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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 mal-alignment; 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 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.

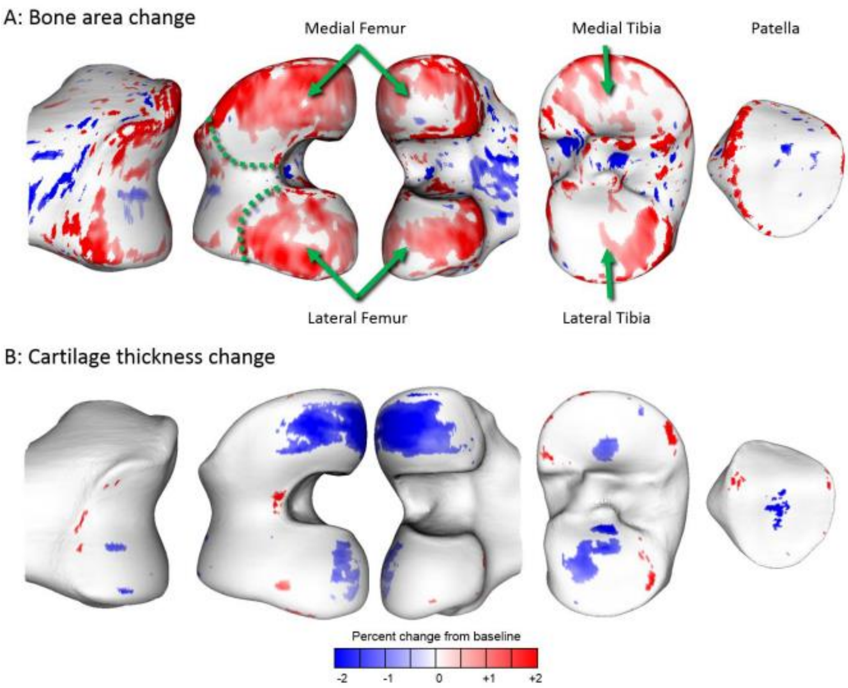

Figure 1 - Spatial change of bone area (top) and cartilage (bottom), displayed on the mean bone shapes. Blue represents decrease in measure, red represents increase (see scale). Regions used in this study are shown on the bone area figures at the top, and the boundary of the medial and lateral femur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

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 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 Students t-test.

	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

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.

