older adults. This first results showed effects after the intensive support phase, but not in the moderate support phase. Although, this new lifestyle intervention seems promising for migrant older adults in order to counteract sarcopenia. Further RCT outcomes, including qualitative data, will be analyzed upcoming months.

**Disclosure of Interest:** The study is funded by NWO – RAAKSIA MKB grant.

**Keywords:** aging, behavior change, cultural sensitive, muscle mass, protein intake, sarcopenia

## Poster № 63

### ***Reduced cardiorespiratory fitness is associated with prefrailty status in the community-dwelling population***

**Introduction:** The concept of prefrailty, preceding clinically identifiable frailty, presents an opportune stage for preventive interventions, given its reversible nature. Recently, the importance of identifying prefrailty has been emphasized due to its higher efficacy in preventing progression to frailty.

However, previous studies focused mainly on the relationship between cardiorespiratory fitness (CRF) and frailty in the older elderly. Therefore, this study explored the relationship between prefrailty and cardiorespiratory fitness (CRF) in community-dwelling individuals.

**Methods:** 419 participants (55 to 75 years) were included in this cross-sectional observational study, conducted as part of the Amersfoort cohort study on functional decline, healthy ageing and frailty (AMCOHF). Frailty status was assessed using three instruments (i.e. Rockwood frailty index, Groningen frailty indicator, and Fried phenotype) and cardiopulmonary exercise testing (CPET) was utilized to evaluate CRF. Statistical analysis performed to assess the correlation between frailty status and CRF parameters considered the potential mediating effects of age, sex, and lean body mass.

**Results:** Prefrailty was observed in 129 of the 419 (30.8 %) participants. Independent t test analysis showed that  $VO_{2peak}$  was higher in non-frail ( $30.90 \pm 6.13$  mL/min/kg) compared to prefrail ( $28.2 \pm 6.2$  mL/min/kg) participants ( $t(419) = 4.098$ ,  $p = 0.05$ ).  $WR_{peak}$  was significantly higher in non-frail ( $30.9 \pm 6.1$ W) compared to prefrail ( $28.23 \pm 6.24$  W) participants ( $t(419) = 4.098$ ,  $p < 0.05$ ). The correlation analysis showed a low significant relationship between Fried Phenotype and  $WR_{peak}$ ,  $VO_{2peak}$ ,  $VE_{peak}$ ,  $O_2pulse_{peak}$ ,  $VT_{peak}$ , VAT and OUES respectively.

**Conclusion:** This study revealed a significant correlation between prefrailty status and CRF, highlighting CRF as a potential marker of a declining intrinsic capacity and the onset of frailty. By investigating these associations, targeted interventions to prevent prefrailty might be developed specifically aimed for those at risk of developing frailty. Further research could focus on identifying potential markers for accelerated decline in CRF.

## Poster № 64

### Finding cycling ergometry Thresholds using different Protocols (FTP)

*Graafland W.H., Panyrek J., Reurink G.*

#### Abstract

**Introduction:** Cardiopulmonary exercise testing using cycling ergometry is often utilized in sports medicine in a healthy athletic population to determine maximum oxygen uptake ( $\dot{V}O_2$  peak) and thresholds (aerobic threshold (AT), respiratory compensation point (RCP)). Shorter protocols, such as the Ramp and 1-minute step are used to determine maximum values and measure performance, whereas longer protocols such as the 3-minute step are used to determine threshold values used in exercise prescription and pacing strategies.

**Purpose:** To examine the differences between three different cycling ergometry protocols (Ramp, 1-minute step and 3-minute step) for power output (Watt) oxygen consumption ( $\dot{V}O_2$ ) and heart rate on AT, RCP and maximum values in healthy athletes.

**Methods:** 17 healthy athletes (15 male, 2 female, mean age 33) that regularly participated in endurance sports performed three different cycling ergometry protocols (Ramp, 1-minute step and 3-minute step) in random order within a 6-week period and with at least 5-days between tests. Watt,  $\dot{V}O_2$  and heart rate were assessed. Participants were asked to report their functional threshold power (FTP). Differences between the protocols were analysed with a repeated-measures ANOVA.

