1. Title page

Title:

Estimation of the effect of body weight on the development of osteoarthritis based on cumulative stresses in cartilage: Data from the Osteoarthritis Initiative

Running title:

Effect of BW on cumulative stresses in cartilage

Olesya Klets* (1,2), Mika E. Mononen (3), Mimmi K. Liukkonen (3), Mika T. Nevalainen (4), Miika T. Nieminen (1,2,4), Simo Saarakkala (1,2,4), Rami K. Korhonen (3,5)

Institutions:

(1) Research Unit of Medical Imaging, Physics and Technology, University of Oulu, P.O.Box 8000, Oulu, Finland
(2) Medical Research Center Oulu, University of Oulu, P.O.Box 8000, Oulu, Finland
(3) Department of Applied Physics, University of Eastern Finland, PL 1627, Kuopio, Finland
(4) Department of Diagnostic Radiology, Oulu University Hospital, P.O.Box 50, Oulu, Finland
(5) Diagnostic Imaging Centre, Kuopio University Hospital, P.O.Box 100, Kuopio, Finland

*Corresponding author: Olesya Klets (Research Unit of Medical Imaging, Physics and Technology, University of Oulu, P.O.Box 8000, 90014, Oulu, Finland, contact phone number: +358 466470989, e-mail: olesya.klets@oulu.fi).
2. Abstract and key terms

Evaluation of the subject-specific biomechanical effects of obesity on the progression of OA is challenging. The aim of this study was to create 3D MRI-based finite element models of the knee joints of seven obese subjects, who had developed OA at 4-year follow-up, and of seven normal weight subjects, who had not developed OA at 4-year follow-up, to test the sensitivity of cumulative maximum principal stresses in cartilage in quantitative risk evaluation of the initiation and progression of knee OA. Volumes of elements with cumulative stresses over 5MPa in tibial cartilage were significantly (p < 0.05) larger in obese subjects as compared to normal weight subjects. Locations of high peak cumulative stresses at the baseline in most of the obese subjects showed a good agreement with the locations of the cartilage loss and MRI scoring at follow-up. Simulated weight loss (to body mass index 24 kg/m²) in obese subjects led to significant reduction of the highest cumulative stresses in tibial and femoral cartilages. The modeling results suggest that an analysis of cumulative stresses could be used to evaluate subject-specific effects of obesity and weight loss on cartilage responses and potential risks for the progression of knee OA.

Key terms: Finite element analysis; articular cartilage; knee joint; obesity; weight loss; magnetic resonance imaging
3. Introduction

Osteoarthritis (OA) is a joint disease that primarily affects articular cartilage and subchondral bone and leads to pain and disability for a significant portion of the population. The precise etiology of OA is unknown, though several clinical risk factors have been identified, including age and gender\textsuperscript{17}, while the most important modifiable risk factor for the progression of OA is obesity\textsuperscript{18}. Currently, only successful therapy for severe/advanced knee OA is an expensive joint replacement surgery, which may not offer an ultimate solution in a long run due to durability of joint implants\textsuperscript{32}. Thus, more effective solution would be prevention with conservative treatment such as weight loss. A tool, which could quantitatively evaluate the joint condition before conservative treatments, would be a great asset in subject-specific clinical evaluation.

Obesity increases the risks for knee OA by nearly five times in men and four times in women when compared with normal weight men and women\textsuperscript{3}. The knee joint in obese persons experiences significantly higher mechanical loads that may eventually change the structure, composition and mechanical properties of articular cartilage\textsuperscript{47}. Each additional kilogram of body mass in obese adults increases the compressive load on the knee joint by approximately 4 kilograms during walking\textsuperscript{34}. Coggon et al.\textsuperscript{10} reported that subjects with body mass index (BMI) \textgreater{} 30 kg/m\textsuperscript{2} have 6.8 times higher chances to develop knee OA than normal weight subjects. Accordingly, weight loss can reduce the risk of symptomatic knee OA\textsuperscript{18}. It was previously shown that an average weight loss of 5\% over 18 months in overweight and obese adults with knee OA results in an 18\% improvement in knee function\textsuperscript{34}. However, not all obese subjects have OA\textsuperscript{47} and it is currently not possible to predict whether mechanical overloading could lead to onset and progression of OA or not.
OA is usually diagnosed by clinical examination and conventional radiography. However, traditional diagnostic tools are insensitive to the early stages of OA. The Kellgren–Lawrence (KL) grading is the most commonly used radiography-based grading criteria for assessing the severity and progression of knee OA and making treatment decisions. Even though KL scale takes into account joint space narrowing and osteophyte development, it cannot directly assess changes in cartilage structure and properties. Instead of radiography, magnetic resonance imaging (MRI) offers a powerful tool for detecting and measuring changes in articular cartilage morphology from early- to end-stage OA. However, it cannot assess mechanical risks (stresses/strains) associated with the progression of knee OA.

