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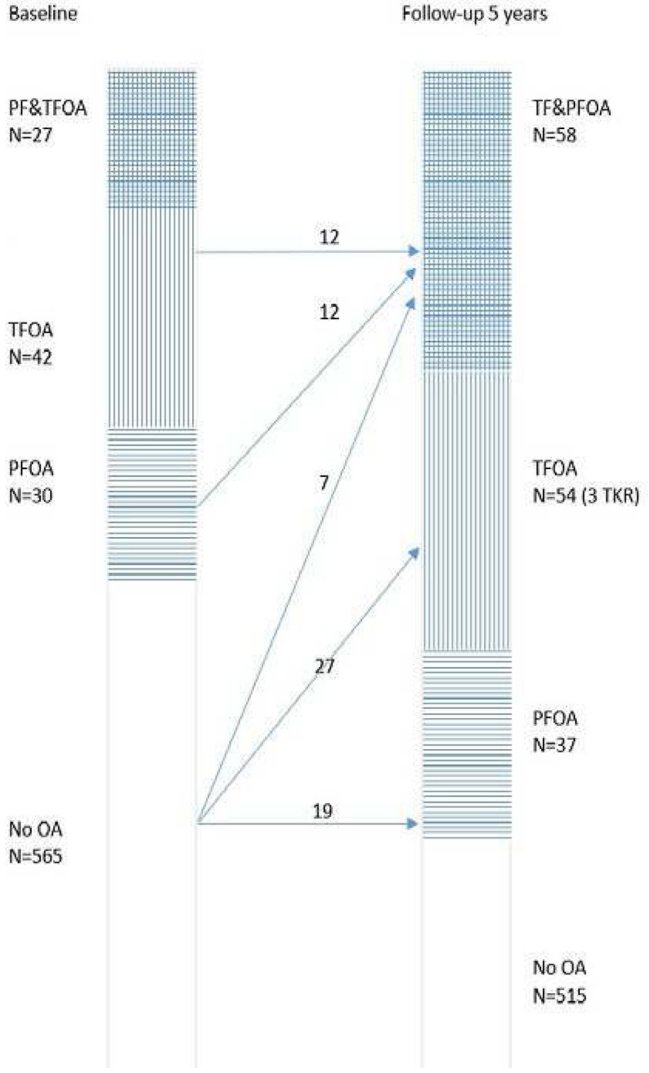
595 knees of 319 women have no TFOA at baseline (25 women are in the analysis with just one knee). Of these 595 knees 30 knees have PFOA at baseline; 56 knees (9.7%) have PFOAMRI at follow up and 46 knees (7.9%) have TFOAMRI at follow up. PFOA was associated with TFOA at follow-up with an odds ratio (OR) of 7.3 (3.2-17.0; p<0.001) independent of the K&L-score (OR=3.0 (1.6-5.8); p=0.001). Pretest predictive value was 7.7% (46/595); posttest predictive value is 40% (12/30). In the knees without PF OA (n=607) at baseline 42 knees were defined with TFOA at baseline, 73 were defined with TFOA at follow-up (3 knees had a TKR) and 37 knees were defined with PFOA at follow-up. TFOA at baseline was associated with PFOA at follow-up (OR=6.5 (2.5-17.0) p<0.001) independent of age, BMI and K&L score. K&L score was not associated with PFOA at follow-up at all (OR=0.92 (0.4-2.3); p=0.85). Pretest predictive value is 6.3% (38/607) and posttest predictive value is 28.6% (12/42).

Conclusions: Structural PFOAMRI at baseline is predictive for structural TFOAMRI at follow-up independent of K&L score. TFOAMRI at baseline is predictive for PFOAMRI at follow-up independent of K&L score. These results will be validated in the second subsample of the cohort.



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CHANGE IN BONE AREA DOES NOT CORRELATE WITH CARTILAGE LOSS OVER 12 MONTHS IN INDIVIDUALS WITH KNEE OA: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: The involvement of subchondral bone in knee osteoarthritis (OA) is well known, and it has been proposed that changes of bone shape may be a marker of disease progression, and contribute to an understanding of OA pathogenesis.

It is not known how this new measure relates to the more established measure of cartilage thickness. This study used statistical shape modelling to study whether bone changes correlate with cartilage change within anatomical regions, and whether the same individuals change more than measurement noise using the two measures over a one-year period, a typical period for a clinical trial.

Methods: A convenience cohort of 88 subjects with medial knee OA was identified from the NIH-OAI dataset. Subjects had K-L scores of 2 or 3; medial JSN > lateral JSN, medial osteophytes and ≥1° of varus malalignment; 43 were female.

