Modeling osteoarthritis through biomechanics and imaging (MOBI)

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Ethical review	Approved WMO
Status	Pending
Health condition type	Joint disorders
Study type	Observational invasive

Summary

ID

NL-OMON57122

Source
ToetsingOnline

Brief title
MOBI

Condition

- Joint disorders

Synonym
degenerative joint disease, Osteoarthritis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: biomechanics, imaging, Modeling, osteoarthritis

Outcome measures

Primary outcome

The association between biomechanical patterns at baseline with progression of structural OA-features on MRI after two years.

Secondary outcome

Evaluate test-retest reliability of the biomechanical measurement protocol and processing pipeline.

- Assess sensitivity of the biomechanical models to changes in model parameters.

- Validate a 3D-2D image registration algorithm.

- Assess the correlation between subchondral bone metabolism at baseline and progression of compositional or structural OA-related features after two years.

- Explore associations among the data collected to generate hypotheses to inform future research.

Study description

Background summary

OA is expected to be the most prevalent disease in the Netherlands by 2040. The knee is the most common joint affected by OA, and knee OA is responsible for more physical disability than any other disease among older adults.

Knee OA is predominantly held to be caused by pathomechanics: biomechanical factors that lead to increases in cartilage stress, promoting its degeneration.

Current methods used to evaluate knee biomechanics contain substantial error, which prevents accurate estimates of cartilage stress. A more accurate and precise measure of stress distribution throughout the cartilage tissue (instead of the average load through the joint) would improve our ability to detect and quantify the relationships between joint/cartilage pathomechanics and OA.

This would have substantial impact on OA research and management by making it possible to incorporate relevant biomechanical factors into personalized prediction models. Moreover, it would inform hypotheses about which interventions might favourably alter biomechanics, potentially leading to improved outcomes including slowing down the progression of OA, reducing pain, and improving function and quality of life.

Study objective

We aim to develop a personalized multi-scale biomechanical model of the knee that integrates joint movement (marker-based motion capture, fluoroscopy), EMG and force data with quantitative cartilage parameters derived from advanced imaging techniques, to yield precise and accurate measures of intra-articular forces and tissue stress distributions. We will then evaluate the associations between these measures and pathophysiological measures (e.g., subchondral bone metabolism and structural OA features) derived from positron emission tomography - magnetic resonance imaging (PET/MRI) over a 2-year period.

We will evaluate test-retest reliability of our biomechanical data collection protocol and processing pipelines and assess the sensitivity of our models to changes of input parameters. We will validate a MRI-based method of image-registration against a CT-based method.

We will assess the correlation between subchondral bone metabolism and structural progression of OA. Finally, we aim to explore associations between our biomechanical parameters and other relevant variables including patient demographics, physical examination tests, and self-reported outcomes like pain. The purpose of these analyses will be hypothesis-generating in nature.

Study design

This study includes a technical development phase and a 2-year prospective observational study.

Study burden and risks

Participants involved in the technical development will attend a single visit involving biomechanical assessment, photon-counting CT (PCCT) and MR image acquisition. They will be exposed to a maximum total radiation of 0.07 mSv. Those in the prospective study will be physically assessed at baseline and

2-year follow-up and fill out questionnaires at 1-year follow-up.

The physical visits will include biomechanical assessment (performing walking and lunging tasks), PET/MR image acquisition, physical examination, completion of questionnaires, and blood draw. Total radiation exposure will not exceed 2.47 mSv. Time for data collection will be approximately 4-6 hours at baseline and 2-year follow-up, divided into two 2-3-hour visits.

At the one year follow-up, questionnaires will take approximately 30 minutes to complete, these will be performed remotely. In total, the time commitment for 4 visits plus completion of questionnaires at home will be 8-13 hours

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Part 1
Eligible participants will meet the following criteria:
(i) aged 18 years or older;
(ii) never diagnosed with KOA;
(iii) no pain in the ankles, knees, hips or low back for at least 6 months;
(iv) no other diagnosed conditions that might impact mobility (e.g. inflammatory conditions, cancer, neurologic conditions); and
(v) no contraindications to radiation exposure or MRI.

Part 2. Eligible participants will belong to one of the following three populations:

• Post-ACLR group:
(i) aged 18-45 years;
(ii) unilateral ACLR; between 12 and 18 months post-ACLR, with or without concomitant meniscal injuries;
(iii) condition of index knee is stable;
(iv) no complaints in contralateral knee (e.g., no pain, no history of injury);
(v) no early KOA symptoms (no joint line tenderness, no pain while walking or climbing stairs);
(vi) no radiographic OA (defined as Kellgren and Lawrence grade >= 2) on most recent radiograph if available
(vii) no history of knee dislocation/multi-ligament injury.

• Early knee OA group:
(i) aged 45-65 years;
(ii) body mass index (BMI) between 27 - 35 kg/m2;
(iii) knee pain aggravated by weight-bearing activities for at least 6 months, but no longer than 2 years;
(iv) no history of traumatic knee injury (defined as injury that required non-weight-bearing for >24 hours (e.g. fracture, dislocation, complete ligament rupture);
(v) no previous knee surgery.

• No OA group, matched to early OA participants on sex and age:
(i) aged 45-65 years;
(ii) never diagnosed with KOA;
(iii) no pain in the ankles, knees, hips or low back for at least 6 months;
(iv) no history of traumatic knee injury (defined as injury that required non-weight-bearing for >24 hours (e.g. fracture, dislocation, complete ligament rupture);
(v) no previous knee surgery.

Exclusion criteria

Part 1
(i)diagnosed with KOA;
(ii) pain in the ankles, knees, hips or low back for at least 6 months;
(iii) other diagnosed conditions that might impact mobility (e.g. inflammatory conditions, cancer, neurologic conditions); and
(iv) contraindications to radiation exposure or MRI.

Part 2
• Morning stiffness in the index knee lasting more than 30 minutes
• Complaints of knee locking
• Any other diagnosed or expected conditions that might impact the participant*s gait pattern (e.g.,
inflammatory conditions, cancer, neurologic conditions)
• Musculoskeletal conditions affecting the ankles or hips, such as osteoarthritis or inflammatory arthritis
• Body mass index > 35 kg/m2
• Contraindications to PET/MRI
• Known renal insufficiency
• Known allergy or contraindications to contrast agents
• Contraindications to radiation exposure
• Use of bisphosphonates
• Unable to communicate in either Dutch or English

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Pending

Start date (anticipated):	01-09-2024
Enrollment:	85
Type:	Anticipated

Ethics review

Approved WMO Date:	21-11-2024
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL87368.078.24