Finite element (FE) modeling can detect changes in tissue-level stresses and strains and describe how these changes might relate to the development and progression of OA. For example, FE models have been applied to study the effects of simulated osteochondral defects on cartilage biomechanics and to analyze cartilage stresses during gait.

It has been previously suggested that there are two primary causes of overloading-induced cartilage damage; i) the application of single excessive loading (above failure limit), which can happen because of injurious joint loading, or ii) the application of cumulative and chronic overloading, which can occur during normal daily activities. Mononen et al. developed a novel theoretical method to predict the progression of collagen degeneration in the knee joint cartilage of overweight subjects. The method was based on overloading of cartilage so that cumulatively accumulated excessive tensile stresses would lead to collagen network damage and OA with time. However, that method used fibril reinforced material models of cartilage and applied iterative degeneration simulation. These both cause numerical difficulties and increase
computational time, and limit the applicability of the method in clinical use when many
patients need to be analyzed. Therefore, certain simplifications are necessary to be
done.

There are no studies that would have evaluated the predictive value of cumulative
stresses in the knee joint cartilage against patient-specific follow-up MRI data of the
progression of OA using a relatively simple and fast modeling approach. In this study,
we hypothesize that cumulative tensile stresses of cartilage during a single gait cycle
are able to show locations of the initiation and progression of knee OA. For this, we
test the sensitivity of cumulative maximum principal (tensile) stresses (instead of
computationally time-consuming iterative degeneration) in transversely isotropic
poroelastic cartilage (instead of more complex material) during simplified gait cycle
loading in quantitative risk evaluation for the initiation and progression of knee OA
within normal weight and obese subjects. Outcomes of simulated cumulative stresses
are compared against 4-year follow-up radiographic gradings (KL) and MRI scorings
(MRI Osteoarthritis Knee Score, MOAKS)\textsuperscript{22}. Furthermore, ability of the cumulative
stress parameter as an indicator to estimate the effect of weight loss on possible
cartilage degeneration within obese subjects is evaluated.
4. Materials and methods

**Magnetic resonance imaging**

MRI data of the baseline and 4-year follow-ups of seven obese subjects, who had developed knee OA at 4-year follow-up (KL ≥ 2), and seven normal weight subjects, who had not developed knee OA at 4-year follow-up, were obtained from the Osteoarthritis Initiative database (OAI) (http://www.oai.ucsf.edu/). Ethical approval for collecting all subject information was provided by the OAI. Inclusion criteria and information about subjects are presented in Figure 1.

MOAKS grading of tibial and femoral cartilages of six obese (one of the selected obese subjects did not have follow-up MRI) and seven normal weight subjects was performed based on 4-year follow-up MRI by a radiologist with an experience in musculoskeletal imaging. We considered MOAKS grading only for the tibiofemoral contact region, since we did not have patella in the models. MOAKS grades for cartilage loss can be divided into four categories (grade 0: no cartilage loss, grade 1: cartilage loss is <10%, grade 2: cartilage loss is 10 - 75%, and grade 3: cartilage loss is > 75% of the region of the cartilage surface area)\(^{22}\).

**Finite element analysis**

**Geometry and material models**

The workflow of building the 3D FE models of the knee joints is presented in Figure 2. For more detailed information on the models’ geometries and FE meshes, see Supplementary material.