**Results:** Watt for the 3-minute step protocol was lower on maximum (Ramp:  $-105,35 \pm -77,16$  Watt, 1 min  $-77,09 \pm -52,51$  Watt) and lower on RCP (Ramp:  $-93,65 \pm -63,65$  Watt, 1 min:  $-64,14 \pm -28,80$  Watt). Watt on RCP corresponded well with self-reported FTP for the 3-minute step protocol (Ramp:  $65,04 \pm 119,68$  Watt, 1 min:  $47,36 \pm 78,54$  Watt, 3min:  $-4,78 \pm 22,66$  Watt). The 3-minute step protocol showed a higher maximum heart rate compared to the Ramp and 1-minute step protocol (Ramp:  $0,43 \pm 8,0$ /min, 1 min:  $0,58 \pm 8,36$  /min) and similar  $\dot{V}O_2$  peak (Ramp:  $-0,94 \pm 2,62$  ml/min/kg, 1 min:  $-1,11 \pm 2,75$  ml/min/kg). Heart rate on RCP was significantly higher for the 3-minute step protocol compared to the 1-minute step (Ramp:  $-1,52 \pm 9,28$ /min, 1 min:  $0,2 \pm 10,27$  /min) and was significantly higher on AT compared to the Ramp protocol (Ramp:  $2,08 \pm 18,98$ /min, 1min:  $-1,82 \pm 18,05$ /min).

**Conclusions:** For both the Ramp and 1-minute step protocol Watt at RCP is higher by a large margin compared to the 3-minute step protocol. Watt on RCP for the 3-minute step protocol corresponds well with self-reported FTP. The 3-minute step protocol had similar maximum oxygen uptake ( $\dot{V}O_2$  peak) and a higher maximum heart rate compared to the Ramp and 1-minute step protocol. Heart rates on thresholds (AT and RCP) are higher in the 3-minute step protocol. This suggests that for both determination of maximum values and threshold determination for exercise prescription the 3-minute step protocol is superior to the Ramp and 1-minute step protocol.

**OSTEOGENIC ACTIVITY ON NAOH-ETCHED 3D-PRINTED PCL SCAFFOLDS IN PERFUSION OR SPINNER FLASK BIOREACTOR**

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**Introduction:** Bioreactor systems, e.g., spinner flask and perfusion bioreactors, and cell-seeded three-dimensional (3D)-printed scaffolds are used in bone tissue engineering strategies to stimulate cells and produce bone tissue suitable for implantation into the patient. Construction of functional and clinically relevant bone graft using cell-seeded 3D-printed scaffolds within bioreactor systems is still a challenge. Bioreactor parameters, e.g. fluid shear stress and nutrient transport, will crucially affect cell function on 3D-printed scaffolds. Therefore, fluid shear stress induced by spinner flask and perfusion bioreactors might differentially affect osteogenic responsiveness of pre-osteoblasts inside 3D-printed scaffolds.

**Purpose:** We designed and fabricated surface-modified 3D-printed poly-ε-caprolactone (PCL) scaffolds, as well as static, spinner flask, and perfusion bioreactors to determine fluid shear stress and osteogenic responsiveness of MC3T3-E1 pre-osteoblasts seeded on the scaffolds in the bioreactors using finite element (FE)-modeling and experiments.

**Method:** FE-modeling was used to quantify wall shear stress (WSS) distribution and magnitude inside 3D-printed PCL scaffolds within spinner flask and perfusion bioreactors. MC3T3-E1 pre-osteoblasts were seeded on NaOH surface-modified 3D-printed PCL scaffolds, and cultured in customized static, spinner flask, and perfusion bioreactors up to 7 days. The scaffolds' physicochemical properties and pre-osteoblast function were assessed experimentally.

**Results:** FE-modeling showed that spinner flask and perfusion bioreactors locally affected WSS distribution and magnitude inside the scaffolds. WSS distribution was more homogeneous inside scaffolds in perfusion than in spinner flask bioreactors. The average WSS on scaffold-strand surfaces ranged from 0–6.5 mPa for spinner flask bioreactors, and from 0–4.1 mPa for perfusion bioreactors. Surface-modification of scaffolds by NaOH resulted in a surface with a honeycomb-like pattern and increased surface roughness (1.6-fold), but decreased water contact angle (0.3-fold). Both spinner flask and perfusion bioreactors increased cell spreading, proliferation, and distribution throughout the scaffolds. Perfusion, but not spinner flask bioreactors more strongly enhanced collagen (2.2-fold) and calcium deposition (2.1-fold) throughout the scaffolds after 7 days compared to static bioreactors, likely due to uniform WSS-induced mechanical stimulation of the cells revealed by FE-modeling.

