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## Three-Dimensional Magnetic Resonance Imaging Knee Bone Shape Predicts Total Knee Replacement: Data From The Osteoarthritis Initiative

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**Background:** MRI provides more accurate image biomarkers of structural progression than conventional radiography. Active appearance modelling (AAM) enables accurate, 3D quantification of MRIs. Changes in 3D subchondral bone shape are integral to structural progression of knee osteoarthritis (OA) and are predictive of incident radiographic knee OA. However, the association of 3D subchondral bone shape with total knee replacement (TKR) is unknown.

**Objectives:** To determine the relationship between scalar 3D bone shape and TKR.

**Methods:** This is a nested case-control analysis, within the osteoarthritis initiative (OAI) cohort. Case knees that underwent TKR were matched 1:1 with controls that “survived” the 6 years of follow up, using stratification (propensity) score matching based upon baseline age, gender, BMI category (<24.9, 25-34.9, >35), ipsilateral knee pain severity numeric rating scale, knee side and recruiting centre. Active appearance modelling of the femur, tibia and patella and linear discriminant analyses identified vectors that were best at classifying knees as having OA vs. no OA, scaled such that -1 and +1 represented the mean non-OA and mean OA shapes, respectively. Vector values were compared within matched case-control pairs using paired t-tests and the odds of TKR associated with baseline 3D bone shape were obtained using conditional logistic regression.

**Results:** Case-control pairs (n=311) of knees were well matched in terms of propensity scores. In cases of TKR the mean baseline 3D bone shape vector was more positive relative to controls, indicating more advanced OA, for the femur [mean 0.98 vs. -0.16; difference (95% CI) 1.14 (0.92,1.37)], tibia [mean 0.86 vs. -0.05; difference (95% CI) 0.90 (0.69,1.12)] and patella [mean 0.95 vs. -0.07; difference (95% CI) 1.02 (0.74,1.31)]. Unadjusted conditional odds ratios (95% CI) for the femur, tibia and patella revealed increased odds of TKR with increasingly positive 3D bone shape vector values (increasing OA structural severity) (Table 1). After adjusting for Kellgren Lawrence (KL) grade in a multivariable analysis, the femur 3D shape vector was independently associated with TKR [OR 1.21 (1.01, 1.45)] with a slight improvement in model fit (AIC) compared with KL grade.

**Conclusions:** 3D bone shape predicts TKR. Femur shape has the greatest association with TKR. This provides evidence of predictive validity of 3D bone shape and its potential utility in trials of prospective disease modifying OA drugs.

Imaging variable	Univariable (unadjusted)				Multivariable*		
	OR	95% CI	p value	AIC	OR	95% CI	AIC
Femur vector	1.79	1.54, 2.09	<0.001	309.51	1.21	1.01, 1.45	228.33
Tibia vector	1.64	1.42, 1.90	<0.001	334.86	1.02	0.84, 1.24	232.66
Patella vector	1.4	1.26, 1.56	<0.001	346.33	1.09	0.95, 1.26	231.24
KL grade (ref: KL 0)							
1	2.42	0.75, 7.82	0.14				
2	9.08	3.36,24.49	<0.001				
3	31.55	11.23,88.63	<0.001				
4	72.77	22.62,234.07	<0.001	230.7			

Table 1 - Associations between 3D bone shape vectors or KL grade with TKR. \*Adjusted for KL grade.