In the models, cartilage was considered as a transversely isotropic poroelastic material, instead of a more complex fibril-reinforced poroelastic material, because it
works fast in FE simulations, is easy to implement, and maximum principal stresses of these two materials are close to each other with a proper choice of the material parameters as it was proven in a recent study\textsuperscript{27}. Due to short term dynamic loading and focus being on cartilage, the menisci were modeled as a transversely isotropic and elastic material. In this material, the fluid load support was considered with a proper choice of the material parameters from previous experimental studies\textsuperscript{12, 16, 19, 39}. All material parameters are presented in Table 1.

\textit{Simplified gait}

Since the OAI dataset does not include subject-specific gait data, the generic gait loading was used (Figure 2b), which was based on axial forces and flexion-extension rotations\textsuperscript{6, 29} with free varus-valgus rotations, similarly as in a previous study\textsuperscript{27}. It was assumed that the forces in \% of body weight (BW) and flexion angles are the same for all subjects and those after simulated weight loss (maximum of about 220\% of BW). Therefore, the absolute values of the implemented loading forces (in Newtons) were calculated separately for each model with respect to subjects’ BW. More detailed description on the boundary and loading conditions can be seen from Supplementary material and a previous study\textsuperscript{27}.

\textit{Simulations}

As cumulatively accumulated chronic overloading, which obese subjects presumably experience, has been suggested to cause a significant risk for the onset and progression of cartilage degeneration\textsuperscript{24, 36, 44}, and maximum principal stress is typically considered as a parameter to analyze the point of failure\textsuperscript{5, 15}, cumulative maximum principal stresses were analyzed and calculated for each element of tibial and femoral cartilages. In our model, this parameter represented tensile failure limit of cartilage\textsuperscript{11}. 
Cumulative maximum principal stresses in each element of cartilage, $\text{cum} S_{el}^+$, were calculated based on the following equation:

$$\text{cum} S_{el}^+ = \sum_{t=1}^{N} \left( S_{el_t}^+ \times \frac{\text{INC}_t}{T} \right)$$

where $S_{el_t}^+$ is the maximum principal stress in certain element $(el)$ during each time increment $(t)$, $N$ is the total number of time increments, $\text{INC}_t$ is the duration of time increment $t$, and $T$ is the total time (0.8 s). Then, peak cumulative maximum principal stresses (the maximum value in the elements of femoral/tibial cartilage) and volumes of elements where cumulative stresses exceeded certain thresholds (>5 MPa$^{11}$, > 6 MPa, > 7 MPa$^{36}$) were analyzed and compared between normal weight and obese subjects. Identical analyses were also performed to obese subjects after weight loss, which was simulated by reducing the axial forces implemented to the reference point during gait according to the new BW (BMI = 24 kg/m$^2$).

In addition to cumulative stresses, average maximum principal stresses, maximum principal logarithmic strains, fluid pressures and cartilage-cartilage contact pressures over the cartilage-cartilage contact area of tibial cartilage were analyzed from the second peak force of the stance (when cartilage experienced the highest forces). The results were compared between the groups (more details in Supplementary material).

**Statistical analysis**

Statistical analysis was performed by using SPSS 24 (IBM SPSS Statistics). Mann-Whitney test was used when comparing cumulative stresses and volumes of elements of normal weight and obese subjects. Wilcoxon test was used when comparing obese subjects with those after simulated weight loss. Spearman test was used to analyze correlations between MOAKS/KL scores and peak cumulative stresses, and between
MOAKS/KL scores and total volumes of elements with different threshold levels of cumulative stresses. The level of significance was set to $p < 0.05$. 
5. Results

Stresses, strains, contact pressures and fluid pressures

In the whole femoral cartilage, lateral tibial cartilage and medial tibial cartilage, average values of peak (highest) cumulative maximum principal stresses of obese subjects were 7.2 ± 3.5 MPa, 7.9 ± 1.3 MPa and 7.5 ± 2.3 MPa, respectively, and they were significantly higher ($p < 0.05$) compared to those of obese subjects with simulated weight loss (5.9 ± 2.8 MPa, 6.8 ± 0.8 MPa and 6.6 ± 2.0 MPa, respectively) (Figures 3, 4 and 5a). There were no statistically significant differences when comparing peak cumulative stresses of cartilage between obese subjects and normal weight subjects (5.4 ± 2.0 MPa, 7.6 ± 1.9 MPa and 6.0 ± 0.7 MPa in the femoral, lateral tibial and medial tibial cartilage, respectively). On the other hand, average contact pressures and maximum principal strains over the cartilage-cartilage contact area were significantly higher ($p < 0.05$) for obese compared to normal weight subjects both in the lateral and medial tibial cartilage during the second peak force of the stance (Figure S1 in Supplementary material). This difference was also observed for average fluid pressures and maximum principal stresses in the medial tibial cartilage.

