method of lesion segmentation. Number of BML lesions correlates less well than WOMRS score with their volume. There is a fixed error due to the nature of the WOMRS method which biases the results in favour of higher WOMRS measurements.

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SENSITIVITY OF CEST MRI OF HUMAN KNEE CARTILAGE IN VIVO AT 3 T AND 7 T

Purpose: To evaluate the sensitivity of chemical-exchange-saturation transfer imaging of glycosaminoglycans (GAG) (gagCEST) on human knee cartilage in vivo at 3T and 7T.

Methods: The study was conducted under an approved Institutional Review Board protocol of the University of Pennsylvania. With an informed consent CEST imaging was performed on the knees of six healthy volunteers using 18-cm diameter, eight-channel transmit-receive phased-array (PA) knee coil on Siemens 3T (Magnetom Tim Trio, Siemens Medical Solutions, Malvern, PA) and 7T MR scanner (Siemens Medical Solutions, Malvern, PA). A new pulse sequence was designed to use a frequency selective saturation pulse train followed by a segmented RF spoiled gradient echo (GRE) readout sequence. The sequence parameters were: slice thickness = 5 mm, GRE flip angle = 10°, GRE readout TR = 5.6 ms, TE = 2.7 ms, field of view = 140 × 140 mm², matrix size = 128×128, and one saturation pulse and 128 segments acquired every 10 sec to enable full T1 recovery. Multiple CEST images were collected using a saturation pulse with average B1rms of 31 (0.7 mT), 62 (1.4 mT), 93 (2.1 mT), and 124 Hz (2.8 mT) and saturation offsets relative to water ranging from −3.0 to +3ppm in steps of 0.1ppm. The total scan time was ~30 minutes. To alleviate B0 and B1 inhomogeneity contribution from CEST effect, B0 and B1 maps from the same imaging slices were also obtained.

Results: Without any corrections for B0 inhomogeneity a clear shift (~0.5–0.6ppm) in the Z-spectra was observed in the human knee cartilage. This shift in the human data is removed after correcting for the B0 inhomogeneity. Without any correction for B0 large gagCEST effect (~20–25%) was observed in cartilage (Figures 1, 2). After B0 correction, with the imaging and saturation pulse parameters used, the calculated average gagCEST from cartilage was ~1% at 3T (Figures 1, 2) and 7.4±0.3% at 7T (Figure 3). The effect of B1 inhomogeneity was minor in the current study.

Conclusion: Because of the uneven geometry of human knee, despite extensive shimming of B0 field, there is a substantial B0 field variation in knee cartilage. Without correction for the B0 field inhomogeneity, a surprisingly large (20–30%) gagCEST effect is observed in knee cartilage in vivo. Correction of the B0 inhomogeneity has shown that there is only a very small (~1%) gagCEST observable in cartilage in vivo at 3T and a significantly larger gagCEST of ~7% at 7T. Since GAG loss from cartilage is expected to result in further reduction in gagCEST, this method is not expected to lead to accurate quantification of GAG content in healthy as well as in degenerated cartilage at 3T. However, given the magnitude of gagCEST measured at high fields such as 7T, this technique holds promise for studying cartilage degeneration at 7T and higher fields.

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THE MINIMAL CLINICALLY IMPORTANT DIFFERENCE (MCID) IN CARTILAGE VOLUME AND THICKNESS CHANGE IN PERSONS WITH KNEE OSTEOARTHRITIS
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Purpose: Investigators use quantitative cartilage morphometry to document longitudinal changes in osteoarthritic knees. With rapid evolution in the capacity of MRI to detect small changes, clinicians confront the question of how much change is clinically meaningful. We sought to establish the minimal clinically important difference in MRI-based longitudinal cartilage evaluation of persons with knee OA.