**Conclusions:** Our findings indicate the importance of using accurate FE models to estimate WSS and determine experimental conditions for designing cell-seeded 3D-printed scaffolds in bioreactor systems.

**EXPLORING THE CORTICOSPINAL TRACT'S ROLE IN MEDIOLATERAL GAIT STABILITY CONTROL: A TMS STUDY:**

**Raven Huiberts**

Organisation: AMS

Institute: Vrije Universiteit Amsterdam

Faculty: human movement sciences

**Introduction/purpose:** Corticospinal excitability modulation during gait in response to stability demands remains underexplored, particularly concerning mediolateral gait stability, a critical factor in fall risk. We investigated if corticospinal excitability adjusts to accommodate mediolateral stability demands during gait.

**Methods:** Ten neurotypical adults performed steady-state gait and gait on a laterally oscillating treadmill. Transcranial magnetic stimulation (TMS) was administered pseudorandomly at 110% of the tibialis anterior standing motor threshold. Kinematic data were captured using Vicon motion tracking software. Differences in local divergence exponent (LDE), step width, and stride duration were tested to confirm lateral instability. Surface electrodes recorded Motor-evoked potentials (MEPs) of four upper leg muscles and three lower leg muscles. From these MEPs, a paired samples temporal resolution was made.

**Results:** Gait with lateral oscillations decreased stride duration (walk $\approx$ 1.13 seconds, oscillated $\approx$ 1.08 seconds,  $p < 0.01$ ) and increased LDE (walk $\approx$ 9.11, oscillated $\approx$ 10.74,  $p < 0.001$ ), however, no significant difference in step width was observed ( $p > 0.05$ ). While most muscles showed significant differences in absolute MEPs, after normalizing to baseline muscle activity, only the upper leg muscles exhibited periods of significant increases within the oscillated condition. All of these increases were in the mid to late stance phase. Antagonistic muscles did not show increases in normalized MEPs within the same period (biceps femoris 33-46.5% and 52.5-62.5% of the gait cycle vs quad femoris 18-27.5%, glute medius 47.5-57% vs adductor 37-42.5%,  $p < 0.05$ ).

**Conclusions:** These condition-dependent increases in corticospinal excitability during the mid to late stance phase suggest a motor cortex control to overcome the mediolateral stability demands. The exclusive increases in normalized MEPs among all upper leg muscles, without concurrent changes in antagonistic muscles, indicates that there is a corticospinal strategy to overcoming the task-induced instability, which did not require modulation of lower leg muscles. The results indicate that the motor cortex can effectively contribute to maintaining lateral gait stability, by coordinatively controlling multiple upper leg muscles. Future research should explore additional stabilization tasks to better understand the motor cortex's involvement in fall prevention.



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### SHORT-TERM EFFECT OF PULSATING FLUID SHEAR STRESS ON THE ACTIVATION OF MACROPHAGES IN VITRO

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#### Abstract

**Introduction:** The muscle stem cell niche plays a pivotal role in the regeneration and repair of skeletal muscle after traumatic injuries or diseases. As one of the most physically dynamic systems in the human body, the contraction and elongation of muscles give rise to multiple mechanical loadings including shear stress that influence satellite cells (*Haroon, et al. 2021*) and conceivably also neighboring cells within the interstitial space between muscle fibers (*Zhong-Dong Shi, et al. 2011*). Among these cells, macrophages are key for governing the early inflammatory response after muscle damage and also participating in the remission of inflammation and long-term repair and remodeling of muscle tissue. However, the impact of mechanical loading on macrophages and its underlying mechanisms are unknown. **Purpose:** To investigate the effects of one-hour pulsating fluid shear stress (PFSS) on the expression of pro- and anti-inflammatory cytokines and NO production in macrophages during PFSS and variable post-incubation. **Methods:** RAW 264.7 macrophages were seeded on a 3.6 cm x 7.9 glass slide ( $1 \times 10^6/\text{cm}^2$ ) and subjected to PFSS (Peak stress: 6.5 Pa/s, 1Hz) for 1h, followed by 0h, 3h, 6h or 24h post incubation. RT-qPCR was used to assess mRNA levels, and the Griess assay was used to quantify NO production. **Results:** The expression of pro-inflammatory genes such as *IL1 $\beta$* , *IL6*, and *TNF $\alpha$*  peaked 6 hours after PFSS varying from 3- to 12-fold. In contrast, *IL10*, *TGF $\beta$* , *Arg1*, and *iNOS* mRNA levels showed no difference compared to those in the control group. Medium NO concentration increased 6-fold during the 1h PFSS. **Conclusions:** Mechanical loading of macrophages stimulates a pro-inflammatory profile of mRNA transcript. These data suggest that mechanical loading shortly after muscle injury may activate the innate immune response which could be beneficial for the clearance of debris and activation of muscle stem cells. Further research is warranted to investigate whether macrophages are functionally activated by PFSS and which cytokines are expressed and secreted into the culture medium.