Total volumes of elements with different levels of cumulative stresses

In the femoral cartilage, total volumes of elements with cumulative maximum principal stresses exceeding the chosen thresholds were not significantly different between the groups (Figure 5b). In the lateral tibial cartilage in obese subjects, the simulated weight loss demonstrated a significant ($p < 0.05$) reduction (by ~2 times) of total volumes of elements with cumulative stresses exceeding 5 MPa, 6 MPa or 7 MPa. In the same location, total volumes of elements with cumulative stresses over 5 MPa were
significantly ($p < 0.05$) higher (by $\sim 2$ times) for obese compared to normal weight subjects.

In the medial tibial cartilage in obese subjects, total volumes of elements with cumulative stresses over 5 MPa were significantly ($p < 0.05$) higher (by $\sim 2$ times) compared to those of subjects after weight loss (Figure 5b). When comparing total volumes of elements of obese and normal weight subjects, there were no significant differences in this location.

**Comparison to radiography and MRI**

Locations of high cumulative stresses in most of the overweight and normal weight subjects were in a good agreement with the locations of the cartilage loss shown by 4-year follow-up MRI and MOAKS grading from the central part of tibial cartilage (Figure 6). Furthermore, for one normal weight subject (the fifth image on the right of Figure 6), relatively high cumulative stresses were observed in the lateral compartment of tibial cartilage. This location showed also changes in MOAKS during the 4-year follow up (from 0 to 3), while the KL grade remained zero. On the other hand, cumulative stresses of one obese subject were relatively low both in the lateral and medial compartments and also the MOAKS grade remained zero during the follow-up (the third image on the left of Figure 6).

There was no significant ($p > 0.05$) correlation between the peak cumulative stresses in femoral and tibial cartilages at the baseline and MOAKS or KL scores at 4-year follow-up in obese and normal weight subjects. On the other hand, there was a significant correlation between MOAKS scores and total volumes of elements in the femoral cartilage with cumulative stresses over 6 MPa ($p < 0.05$) and 7 MPa ($p < 0.01$); and in the lateral tibial cartilage with cumulative stresses over 6 MPa ($p < 0.05$).
6. Discussion

Given the strong evidence linking obesity and knee OA\textsuperscript{17} and that chronic, cumulative overloading has been suggested to be an important factor for the initiation and progression of OA\textsuperscript{36, 44}, we performed a FE analysis by calculating cumulative maximum principal stresses in obese and normal weight subjects during simplified gait loading. The results were compared with radiographic and MRI findings. We also simulated the effect of weight loss on cartilage responses. Peak cumulative stresses of cartilage could not show differences between obese and normal weight subjects.

However, it was demonstrated that obese subjects, compared to normal weight subjects, have significantly larger volumes of elements exceeding cumulative stresses of 5 MPa in the tibial cartilage. These results propose that the area/volume may be more relevant than just the peak cumulative stress value when predicting knee OA.

For most subjects, MOAKS grading was consistent with the biomechanical analysis. Simulated weight loss in obese subjects reduced mostly the volumes of elements with high stresses in the tibial cartilage. These results suggest that the relatively simple cumulative stress parameter might be feasible for prediction of the risk areas/volumes for the onset and progression of knee OA in obese subjects.

Several studies have reported that BMI is negatively associated with tibial cartilage volume\textsuperscript{2, 14}. In our study, volumes of elements with cumulative stresses over 5 MPa were specifically higher in the lateral tibial cartilage in obese subjects compared to healthy controls. Moreover, a significant correlation was observed between 4-year follow-up MOAKS scores in the lateral tibial cartilage and total volumes of elements with cumulative stresses over 6 MPa at the baseline. Cicuttini et al.\textsuperscript{8} have also demonstrated that greater BMI is significantly associated with increased progression of lateral but not medial cartilage defects.
For most of the obese subjects, locations of high cumulative stresses in central regions of tibial cartilage at the baseline were able to indicate possible cartilage degeneration areas (Figure 6) shown by 4-year follow-up MRI. This was true except for one obese subject (Figure 6, top left image), who had high cumulative stresses in the lateral compartment of tibia at the baseline while MOAKS showed cartilage degeneration in the medial compartment at 4-year follow-up MRI. This difference may be due to the generic gait data because the OAI database does not include subject-specific loading.

