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The role of periarticular adipose tissue in knee osteoarthritis: data from the osteoarthritis initiative (OAI)

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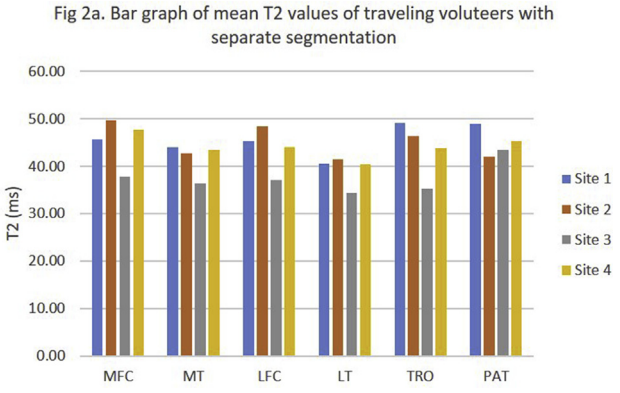
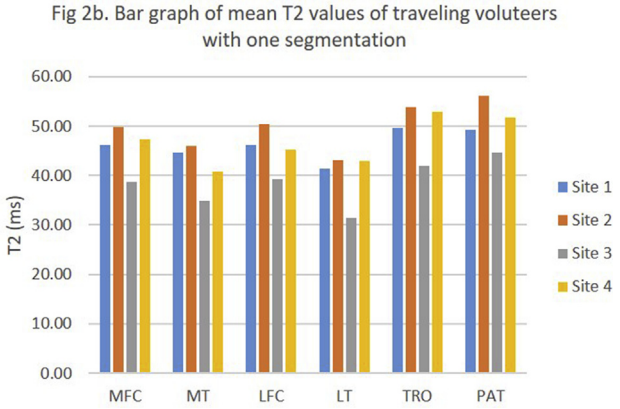
Table 3b
Intra- and inter-site CV of cartilage using the one segmentation with registration (In-vivo)

	Cartilage	MFC	MT	LFC	LT	TRO	PAT
Intra-siteCV (%)	Site 1	1.92	4.23	2.70	2.82	2.49	3.01
	Site 2	3.52	2.51	1.24	0.28	1.23	3.34
	Site 3	6.97	2.07	1.23	4.95	4.20	3.71
	Site 4	4.52	0.76	0.77	2.98	3.63	2.41
Inter-site CV (%)		13.05	13.70	10.60	15.19	14.77	7.76





Results: In phantoms, the average intra- and inter-site CVs were 1.33 % and 5.96% respectively (Table 2, Figure 1). In human subjects, using separate segmentations, the average intra and inter-site CVs were 3.12% and 12.47% respectively, Table 3a. The average intra and inter-site CVs were 2.81% and 12.51% respectively, using the same segmentations after registration, Table 3b. Mean T2 values for each cartilage compartment segmented are shown in Figure 2a and Figure 2b for separate and same segmentations respectively. There were significant differences in T2 measures in all compartment across the sites ($P < 0.05$).
Conclusions: The intra-site repeatability of T2 mapping using MESE sequences were excellent at all sites and on all MR systems (CV < 5%). However, significant differences and large variations of T2 measures across the vendors were observed in this study. T2 derived from MESE sequence is known to be susceptible to B1 inhomogeneity invoked stimulated echoes. The variations we observed may be explained by the different B0 and B1 inhomogeneity at each MR system with different RF coils, and different implementations of the sequence at each MR platforms including acquisition and reconstruction details. T2 mapping techniques which are robust to B0 and B1 inhomogeneity and provide reproducible measures across vendors and sites are needed for large-scale clinical trials. The results need to be confirmed by large scale studies in the future.

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THE ROLE OF PERIARTICULAR ADIPOSE TISSUE IN KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE (OAI)

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Purpose: The relationship of periarticular adipose tissue to knee osteoarthritis (OA) is getting more attention as local inflammatory adipokine production may influence the development and progression of OA. Studies have evaluated supra- and infrapatellar fat pads as intra-articular sources of inflammation. However, associations with local extra-articular subcutaneous fat (SCF) and OA are less well characterized. The aims of this study were to 1) investigate the cross-sectional relationship between the local fat distribution and knee OA and 2) the association between local fat distribution and change in knee OA over 4 years using WORMS as semiquantitative and Magnetic resonance (MR) cartilage T2 relaxation times as quantitative outcome measurements.
Methods: For this study, we selected 278 subjects from the Osteoarthritis initiative (OAI), using the following criteria: (i) availability of MRI of the right knee at baseline and 4-year follow-up, (ii) availability of MRI of the thigh at baseline, (iii) WORMS readings and T2 values available at baseline and 4-year follow-up, (iv) BMI $\geq$ 25 at baseline, (v) Kellgren-Lawrence score of the right knee of 0 - 1 at baseline and (vi) no history of knee surgery or inflammatory arthropathy. Fat distribution around the right knee was measured as thickness of SCF on coronal 3D Flash sequences (medial and lateral; average of measurements on the level of the medial tibial spine and the medial joint space) (Fig.1). Fat thickness anterior to the patellar tendon was obtained on sagittal DESS sequences (perpendicular, level of the lateral tibial spine, mid-level of patellar tendon) (Fig.2).

