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Bone Shape Does Not Cause OA – but OA Does Change Bone Shape; a Study on Data From 4654 Knees From the Osteoarthritis Initiative

Michael A. Bowes¹, Christopher B. Wolstenholme¹, Graham R. Vincent¹, Philip G. Conaghan²

¹ imorphics Ltd, Manchester, UK, ² Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

Purpose: The involvement of subchondral bone in knee osteoarthritis (OA) is well known, and 3D changes in bone shape and area are associated with future development of OA, and with the likelihood of knee replacement. If OA has a predominantly biomechanical origin, then we might expect certain shapes within the population to result in differential loading at the knee, and predispose the knee towards OA. Statistical shape modelling (SSM) provides a convenient method for regression analysis of shape as an explanatory variable for future change in 3D bone area, or radiographic OA progression. We therefore examined whether the shape of a person's distal femur contributes to the onset of OA, or whether it is the OA process which changes the bone shape.

Methods: Bone shape was analysed from all knees from the Osteoarthritis Initiative, which had Dual Echo Steady State water-excitation images (DESS-we) at baseline, 12, 24, 48 and 60 months, regardless of KL score. Two measures of OA progression were defined for this study: (i) slope of annual change in the area of the medial condyle of the femur over 6 years, as a proportion of the baseline area for each individual, and (ii) radiographic progression, defined as a change in KL grade of 1 or more from baseline at 6 years. All baseline femurs were searched with active appearance models, a form of SSM. This method records the shape as a series of principal components; we used the first 20 principal components (representing 90% of all of the variance in the shape model). Values for the 20 principal components were used as explanatory variables in a linear regression model for the bone area slope, and in a logistic regression model to explain the radiographic change as a binary outcome. ANCOVA models were used to assess the contribution of other covariates as explanatory variables for bone area slope.

Results: 4,654 knees had DESS-we images available at all time points, from 2429 individuals, a total of 23,295 images. Linear regression models showed that although some principal components were significantly associated with the slope of change in the femur, the goodness of fit for the model was very weak (r^2 of 0.05). A similar weak fit was seen in logistic regression with radiographic progression ($r^2 = 0.04$). ANCOVA models of commonly used covariates (BMI, gender, KL score and alignment) had a slightly better fit (r^2 of 0.135 with slope, Figure 1). Knee alignment (varus/valgus) had no effect and was excluded from the model. The probability distribution of slope (percent change from baseline), based on KL score is shown in Figure 2. Average slope increased as the KL grade increased, and the SD of the distribution also increased.

Conclusions: It is notable that there was no femur shape which was strongly associated with the onset of radiographic OA, or increased change in bone area. This is not the case in this study. Mechanical covariates may play some role in the development of the disease, as BMI had a small effect on the slope of bone area change. We have previously shown that 3D

bone shape is associated with subsequent OA. In the context of the current findings, this can be interpreted as the detection of small changes in overall 3D progression, which are not visible in radiographs (pre-radiographic OA). In conclusion, the most significant covariate associated with increase in femur bone area is the KL grade, and the shape of the bone has minimal effect. This implies that the OA process causes changes in knee bone shape, and that increasing bone deformity in turn leads to more rapid change in bone area. This work suggests that for knee OA, subsequent events rather than knee morphology are critical in driving the OA process.

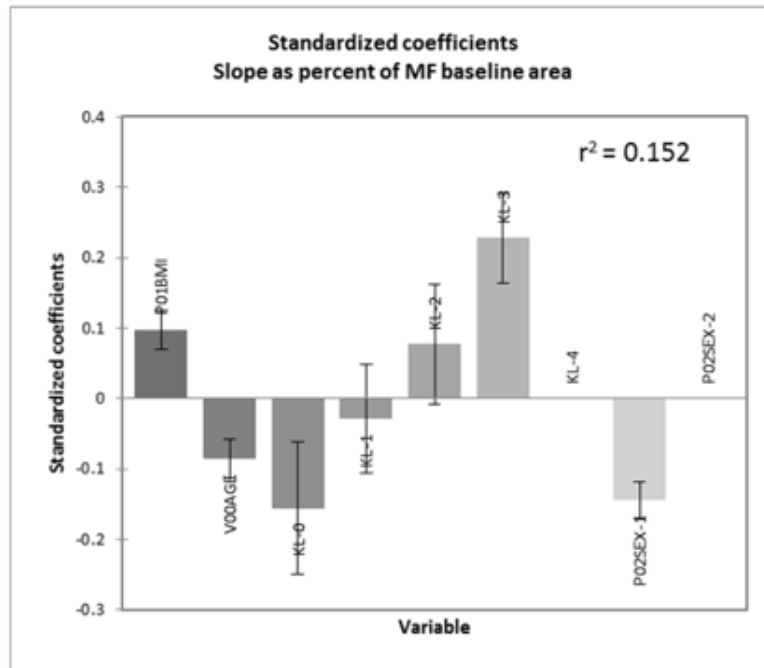


Figure 1 – Standardised coefficients for explanatory variables in an ANCOVA model of bone area slope (expressed as percent of baseline area).

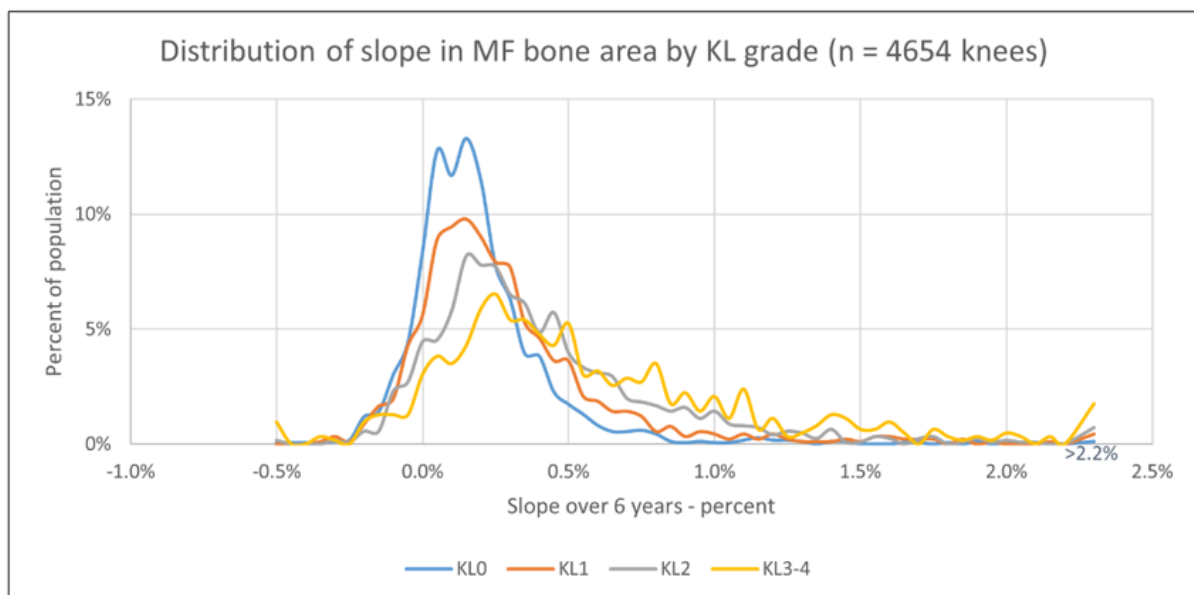


Figure 2 – Distribution of 6-year slope in MF bone area, using all available knees from the OAI which had images at 0, 1, 2, 4 and 6-year time points. Note: pace of change for population quickens with increasing KL grade, and SD distribution increases.