Methods: We used data from one knee per person of 429 participants of the Progression Cohort of the Osteoarthritis Initiative (OAI), defined by the presence of frequent symptoms and definite radiographic knee OA, who had baseline and 24 month quantitative MRI assessment. Manual tracing of the total subchondral bone area of the medial/lateral tibia (MT/LT) and central (weight-bearing) medial/lateral femoral condyle (cMF/cLF) was performed by Chondrometrics GmbH (Anning, Germany) and publicly released. We considered the mean cartilage thickness over the entire subchondral bone area with (ThCtAB) and without (ThCcAB) denuded areas. Results for the medial and lateral femorotibial compartments were obtained by summing values of MT+cMF and LT+cLF respectively. We defined the MCID in cartilage volume and thickness changes from baseline to 24 months using the indirect anchor method, in which changes exceeding a previously established minimum difference were considered to be clinically important. The anchor was defined by worsening by at least 13 points on WOMAC Function scale (Angst, 2001). MRI-based morphologic measures were compared between knees that showed discrimination between those who did and who did not achieve the MCID at a 0.05 significance level.

Results: Among 429 knees, 43% had K-L grade 2 and 54% K-L grade 3. 68% had OA in medial compartment. 11% worsened by at least 13 points in WOMAC Function score over 24 months. A limited set of MRI-based cartilage morphology measures discriminated (at p = 0.05) between those who did and those who did not worsen in WOMAC Function by the MCID. These included cartilage volume, cartilage thickness (including and excluding denuded area) as well as the area of subchondral bone covered by cartilage – all measured in the central (weight-bearing) medial femur.
The other measures that discriminated between those reaching the MCID and those who did not were cartilage volume and thickness of total medial femorotibial compartment. The Figure illustrates SRM thresholds corresponding to the MCID in cartilage morphology measurements, where the differences between those who achieve worsening defined by MCID were statistically significantly different (p < 0.05) from those who did not. MCID for cartilage volume loss over the central medial femoral and medial femorotibial compartment was estimated at 6.6% and 6.7% respectively. MCID for cartilage thickness loss in the central medial femoral compartment was estimated at 6.3% including denuded area and 3.3% excluding it. These 3–7% losses correspond to SRMs (mean change / SD change) of approximately 0.5 to 0.65 (Figure).

Figure: Changes over 24 months in cartilage morphology stratified by achieving MCID in functional worsening.

Conclusions: These data offer clinically meaningful thresholds in quantitative cartilage morphology changes measured by MRI. Planning clinical trials based on changes in cartilage volume and thickness in the central medial femur may lead to the most efficient design in terms of sample size.

386 MAGNETIC RESONANCE IMAGING; CARTILAGE DEFECT ASSESSMENT IS LESS SENSITIVE THAN THE QUANTIFICATION OF CARTILAGE VOLUME LOSS IN A KNEE OSTEOARTHRITIS DMOAD TRAIL
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Purpose: Magnetic resonance imaging (MRI) has become the tool of choice for the assessment of knee osteoarthritis (OA) structural changes and disease severity in cross-sectional and longitudinal studies. Amongst methods currently used for cartilage evaluation are semiquantitative scoring systems and quantitative volumetry. For the former method, MRI sequences vary greatly among studies and are subject to debate. This study aimed to evaluate both the impact of the choice of MRI sequences on the cartilage defect assessment and the sensitivity to change of semiquantitative and quantitative methods.

Methods: Post-hoc analysis of the MR image database of two recent clinical trials in knee OA (Cohort 1, n=24 and Cohort 2, n=143) was performed. Standard inclusion and exclusion criteria were employed. For both cohorts, a gradient echo fat suppressed T1-weighted (T1) sequence was used, and patients of Cohort 1 underwent an additional fast spin echo fat suppressed proton density (PD) sequence. MRI images were performed at baseline and 2 years. Cohort 2 included patients from a trial examining the chondroprotective effect of licofoleone (200 mg bid) versus naproxen (500 mg bid). Cohort 1 was used to assess the impact of the two MRI sequences on cartilage defect scores, and Cohort 2 to evaluate, for the two methods, the sensitivity to change and detectability of the treatment effect. The cartilage defects and cartilage volume were evaluated using the semiquantitative WORMS5 method and the proprietary software Cartiscope™, respectively, on the same patient. Evaluation was performed for the global knee (GK) as well as medial (MC) and lateral (LC) compartments and subregions. Statistical analysis for Cohort 1 included the Wilcoxon signed rank test and for Cohort 2 the Student’s t-test and the standardized response mean (SRM) of change.