#### Reference

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**MRI-based Lumbar Epimuscular and Intramuscular Structural Changes are associated Clinical Outcomes**

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**Abstract (428 words)**

**Introduction:** Low Back Pain (LBP) contributes to functional disability and tissue degeneration. In individuals with LBP, intramuscular fat infiltration (IMF) appears to replace muscle fibers (MF), and an increase in lumbodorsal epimuscular connective tissue thickness is reported. Whether these morphological changes are associated with pathology in MRI findings and clinical outcomes in LBP is unknown. Besides pain and perceived disability, fear and depression are also considered since decreased muscle activity is expected in this population.

**Purpose:** To test whether percentage of segmental lumbodorsal epimuscular fat (EMF) and lumbar paraspinal IMF is associated with clinical outcomes (i.e., pain intensity, perceived disability, psychological factors, disc degeneration, Modic changes, and recurrent LBP).

**Method:** MRI T2 spin echo of 76 asymptomatic individuals were automatically segmented using Gaussian mixture models. Paraspinal IMF and EMF are calculated as muscle-fat ratios per segment. Associations between muscle-fat ratios and clinical outcomes were tested with regression analysis.

**Results:** Perceived disability was positively related to multifidus MF and negatively associated with EMF. EMF at L1-2, L2-3, and L4-5 exhibited negative associations with pain intensity, contrasting with positive associations observed for psoas IMF at L4-5. Negative associations with depression were found for EMF and psoas FI at L1-2 and L3-4, whereas positive associations with were observed for multifidus IMF at L4-5 and psoas MF at L4-5. Positive associations with anxiety were identified for erector spinae IMF at L3-4, while negative associations were shown for erector spinae MF at L5-S1.