Fat ratios (lateral / medial side) and total knee fat measurements (lateral + medial + anterior) were calculated. SCF of the right thigh was semi-automatically segmented (Fig.3) to assess cross-sectional area (CSA). Knee cartilage of five compartments (patella, medial and lateral femur,

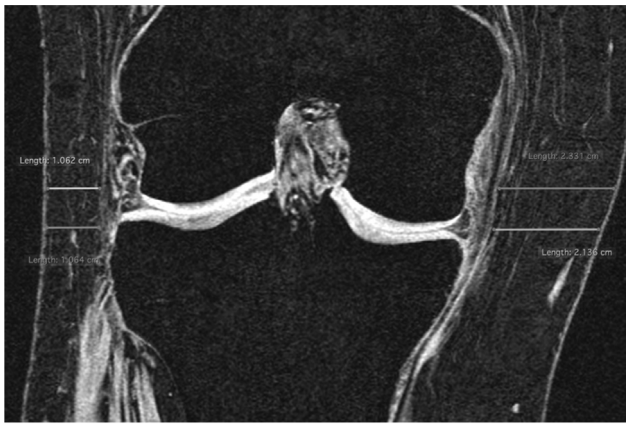

Fig. 1: Example of measurements of subcutaneous fat thickness on the medial and lateral side of the knee.

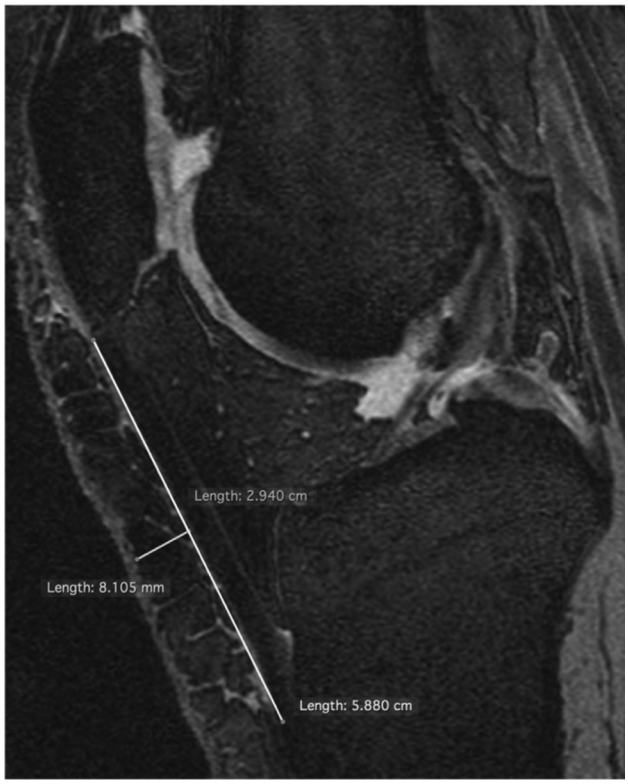

Fig. 2: Measurement of subcutaneous fat anterior to the patellar tendon.

