Title

021 PREDICTION OF INCIDENT CONSTANT AND INTERMITTENT KNEE PAIN BY CARTILAGE THICKNESS AND T2 VALUES: DATA FROM THE OAI

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In this study we observed a substantially greater rate of cartilage loss for readings performed unblinded to time point. It is likely that rates of change observed with blinded analysis are closer to reality, as readers may be biased towards cartilage loss, knowing the natural progression of OA, with unblinded reading. Our results do not confirm that, in case of sprifermin, detection of DMOAD treatment is enhanced when longitudinal MRIs are read unblinded to order, but the sensitivity was similar to blinded analysis. Hence, the choice on blinded vs. unblinded analysis may be based on other criteria, such as whether determining non-biased rates of structural progression is key, whether time delays at study end are acceptable with blinded readings, and/or whether interim analysis is desired.

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PREDICTION OF INCIDENT CONSTANT AND INTERMITTENT KNEE PAIN BY CARTILAGE THICKNESS AND T2 VALUES: DATA FROM THE OAI

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Purpose (the aim of the study): Treatment strategies in osteoarthritis (OA) aim to prevent the loss of cartilage and relieve pain. Evidence suggests that focal cartilage loss explains worsening knee pain to a limited extent. Compositional MRI including T_2 values can detect degeneration before cartilage loss is apparent. But knowledge is limited as to whether changes in cartilage composition or thickness precede pain. The goal of our study was to investigate whether incident knee pain is associated with cartilage thickness and T_2 values assessed in MRI scans 1 to 4 years before the onset of knee pain.

Methods: Participants who had Intermittent and Constant Osteoarthritis Pain (ICOAP) scores at the 48-month visit (defined as baseline [BL]) were selected from the Osteoarthritis Initiative (OAI). Right knee magnetic resonance imaging (MRI) at yearly visits 1 to 4 years before BL were collected. Participants with pain, aching, or stiffness in the right knee more than half the days of a month for the past 48 months before BL were excluded to focus only on participants with incident pain (Fig. 1). Cartilage was automatically segmented in a three-dimensional double-echo steady-state (3D-DESS) sequence using a 3D V-Net architecture. Quantitative T_2 imaging was performed using a sagittal multi-echo spin-echo T2 mapping sequence. Average cartilage thickness and T_2 values were extracted in medial femoral (MF), lateral femoral (LF), medial tibial (MT), lateral tibial (LT), and patellar regions (PAT). Femoral cartilage thickness was limited to the central weight bearing areas. Associations of cartilage measures with ICOAP (linear scale from 0-100) were calculated using mixed-effects linear regression models with repeated observations (visits before BL) and a Bonferroni-corrected p-level of < 0.0025. Models were adjusted for age, gender, race, body mass index (BMI), and Physical Activity Scale for the Elderly (PASE) score.

Results: ICOAP scores were available in 1592 participants (968 women) without previous symptomatic knee OA. Participants had a mean age of 61.4 ± 9.2 years, BMI of 27.7 ± 4.5 kg/m^2, mean T_2 values of 38.7 ± 2.9, 35.3 ± 2.6, 30.1 ± 2.2, 28.3 ± 2.3, and 33.4 ± 3.1 as well as cartilage thickness of 1.9 ± 0.3, 1.9 ± 0.3, 1.8 ± 0.3, 2.1 ± 0.3, and 2.2 ± 0.4 mm in MF, LF, MT, LT, and PAT regions, respectively, at 4 years before BL. Associations of cartilage thickness and T_2 values in the 4 years before BL with incident knee pain are shown in Table 1 and Table 2, respectively. Incident intermittent pain was significantly associated with decreasing cartilage thickness in the PAT region ($p < 0.001$), but with increasing cartilage thickness in the LF region (p=0.001). Incident constant pain was significantly associated with decreasing cartilage thickness in the MF, MT, and LT regions (each $p < 0.001$). Incident intermittent and constant pain was significantly associated with increasing T_2 values in the MF region ($p < 0.001$ and p=0.001, respectively).