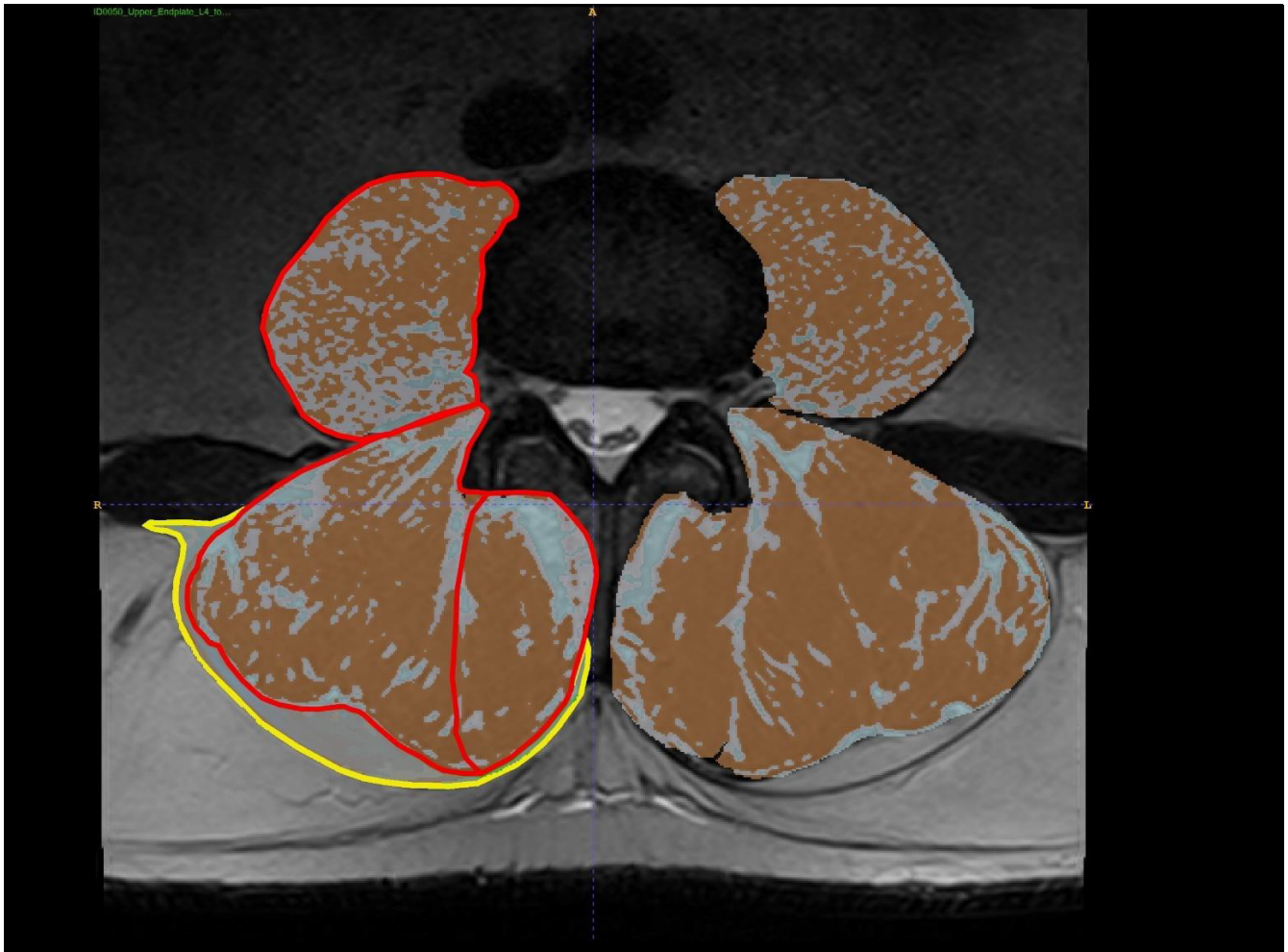
Regarding associations between morphological muscle characteristics, positive associations were observed between EMF and multifidus MF. Negative associations were identified between IMF at L1-2 and the psoas MF at L1-2. In addition, negative associations were found across various segments between EMF and both erector spinae IMF and erector spinae MF.

Multifidus IMF and EMF associated positively with Modic changes. Multifidus IMF at L3-4 and L4-5 associated positively with High-Intensity Zones (HIZ) at L3-5 and L5-S1. Negative associations were found for multifidus MF and PS MF with HIZ at L5-S1, as well as for EMF with HIZ at L2-3. Moreover, EMF at L2-3 was negatively related to the likelihood of recurrent LBP.

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**Conclusions:** This study shows increased IMF in various paraspinal muscles in LBP patients which associated with elevated pain intensity, increased perceived disability, higher levels of anxiety and depression. Conversely, increased EMF is associated with higher levels of depression, decreased pain, reduced perceived disability, and a higher likelihood of recurrent LBP. The complex interplay among lumbar tissues related to LBP indicates that increased EMF and reduced IMF may have beneficial with regard to clinical outcomes.

**Keywords:** Magnetic Resonance Imaging, anatomy, back muscles, fascia, spine, Low Back Pain reported.



**Figure 1.** Model result. This image represents the generated epimuscular and intramuscular fatty connective tissue and the muscle fibers of the back muscles at the height L3-4. Red/brown = muscle fibers and gray/bleu = fatty connective tissue.

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**Background:** Oculogyral illusion (OGI) is the perceived drift of a head-fixed target during self-rotation in healthy individuals. This phenomenon is caused by a mismatch between predicted visual input and vestibular signals. An OGI theoretical model suggests that semicircular canals generate an opposite efference copy for sensed angular motion, proposing that target position can influence the OGI. Prior research linked OGI to the after-image drift in Meniere's disease patients during the Extended Utermohlen Test (EUT), with optimal prisms reducing drift. Underlying theory remains invalidated. **Aim:** To validate the prediction by exposing subjects to angular motion and assess gaze direction's effect on OGI. **Methods:** 22 healthy subjects sat in a rotating chair in a dark-room, wearing VR goggles displaying a fixation target. The target was positioned straight ahead, 10° to the right, and 10° to the left in separate trials. Participants indicated the apparent target drift direction in a two-alternative forced choice task. **Results:** OGI effect is influenced by the target position. Drift matches motion direction during acceleration and opposes it during deceleration. Leftward target displacement significantly reduced OGI ( $p < 0.05$ ), while rightward displacement showed a reduced but non-significant effect ( $p = 0.4163$ ). **Conclusion:** OGI was successfully elicited using virtual reality, suggesting that altering target position influences motion perception and potentially supports prism application.