Baseline and 12-month DESS images were manually segmented for articular cartilage. Segmenters were blinded to time point but not to subject, using EndPoint software (Imorphics, UK). Bone surfaces were identified by automated segmentation using active appearance models (AAMs). This methodology provides a dense set of anatomically corresponded points on each bone surface, allowing mapping of bone and cartilage in a consistent measurement frame.

Average thickness (ThCtAB) of the cartilage for each major compartment of the femur, tibia and patella was calculated. Bone area (tAB) was measured using anatomical areas identified on the triangulated mean bone shape.

Population maps were prepared to display the mean change in bone and cartilage on the bone surfaces for visual comparison (Figure 1). For each anatomical region, individuals with change greater than the smallest detectable difference (SDD) were identified. SDD was calculated using a set of 29 individuals with DESS images, taken at one week apart. The number of individuals who showed change greater than SDD for both measures were calculated. Correlation between bone and cartilage change was measured using Pearson's correlation coefficient.

Results: Bone area and cartilage thickness both showed significant change in one or more anatomical regions (Table 1). Both types of measure showed similar sensitivity, as judged by the standardised response mean (SRM) The pattern of change for the 2 measures was somewhat different. Change in cartilage thickness was typically negative, representing cartilage loss, and was located in the articulating surfaces of the femorotibial joint, and the lateral facet of the patella (Figure 1). Bone change was typically positive, representing increased bone area. Change was most evident around the edge of all cartilage plates, but was also present, at a lower rate of change, in the articulating surfaces of femur and tibia bones (the areas where cartilage showed change). There was no obvious strong pattern of spatial similarity between the 2 measures, except for this change in the articulating

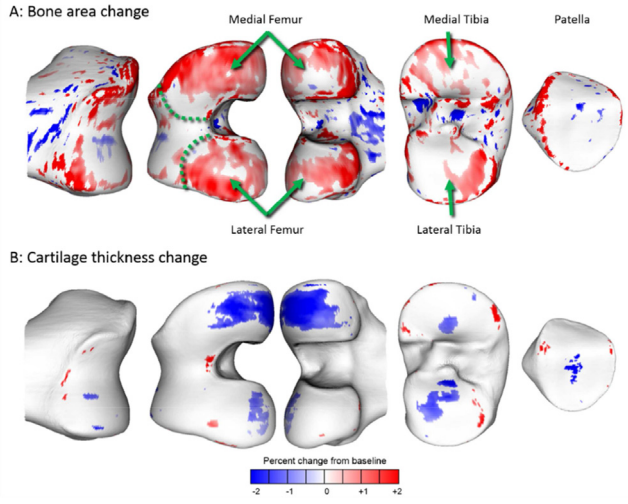

Figure 1. Spatial change of bone area (top) and cartilage (bottom), displayed on the mean bone shapes. Blue represents decrease in measure, red represents increase (see scale). Regions used in this study are shown on the bone area figures at the top, and the boundary of the medial and lateral femur regions is shown as a dotted line. This line represents the anterior edge of the menisci in the mean shape model.

surfaces of the femorotibial joint. Correlation of bone and cartilage change within each anatomical regions was very poor. Individuals who were rapid progressors for cartilage loss were no more likely to be fast progressors for bone change than any other individual (Table 2).

Conclusions: Bone area and cartilage thickness both provide responsive measures of change in knee OA. Within a one year period the spatial location of the change is different in most areas of the knee, though both measures show change in the articulating surfaces of the femorotibial joint.

There is no correlation between the two measures for any of the anatomical regions, and the 'fast progressors' for each method are not found in the same individual more than might be expected by chance alone.

The relationship of bone and cartilage changes with time is not well understood, but within the one year period typical of a clinical trial, the two tissue measurements progress independently of one another.

It is important to understand whether these two tissues change as part of the same overall disease progression, or are unrelated to each other. This experiment cannot answer that question, but the independence of the 2 measures suggests that they could be combined to provide a composite measure of change in the OA knee which provides more information than using the two methods independently.

Table 1
Change in cartilage thickness and bone area in 88 subjects over one year. Standardised response mean (SRM) is calculated as mean change/standard deviation of change. P-values are calculated from paired.

Cartilage thickness (ThCtAB)				Bone area (tAB)			
Region	Percent Change from baseline	p value	SRM	Region	Percent Change from baseline	p value	SRM
Medial Femur	-4.3%	$<10^{-4}$	-0.72	Medial Femur	1.2%	$<10^{-4}$	0.74
Lateral Femur	-1.0%	0.019	-0.25	Lateral Femur	0.9%	$<10^{-4}$	0.63
Medial Tibia	-1.2%	0.198	-	Medial Tibia	0.5%	$<10^{-4}$	0.43
Lateral Tibia	-1.6%	0.001	-0.37	Lateral Tibia	0.4%	0.003	0.41
Patella	-1.6%	0.174	-	Patella	-0.1%	0.461	-

Table 2
Agreement between fast progressors for bone and cartilage thickness, and correlation of the two measures. Correlation coefficient is calculated using Pearson's method.