Conclusions: We found that elevated T_2 values in the medial femoral cartilage predicted future intermittent and constant knee pain. Decreasing patellar cartilage thickness predicted intermittent knee pain. Decreasing medial femoral and tibial as well as lateral tibial cartilage thickness predicted constant knee pain. In contrast, increasing lateral femoral cartilage thickness predicted intermittent knee pain. Unlike previous studies, we were able to demonstrate a strong relationship between quantitative cartilage loss and incident knee pain in all compartments except for the lateral femoral region. Increasing lateral femoral cartilage thickness may be related to cartilage swelling which is found in the early disease stages associated with intermittent knee pain.

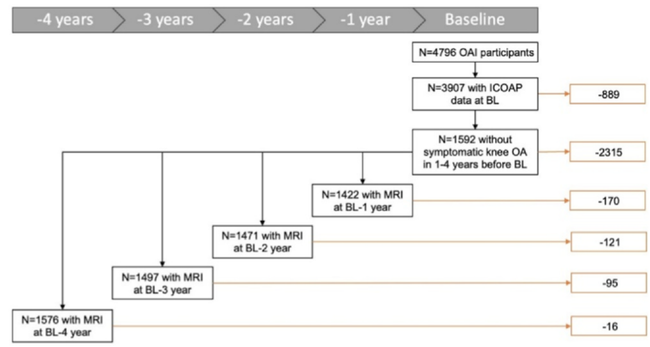

Fig. 1: Selection of study subjects. OAI, Osteoarthritis Initiative; ICOAP, Intermittent and Constant Osteoarthritis Pain; BL, baseline (= 48-months study visit).

022
PATELLA SHAPE ANALYSIS PREDICTS KNEE ARTHROPLASTY RISK ENHANCED BY DIFFUSION MODEL

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Purpose (the aim of the study): Patellofemoral(PF) OA has been revealed to possess stronger associations with knee OA symptoms and functional impairments than tibiofemoral OA, morphological changes that manifest the disease's early development also tend to originate from the PF joint. The dislocation and osteophytes development are major pathological signs of PFOA aggravation reflected in patella morphology.

To enable early interventions for knee OA management, prognostic AI that could accurately forecast and explain the risk of disease deterioration are demanded. Published research has shown benefits of introducing image generative model as an intermediate step prior to predicting knee OA progression from radiographs. By leveraging the remarkable advancement in image generation quality of diffusion models recently, we were able to perform a model-based patella morphology trajectory prediction, significantly enhancing the risk prediction of requiring knee arthroplasty(KA) in the future.

Methods: In our pipeline (Fig1), a course-to-fine patella segmentation model was first developed to extract precise patella mask from lateral knee radiographs. Inferencing on all paired knee radiographs collected at the baseline visit and 60-month follow-up visit from the MOST dataset, we obtained 2540 sets of precise patella masks pairs (Train:Test = 8:2).

A diffusion model generates realistic samples by gradual transformation of a simple to the target distribution by repetitive addition and removal of noise. Inspired by MedSegDiff, a diffusion model architecture designed for medical image segmentation, our image prediction diffusion model instead encodes baseline patella masks as conditional embeddings to the U-Net CNN that trained to reconstruct follow-up patella shapes from noise. By modeling the correlations of latent variables between baseline and future follow-up patella shape pairs, it could predict the trajectory of morphological changes of a patella bone by sampling on baseline data, generating the synthetic follow-up patella shape at 60-month.

To predict whether the subject receives KA within future 60-month period, coordinates of patella shapes are extracted from synthetic masks as model input. Baseline patella shapes are also extracted and analysed in a similar manner to compare the prognostic performance between a common end-to-end learning approach and our novel synthetic prediction approach. We specifically designed a 2-channel 1D-FCN with circular padding to effectively model the shapes as closed line segments.

Results: Our segmentation pipeline reports a 0.9729 Dice score and 0.9472 IoU score, capturing precise patella shapes for further analysis. Fig2 demonstrates that our diffusion model can correctly predict morphological changes of the patella, including deformation and osteophytes