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OA May Not be as Structurally Heterogeneous as Expected: Shape Analysis of All Knees From the Osteoarthritis Initiative Reveals a Consistent Pattern of Bone Shape Change Over 8 Years

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Purpose: Osteoarthritis is often referred to as a heterogeneous disease, even within a single anatomical location, such as the knee. Bone pathology is integral to the OA process, but change in 3D bone shape is difficult to interpret when examining individual radiographs, or slices within an MR image. Statistical shape modelling (SSM) provides a convenient method for study of systematic change, as each bone shape is reduced to a series of principal components. The aim of this study was to determine whether 3D changes in bone shape were similar for all participants in the OAI, or whether clusters were distinguishable.

Methods: All baseline knees from the Osteoarthritis Initiative, which had Dual Echo Steady State water-excitation MR images (DESS-we) were included in the analysis of shape vs KL grade. Images were searched with active appearance models (AAMs) of the femur; AAMs are a form of SSM. Each femur shape is recorded as a series of 70 principal components (PCs); being the number of PCs needed to represent 98% of the variance in the AAM, which was trained using 96 femurs representing a range of KL grades.

In order to visualise a large number of femurs, the number of shapes must be reduced without loss of information. This was achieved using a decimation algorithm which discards shapes which are close to one another, until the number of remaining bones can be visualised (in this case 400 femurs, the “decimated subset”). This subset is then displayed using a Sammon plot, which is a method of reducing multiple dimensions to 2D, while preserving the distance between shapes as far as possible. In a further analysis, 30 fast progressors are added to the Sammon plot, and the change in their shape over 8 years displayed as an arrow. Fast progressors were defined as those bones which changed more than the 95% confidence limits of the repeatability of the method.

A more formal analysis of shape change was performed directly on the 70-dimensional data. All femurs which had been imaged at 0,2,4,6 and 8 years were fitted with a line, using orthogonal least squares. The angle between the fitted line and a known direction (the first PC of the femur shape model) was calculated, and the distribution of angles was plotted. The null hypothesis was that there was no shape change between time points except for measurement noise. The expected distribution under the null hypothesis was estimated by simulating a set of 500 examples (null population) using the covariance matrix of non-OA femurs imaged at baseline and 1 year, but centred on 0.

Results: Figure 1A shows the shape distribution of the decimated subset, which reduced 9,213 femurs (from 4,791 people) from the baseline images to 400. The figure also shows the 95% confidence ellipse of each group. The presence of OA contributes about half of the variability in shape in this distribution (the area enclosing those with KL 0-1 is about half of the total area). The shapes of femurs with KL 3-4 are almost substantially separated from those with KL 0 or 1. The group of KL 2 femurs bridges the region between these groups.

Figure 1B shows the progression of 30 fast progressors, displayed on the same Sammon plot. For each of the femurs, the direction of travel is approximately parallel to a line drawn through the mean shapes of each group.

The formal analysis of the direction of shape change for the fast progressors, showed that the direction of shape change differed significantly from the null population (p<0.0001, Figure 2).

Conclusions: At the population level, femur bone shape changes in a unidirectional manner, with KL3-4 femurs further away from the KL 0 group than a group of KL 2 femurs.

To visualise the shape change in this study we focussed on fast progressors, and these individuals demonstrated unidirectional change, which in the Sammon plot was similar in direction to the overall direction of population shape change.

This is an important finding for both pathogenesis, and for treatment of knee OA. Given the unidirectional change in 3D bone shape, it should be possible predict future shape (a benefit for intervention studies), and also for historic shape (which would for example allow surgery to reconstruct the knee to an earlier time point).

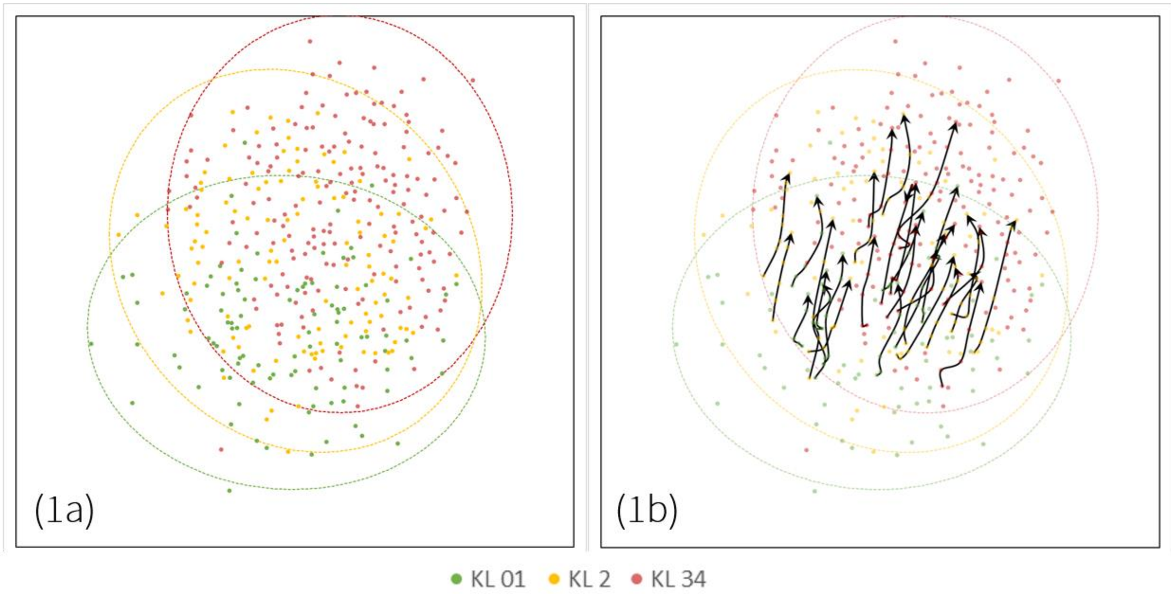

Figure 1 – Figure 1a shows Sammon plot representing 9,313 femurs at baseline, decimated to 400 examples, grouped based on KL grade. Figure 1b additionally shows direction of travel of 30 fast progressors over 8 years within the same Sammon plot.

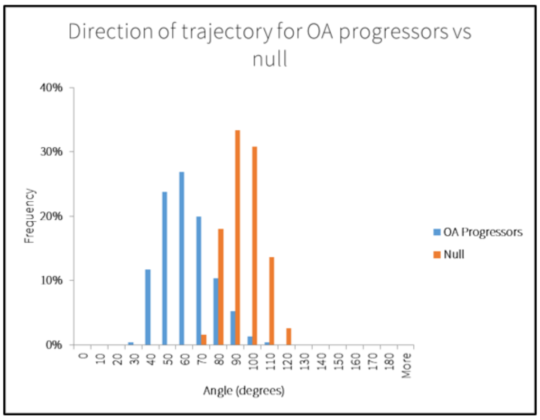

Figure 2 – The distribution of angles of shape change (in 70-dimensional space) of a group of fast progressors over 8 years. The null distribution was based on a simulated set of 500 examples using the covariance matrix of 885 non-OA knees imaged at baseline and 1 year, centred on 0.