Different loading could change the load distribution between lateral and medial compartments\(^{33}\). On the other hand, biomechanical analysis also showed differences for one normal weight subject (the fifth image on the right of Figure 6) who had a MOAKS score of 3 at 4-year follow-up but KL grade stayed at zero. This suggests that the biomechanical analysis conducted for the baseline can possibly predict small changes in cartilage that could not be observed by radiographic grading even after four years\(^{22,23}\). The model also showed low cartilage stresses for one obese subject (the third image on the left of Figure 6) whose MOAKS grade was zero but KL grade was 2. This result suggests that this joint had other osteoarthritic signs than those seen in cartilage and that the biomechanical analysis could reveal minimal risk for cartilage degeneration.

The effect of BW on risk areas/volumes for cartilage degeneration was studied by testing several threshold levels (5 - 7 MPa)\(^{11,36}\) of peak cumulative stresses. The threshold of 5 MPa revealed the most significant differences between the groups, especially in the lateral tibial cartilage (Figures 4 and 5b). This threshold limit is in accordance with a previous experimental study of cartilage failure\(^{11}\). On the other hand, it should be reminded that these threshold values can change from patient to
patient\textsuperscript{38}. If this limit or cartilage properties\textsuperscript{42} could be obtained in a patient-specific manner, the analysis might become more accurate.

Since obesity is a known risk factor for the development and progression of knee OA, it is important to detect the relationship between weight loss and peak stresses in cartilage and to clarify the pathophysiologic role of obesity in knee OA. Much more modest reductions in BW than simulated here have been suggested to show promising results when considering self-reported physical function\textsuperscript{34} and odds for developing osteoarthritis\textsuperscript{18}. Our study showed that simulated weight loss (by \textasciitilde 29\%) to normal BMI in obese subjects leads to a significant (\(p < 0.05\)) reduction of the highest cumulative stresses in tibial and femoral cartilages by \textasciitilde 13\% and \textasciitilde 18\%, respectively, being in the same range as in normal weight controls. Areas of high cumulative stresses in tibial cartilage also decreased after the simulated weight loss. The main reason to the “extreme” weight loss was to reach normal BMI and to have a fair comparison of cumulative stresses with normal weight subjects. This way we might see whether the risk for OA, from the mechanical point of view, reduces to the levels of normal weight subjects who did not get OA during the follow-up. If this would not happen, then there would be probably other factors than just weight (such as knee geometry). We have also tested the weight loss of 10\% BW in one obese subject, and the highest maximum principal stresses in cartilage were decreased only by 2\% in the lateral side and 4\% in the medial side.

We also analyzed average (over the cartilage-cartilage contact area) maximum principal stresses, logarithmic strains, fluid pressures and cartilage-cartilage contact pressures in tibial cartilage (Supplementary material). It was found that, similarly with the volumes of element exceeding the 5 MPa threshold, strains and contact pressures of the lateral tibial cartilage (primary location for elevated MOAKS) were significantly
higher in obese subjects compared to normal weight subjects, suggesting that these
parameters could also be used to estimate risks for osteoarthritis. However, these
parameters did not correlate with MOAKS and KL scores at 4-year follow-up, such as
volumes of elements with high cumulative stresses did in the lateral tibial cartilage.
They also did not take into account the cumulative effect of the cartilage loading during
gait in a location (element) specific manner, which has been suggested to strongly
contribute to osteoarthritis\textsuperscript{9, 41, 44}. Nonetheless, more studies and subjects would be
needed to be investigated before conclusive statements of different parameters and
their ability to correlate with the progression of osteoarthritis can be drawn.