Results: In Cohort 1, the cartilage defect assessment provided consistent and significantly higher scores in PD than in T1 sequences both at baseline and 2 years (p < 0.001). Interestingly, in all regions studied, the change from baseline to 2 years was not significantly different (p > 0.377). In Cohort 2, the SRM for the cartilage defects and volume loss were respectively 0.365 and 2.000 for GK; 0.293, 1.473 MC; and 0.252, 1.165 LC, indicating that the quantitative cartilage volume evaluation demonstrated greater sensitivity to change. With regard to treatment effect, data revealed no significant difference in cartilage defect score change over 2 years between the two treatment groups, while the change in cartilage volume loss demonstrated a significant difference in GK (p = 0.009) and LC (p = 0.026) as previously published[1].

Conclusions: OA cartilage defects assessed with the PD MRI sequence showed a higher score than T1 in cross-sectional evaluation. However, neither of the MRI sequences demonstrated superiority in assessing cartilage defect change over time; therefore both are valuable for evaluating cartilage lesions cross-sectionally. With regard to clinical DMOAD trials, quantitative assessment of cartilage volume loss is more sensitive than the semiquantitative method for the evaluation of changes in OA cartilage lesions over time.

Reference(s)

387 CARTILAGE T2 RELAXATION TIME MEASUREMENTS AT THE KNEE ARE ASSOCIATED WITH METABOLIC SYNDROME AND LIFESTYLE FACTORS
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Purpose: Prevention of osteoarthritis (OA) may be achieved through modification of lifestyle parameters; among these obesity and metabolic syndrome are of particular interest. T2 relaxation time measurements of hyaline cartilage provide information on cartilage water content and collagen degradation; these measurements provide an early assessment of cartilage degeneration, before there is structural cartilage loss. The aim of this study was to study how individual facets of the metabolic syndrome are associated with cartilage degenerative changes measured with T2 values at the knee using 3T MR images in middle-aged individuals from the Osteoarthritis Initiative (OAI) incidence cohort without radiographic osteoarthritis.

Methods: MR images of right knees of 405, 45–60 year old individuals (n = 205 male, n = 200 female) with risk factors for osteoarthritis but without knee pain and without radiographic findings for osteoarthritis (K/L score 0 and 1) were analyzed. Cartilage segmentation was performed in five compartments (patella, medial tibia, lateral tibia, medial femoral condyle, lateral femoral condyle) and T2 relaxation time maps were generated. Factors analyzed included diabetes mellitus type II (DM, self-reported), body mass index (BMI), abdominal circumference, diastolic and systolic blood pressure, as well as fat content of nutrition. Additionally nicotine consumption and alcohol consumption were evaluated. Statistical significance was determined by using analysis of variance and corrected for differences in age, gender and OA risk factors other than BMI (e.g. history of knee injury, family history of knee replacement, Heredon nodes in hands) in a multivariate linear regression model.

Results: As shown in Figure 1 significantly increased cartilage T2 values were found in individuals presenting with DM (p = 0.0122) and systolic hypertension (P = 0.0464), but not for high diastolic blood pressure. BMI and abdominal circumference showed the strongest effect on T2 changes, which were most prominent in the medial compartment (P < 0.0001; Figure 2). While general alcohol consumption had no effect, increased beer consumption showed a non-significant trend (P = 0.0602). Neither nicotine consumption nor pack years of cigarette smoking were