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# The influence of body orientation on length judgements.

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Perceiving the size of a visual object requires the combination of various sources of visual information. A recent paper (Kim et al. [2022], Body Orientation Affects the Perceived Size of Objects. *Perception* 51:25-36) concluded that body orientation played a substantial role. The aim of the present paper is to answer the question whether the reported effect of body orientation on visuo-haptic size matching was due to effects on the visual or on the haptic judgements of size. To do so, we used a within-participant design combining an experiment using visuo-haptic size matching with two experiments that assessed the visual and haptic size-percept using free magnitude estimation. Our experiments produced a systematic visuo-haptic mismatch, but the sign of the mismatch was opposite to that of the original study. Moreover, our study did not reveal a systematic effect of body orientation on this mismatch. Thirdly, we found that the mismatch we determined from participants matching a visual and haptic percept was considerably smaller than the mismatch we derived from their visual and haptic size estimates. In summary, we conclude that conclusions about perceived sizes of objects are very sensitive to details of the experimental approach.

**STOPFOP: A PHASE II CLINICAL TRIAL TO PREVENT HETEROTOPIC OSSIFICATION IN FOP USING SARACATINIB (AZD0530); A STATUS UPDATE**

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**Introduction:** Fibrodysplasia Ossificans Progressiva (FOP) is an invalidating disorder marked by severe heterotopic ossifications (HO), causing diffuse ankylosis and early death. Currently there is no approved treatment for FOP in the world except in the USA and Canada. Saracatinib, originally designed for ovarian cancer treatment, was identified by our team as a potent inhibitor of the ALK2-kinase which, through mutation of the ACRV<sup>1</sup>-gene, causes this rare bone disease.

**Purpose:** The purpose of this study is to investigate the repositioning of saracatinib to treat patients with FOP after it proved effective in preventing HO in FOP mouse models.

**Method:** The Saracatinib Trial to Prevent FOP (STOPFOP) is a phase 2a, double blinded multicentre trial, wherein patients are randomized to receive 6 months saracatinib or placebo, followed by a 12 month open-label phase. Endpoints are objective change in heterotopic bone volume as measured by low-dose whole-body CT, [18F] NaF PET activity and patient reported outcome measures such as the FOP-IADL questionnaire.

**Results:** Although the COVID pandemic resulted in serious study delays, the study is now well underway and 17 FOP patients, aged 18-65 years from 8 European countries are now included. No data is yet available as the study is still ongoing, but to date there have been no drug related SAE's and both the investigators and participants are happy with the progress of the trial.

**Conclusion:** Drug repositioning is especially useful in rare diseases with limited study populations, such as FOP. It represents an ideal solution for limiting risks in early clinical studies and existing pre-clinical and clinical knowledge may also allow more affordable pricing once an indication is approved. With positive study outcome, saracatinib may provide a rapidly translatable therapy for FOP due to the availability of extensive safety data from over 600 patients in more than 28 registered clinical trials. At the time of writing, 17 patients are included and 11 have already completed the study, of whom all have elected to continue the medication in an extended study phase, waiting for more results to be analysed once the study is complete.

**Trial registration:** NCT04307953 / EudraCT number 2019-003324-20

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### BEYOND PLAYING POSITIONS: A NEW APPROACH TO CATEGORIZE SOCCER PLAYERS BASED ON MACHINE LEARNING

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**Introduction** A soccer match involves many explosive actions within the context of a 90-minute endurance performance. Therefore, it is important to optimize the sprint and endurance capacity to the individual requirements of the players. Typically, these requirements are associated with the playing positions. However, it is unknown and arguably questionable if categorizing soccer players by playing position is useful from a physiological perspective.

**Purpose** This study examined sprint, endurance, and match-specific running performance of players, assessed alignment of match-specific running performance with playing positions, and evaluated the potential of unsupervised machine learning for identification of players with similar match-specific running profiles.

**Method** Forty elite male soccer players had match-specific running data collected over two seasons, with 31 undergoing exercise testing, consisting of a 20-meter sprint and a treadmill test to measure maximal oxygen uptake. *k*-means clustering identified subgroups based on players' match-specific running performance. Differences in sprint, endurance, and match-specific running were compared between playing positions and between clusters. Both grouping methods were tested for their ability to identify subgroups with similar total distance (TD), low (LIR), moderate (MIR), high intensity running (HIR) and sprint distance in matches.