This study included the same types of tissues and used the same type of material
models and loading conditions as in Klets et al.\textsuperscript{27}, where the modelling approach was
compared against experiments and other existing models. Model limitations were also
discussed there and sensitivity analysis of the effect of ligaments, motion, material
models and material properties of cartilage was conducted. Efficient computational
models, which can be applied in clinical practice, are not optimal without associated
simplifications for instance in the type of loading and material models. This allows to
study more subjects. Our FE modeling-based study included 14 subjects and 21
models while most FE models, both simplified and advanced, are usually based on
one subject\textsuperscript{25, 30}.

The use of simplified loading is both an advantage (simple implementation and
guaranteed convergence) and a limitation (not all kinematics taken into account) of the
study. Since the OAI database does not have subject-specific gait data, we used
generic gait adopted directly from other studies\textsuperscript{6, 29, 35}. The subject-specific gait data
could improve the accuracy of detecting the locations of potential degeneration areas
in cartilage. Still, in clinical practice, obtaining subject-specific gait data is typically not
feasible. And even with the simplified loading, based only on flexion/extension angles and axial forces with free varus/valgus rotations, our models were still able to predict locations of cartilage degeneration for most of the subjects detected by MOAKS scores at 4-year follow-up. The effect of different gait cycle (with 6 degrees of freedom) was tested previously and compared to the simplified loading used here. It was found that conclusions about the differences in maximum principal stresses between the models with different material models did not change by a more complete set of kinematic parameters.

It was reported previously that weight loss significantly reduces the peak knee flexion angle in obese subjects. On the other hand, that absolute difference was only 0.4 degrees. Furthermore, there is no clear consensus on differences in knee joint kinematics between obese and normal weight subjects. For instance, it was shown that obese subjects have a smaller knee flexion angle during walking compared to non-obese individuals, while another study reported that the range of knee flexion angles during gait in obese subjects is similar to normal weight subjects. Also, no significant differences were reported in internal/external rotations of the knee joints between obese and normal weight subjects, while internal/external moments were shown to be altered after weight loss. Since we did not have gait data available, the FE model did not take into account other biomechanical factors than BW that could change in response to weight loss. However, we have tested how including internal-external rotation in the model affects the result. That model, compared to the model with the used simplified loading, showed 1% difference in maximum principal stresses in cartilage at the first and second peak forces during gait, and the distribution of maximum principal stresses was similar between the models (Figures S2 and S3 in Supplementary material).
It should be noted that we simulated instantaneous weight loss and an example of such a rapid weight loss is a bariatric surgery-induced weight loss. If someone would want to study time-dependent changes of weight loss on subject-specific cartilage stresses, then time-dependent information of several factors should be known.

Our models were purely mechanical and did not include biophysical, biochemical, and metabolic factors, which could also lead to cartilage degeneration especially for obese subjects. However, we did not have this information and there are no such models of the knee joint in the literature where these factors would have been taken into account. Before implementing these factors in the knee model, their effect should be tested and validated first using controlled *in vitro* experiments.

When analyzing the effect of BW on OA, we did not separate muscle mass and fat mass, while it was shown previously that they have opposite effects on knee OA; greater fat percentage increases the risks of OA while greater muscle strength prevents OA progression. If there was more experimental data available for the studied subjects and these factors could be taken into account in the model, their effects could be tested.

We compared cartilage stresses in obese subjects, who had developed OA in 4-years, with normal weight subjects without OA. In the future, normal weight subjects, who develop OA at the follow-up and obese subjects, who do not develop OA at the follow-up, should be included. Also, we did not take into account the effect of gender when comparing obese and normal weight subjects, while it has been proven that females have higher prevalence of knee OA than men. In this study, anatomical factors and alignment for each model were obtained from MRI and gender was therefore implicitly taken into account.
OA is estimated to affect more than 37% of adults over the age of 60 and is associated with considerable loss in productivity, pain and substantial healthcare expenditures. Greater BMI has been associated with higher risk of developing OA.