	Number of IDs with cartilage > SDD	Number of IDs with bone > SDD	Number of IDs with both cartilage and bone > SDD	Expected agreement by chance	Correlation coefficient
Medial Femur	28	36	14	11	0.02
Lateral Femur	15	26	4	4	0.01
Medial Tibia	23	16	6	4	0.03
Lateral Tibia	11	5	0	1	0.00
Patella	9	6	2	2	0.00

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CAN THE PRESENCE OF SUBCHONDRAL CYST – AN INDICATOR OF SUBCHONDRAL BONE DISTURBANCE, BE USED FOR SUBTYPING KNEE OSTEOARTHRITIS?

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Purpose: Subchondral bone cyst (SBC) is a pseudocystic lesion that is frequently reported in advanced osteoarthritis (OA), particularly in hip OA.

Although it is considered as one of the cardinal radiological features in OA, and the presence of SBC in knee OA had been previously reported as a risk factor of cartilage loss and knee replacement, its clinical significance as a radiological feature in knee OA remains debated as they are hard to detect under plain radiographs.

The actual aetiology of SBC is still unsolved but there are two main theories – the synovial fluid intrusion theory and bony contusion theory. The former suggests that intrusion of synovial fluid into the subchondral bone results in SBCs; while the latter states that unresolved bone marrow lesion (BML) could be the precursor of SBCs. More recent longitudinal studies show knee BMLs could progress into SBCs, cohering with the latter theory.

The actual bone structural changes related to the presence of SBCs in knee subchondral bone are yet to be thoroughly investigated; therefore we have employed histology and μCT imaging to elucidate the relationship between SBC and surrounding trabecular bone remodelling activities in OA.

We would like to look into changes in subchondral bone microstructures in relation to SBCs, the possible links between such changes with knee functions, as well the possibility of using this radiological marker for subtyping knee OA.

Methods: A total of 112 advanced OA patients (87 female and 25 male, aged between 48 and 87) undergoing total knee arthroplasty (TKA) were selected in the study. SBC diameter, surrounding trabecular bone parameters and bone mineral density were analyzed in μCT images.

Paraffin sectioning of the resected tibial plateaux was performed with the thickness set at 7μm and subsequently stained with Haematoxylin & Eosin according to our previous protocols.

Patients' knee functions are evaluated by our clinical staff based on the criteria of the Knee Society Knee Score.

Results: SBCs of diameters ranging from 3mm to 12.5mm were present in 73% of the study population, higher than 22.6% as detected by plain X-ray interpreted by our experienced surgeon, or 30% reported by Audrey et al.

Trabecular bone in OA tibial plateaux with SBC underwent remodelling events, having a higher bone volume to tissue volume ratio (BV/TV) of 27.9 (±10.2)% compared to 14.2 (±5.9)% of their SBC-free counterparts; their bone mineral densities (BMD) are also significantly compromised (0.598 ±0.045 g/cm^3) compared the SBC-free specimens (0.623±0.048 g/cm^3). They also have higher trabecular number (1.6495 ±0.51039 mm^-1) compared to 1.4147±0.46550 mm^-1 of their SBC-free counterparts, and less trabecular separation (0.5060±0.19257mm verses 0.6186±0.25439mm).

Subchondral bones with SBCs tend to be of lower BMD, have higher trabecular number and smaller spaces between trabeculae.

From our histology slides, it was found that SBC is correlated to more chaotic de novo bone formation.

Interestingly, we also found out high trabeular number and small trabecular separation, which are features associated with SBCs, are correlated with better pain score, indicating less pain in patients with SBCs.

According to the histology sections, we have found specimens with SBCs have more bone in the marrow space than their SBC-free counterparts. These bones are, rather than lining on top of existing trabecular bones, clustered in the marrow space normally occupied by the marrow; although it is not yet clear whether these bones of poor quality are newly formed "de novo" bones or un-resorbed fragments due to bony contusion as a result of previous traumatic events.

Conclusions: SBCs in knee OA were found to be more common than previously suggested, implying their presence had been vastly underestimated clinically.

With lower BMD and higher bone volume, SBC could be an indicator for disturbance of subchondral bone metabolism; lower BMD, excessive de novo bone formation and uncoupled bone resorption – as observed in our histology.