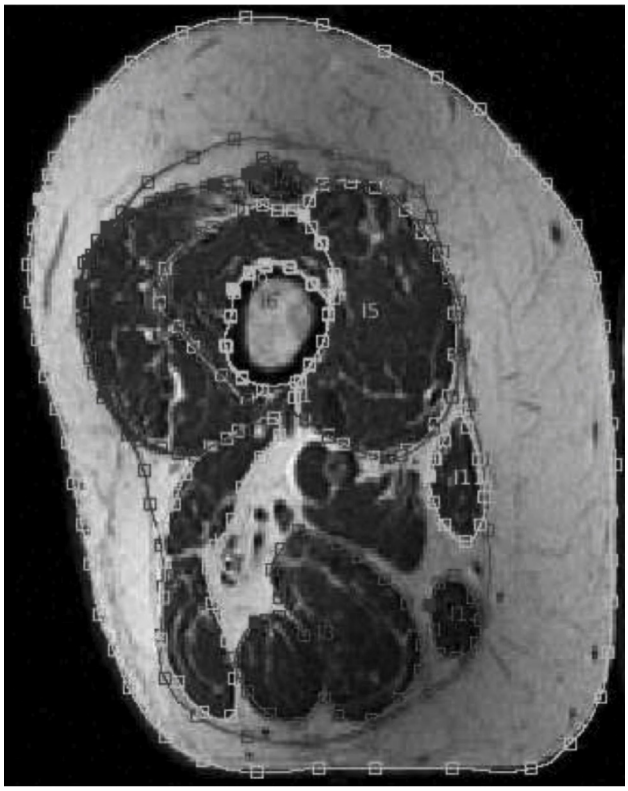

Fig. 3: Semi-automatic segmentation of subcutaneous thigh fat area.

medial and lateral tibia) was semi-automatically segmented and averages of T2 relaxation time measurements were calculated for three joint compartments (medial, lateral, patellofemoral). Compartmental (medial / lateral / patellofemoral) sums of WORMS were calculated as well as compartmental summation-scores for cartilage, menisci and edema-like marrow signal intensity (EMSI). Changes in WORMS and T2 over 4 years were calculated and progression was defined dichotomously (WORMS: increase by $\geq$ 1; T2: increase; both over 4 years). Linear regression models were used to assess the relationship between fat measurements and baseline T2 and WORMS. The relationship between fat measurements and progression of T2 and WORMS were assessed using logistic regression models. All analyses were adjusted for age, gender, physical activity and BMI and all measurements of fat distribution were standardized by converting to Z scores prior to the analyses.

Results: *Cross-sectional analyses:* Total SCF around the knee was positively correlated with overall WORMS sum and T2-values of the lateral joint compartment (Change associated with 1 SD change, [95%-CI], *P*-value) (0.42, [0.02-0.82], *0.04*, and 0.52, [0.16-0.88], *0.01*, respectively). For the fat distribution, we found the strongest correlations between periarticular lateral fat and WORMS and T2-values of the lateral compartment (0.53 [0.12-0.95], *0.01* and 0.43 [0.03-0.83], *0.04*). Thigh fat measurements correlated negatively with WORMS sum in the patellofemoral compartment (-0.79, [-1.55-0.02], *0.05*). *Analyses of progression:* Participants with greater thickness of SCF lateral or anterior to the knee showed a greater risk of worsening of WORMS sum of the lateral compartment after 4 years (Odds ratio per 1 SD change, [95%-CI], *P*-value) (1.50, [1.05-2.15], *0.03* and 1.29, [1.02-1.63], *0.04*, respectively). The fat ratio was found to be the strongest predictor for worsening of the lateral compartment total WORMS sum and cartilage sum as well as for both menisci (1.70, [1.19-2.42], *0.00*; 1.55 [1.06-2.28], *0.02*; 1.59, [1.06-2.36], *0.02*; 1.70, [1.13-2.57], *0.01*, respectively) over 4 years.

Conclusions: The distribution of fat around the knee is associated both with MRI based measures of prevalent knee degeneration and worsening of knee degenerative changes independently of BMI. We found associations between fat thickness on the lateral side of the knee, especially with the adjacent lateral compartment. These observations suggest an impact of adiposity on OA beyond an increase in joint load to local effects, such as an increase in inflammation due to adipokines. Furthermore, this relationship was also observed for cartilage T2 values, suggesting that periarticular fat may be associated with early joint degeneration.

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EFFECT OF CONTRALATERAL RADIOGRAPHIC DISEASE SEVERITY ON THE PREVALENCE AND PROGRESSION OF MRI-DEFINED STRUCTURAL PATHOLOGY IN KNEES WITHOUT ESTABLISHED OSTEOARTHRITIS

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Purpose: Ideally, intervention and prevention of structural joint damage based on pharmacologic or other therapeutic approaches should commence prior to the onset of radiographic change. As preventive treatment is unlikely to be without side effects and risks, it is important to identify patients who would be ideal candidates for preventive treatment of a radiographically normal knee in view of a positive benefit-risk ratio of the intervention. It has been shown that radiographically normal (i.e K-L 0) knees carry a greater risk of developing radiographic OA when the contralateral knee has already established radiographic knee OA compared to those where contralateral knees are radiographically normal, despite other risk factors.

Objective was to test whether radiographically normal knees (K-L 0) with definite contralateral radiographic knee OA (K-L 2 to 4), but without contralateral trauma history (i.e. an 'early OA model'), exhibit greater prevalence and progression of structural joint pathology as defined by MRI than those with bilateral radiographically normal knees (K-L 0) without risk factors ('healthy reference'). In another step we compared the prevalence and progression rates with those previously reported for bilateral K-L 0 knees with risk factors.