The prevalence of obesity has increased over the past three decades. Thus, the presented approach and analyzed parameters might be clinically useful in evaluating subject-specific effects of weight and weight loss on cartilage responses and possible risk for the progression of knee OA.
7. Acknowledgements

The research leading to results in the manuscript has received funding from the University of Oulu (strategic funding), the Medical Research Center of University of Oulu and Oulu University Hospital, Academy of Finland (grants 286526, 268378 and 305138), Sigrid Juselius Foundation, and Finnish Cultural Foundation (North Savo regional fund, grant no. 65142194). The OAI is a public-private partnership comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; N01-AR-2-2262) funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by the OAI Study Investigators. Private funding partners include Merck Research Laboratories; Novartis Pharmaceuticals Corporation, GlaxoSmithKline; and Pfizer, Inc. Private sector funding for the OAI is managed by the Foundation for the National Institutes of Health. This manuscript was prepared using an OAI public use data set and does not necessarily reflect the opinions or views of the OAI investigators, the NIH, or the private funding partners.
8. References


44. Seedhom, B. B. Conditioning of cartilage during normal activities is an important factor in the development of osteoarthritis. Rheumatology (Oxford) 45:146-149, 2006.


Table 1. Material parameters for cartilage and meniscus.

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$E_p$ is in-plane Young’s modulus, $E_i$ is out-of-plane Young’s modulus, $\nu_p$ is in-plane Poisson’s ratio, $\nu_{ip}$ is out-of-plane Poisson’s ratio, $G_i$ is out-of-plane shear modulus, $k$ is permeability and $e_0$ is initial void ratio.
Figure 1. Inclusion criteria from OAI data.

Figure 2. The workflow of building the 3D FE models of the knee joint. (a) Femoral and tibial cartilages, and menisci were manually segmented from the baseline MRI and 3D geometries were reconstructed. (b) 3D FE model meshes were created, with material properties from Table 1, and a simplified gait cycle loading was applied, with free varus-valgus rotation, to the reference point (RP) of the knee joint center\textsuperscript{6, 27, 29}. (c) Cumulative maximum principal stresses and other parameters were analyzed.

Figure 3. Distribution of cumulative maximum principal stresses over the stance phase of gait in femoral cartilage. Values of the highest cumulative stresses over the entire femoral cartilage are in the right corner of each image.

Figure 4. Distribution of cumulative maximum principal stresses over the stance phase of gait in tibial cartilage. Values of the highest cumulative stresses over the entire tibial cartilage are in the right corner of each image.

Figure 5. Comparison of (a) peak (highest) cumulative maximum principal stresses in femoral and tibial cartilages in obese subjects before and after simulated weight loss and in normal weight subjects; and (b) total volumes of elements in femoral and tibial cartilages that have cumulative maximum principal stresses (CS) of >5 MPa, >6 MPa, >7 MPa in obese subjects with and without simulated weight loss and in normal weight subjects. Circle (○) and cross-line (—) represent mean and median values, respectively.

Figure 6. Distribution of cumulative maximum principal stresses in tibial cartilages of obese and healthy subjects together with MOAKS scores from the central part of tibial cartilage and KL scores.
4796 subjects

- Age < 65 years
- KL = 0 at the baseline
- No knee injuries
- Never operated meniscus and cartilage

429 subjects

- BMI ≤ 24 kg/m²
- KL = 0 in 4-year follow-up

Normal weight subjects

- 3 males and 4 females
- Age: 55 ± 4 years old
- Height: 168 ± 9.4 cm
- BW: 66.4 ± 10.9 kg
- BMI: 23 ± 2 kg/m²

*Obese subjects

- BMI ≥ 30 kg/m²
- KL ≥ 2 in 4-year follow-up

- 3 males and 4 females
- Age: 55 ± 3 years old
- Height: 168.1 ± 5.0 cm
- BW: 96.5 ± 14.5 kg
- BMI: 33 ± 3 kg/m²

*One subject was not obese:
BMI = 29.3 kg/m²
Segmentation  3D generation

(a)

3D DESS MRI

FE modeling

(b)

Gait cycle loading

Cumulative stresses

(c)
Obese subjects

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Obese subjects after simulated weight loss

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<tbody>
<tr>
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<tr>
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<tr>
<td>24</td>
<td>11.5MPa</td>
</tr>
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<td>5.2MPa</td>
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<tr>
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<td>2.9MPa</td>
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<td>24</td>
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<td>24</td>
<td>4.8MPa</td>
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Normal weight subjects

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<tr>
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