**Results** Match-specific running performance differed between playing positions, although notable variation was observed per playing position. Clustering based on match-specific running performance revealed less variance within groups (TD:  $P = 0.049$ , LIR:  $P = 0.032$ , HIR:  $P = 0.033$ ) and larger standardized differences between groups (LIR:  $P = 0.037$ , MIR:  $P = 0.041$ , HIR:  $P = 0.035$ , Sprint:  $P = 0.018$ ) compared to grouping by playing position. Moreover, 20-m sprint speed differed between the sprint and high intensity endurance cluster (25.22 vs 23.75,  $P = 0.012$ ), but not between playing positions.

**Conclusions** Utilizing unsupervised machine learning to group soccer players based on match-specific running performance enhances the identification of player groups with distinct physical profiles. This data-driven approach supports performance evaluation and enables training optimization towards groups of players with similar match-specific running performance.

**KEY WORDS:** Artificial intelligence, clustering, football, physiology, sprint speed,  $V \cdot O_{2max}$

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### DETERMINING $\dot{V}\text{-O}_{2\text{MAX}}$ IN COMPETITIVE SWIMMERS: COMPARING THE VALIDITY, RELIABILITY, PRACTICAL APPLICABILITY, AND SPORT-SPECIFICITY OF CYCLING, ARM CRANKING, ERGOMETER SWIMMING, AND TETHERED SWIMMING

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**Introduction** Maximal oxygen consumption ( $\dot{V}\text{-O}_{2\text{max}}$ ) is a critical success factor in most endurance sports including competitive swimming, especially in races beyond 100-m. Measuring  $\dot{V}\text{-O}_{2\text{max}}$  is an indispensable tool for coaches, researchers, and athletes striving for excellence in training and performance. However, the optimal way of determining  $\dot{V}\text{-O}_{2\text{max}}$  in competitive swimming remains unknown.

**Purpose** This study aims to identify the optimal method for determining  $\dot{V}\text{-O}_{2\text{max}}$  in competitive swimmers in terms of validity, test-retest reliability, practical applicability, and sport-specificity.

**Method** Twenty competitive swimmers performed four maximal incremental exercise tests: cycling, arm cranking, ergometer swimming, and tethered swimming. Gas analysis was conducted to estimate  $\dot{V}\text{-O}_{2\text{max}}$ . Validity was assessed in terms of the amount of variance explained by the estimated  $\dot{V}\text{-O}_{2\text{max}}$  of the performance on a 1500-m time trial. Test-retest reliability was evaluated using the intraclass correlation coefficient (ICC). Practical applicability and sport-specificity were evaluated qualitatively.

**Results**  $\dot{V}\text{-O}_{2\text{max}}$  obtained from tethered swimming, ergometer swimming, and cycling explained a similar amount of variance of the 1500-m performance ( $R^2 = 0.64, 0.64, 0.65$ , respectively). However, ergometer swimming yielded significantly lower  $\dot{V}\text{-O}_{2\text{max}}$  estimates ( $40.54 \pm 6.55$  ml/kg/min) than tethered swimming ( $54.40 \pm 6.21$  ml/kg/min) and cycling ( $54.39 \pm 5.63$  ml/kg/min). Arm cranking resulted in both a lower explained variance ( $R^2 = 0.41$ ) and a significantly lower  $\dot{V}\text{-O}_{2\text{max}}$  ( $43.14 \pm 7.81$  ml/kg/min). Tethered swimming showed a good reliability (ICC=0.81). In terms of practical applicability, the methods ranked from cycling, arm cranking and ergometer swimming to tethered swimming, but in the opposite order in terms of sport-specificity.

**Conclusions** Bicycle and tethered swimming tests demonstrated high validity with comparable  $\dot{V}\text{-O}_{2\text{max}}$  estimates, explaining a large proportion of differences in endurance performance. Choosing between these two methods involves a trade-off between a higher practical applicability and reliability of the bicycle test versus the more sport-specific nature of the tethered swimming test.

**KEY WORDS:** Athletes, endurance capacity, exercise testing,  $\dot{V}\text{-O}_{2\text{peak}}$ , test-retest reliability, reproducibility