

# qMRI-Based Risk Factors for Symptomatic Knee Pain: Data from the OAI

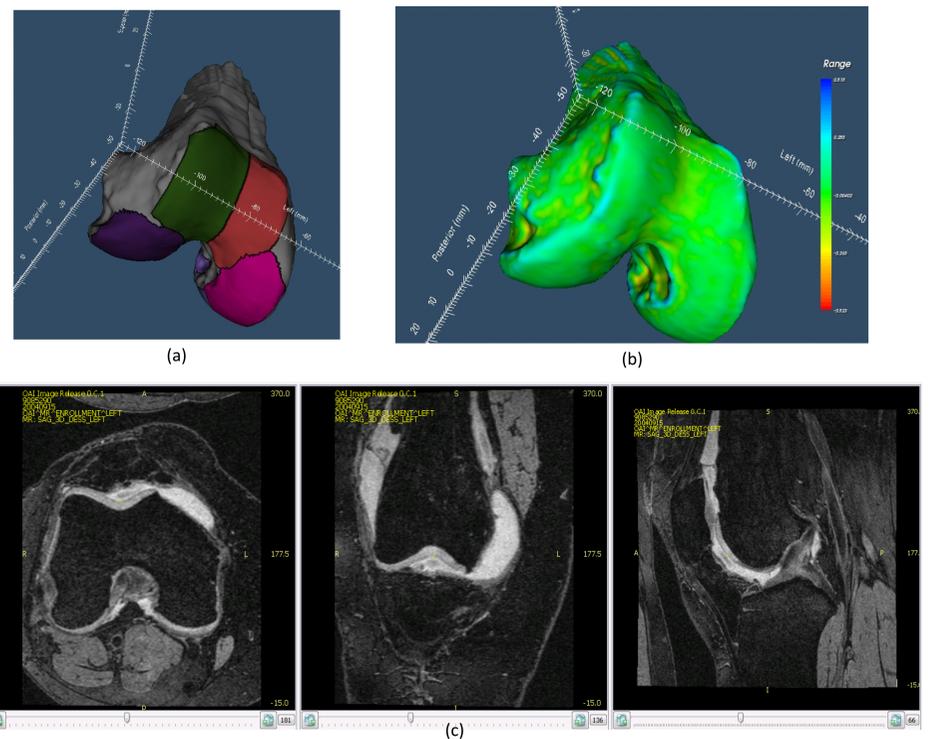
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**INTRODUCTION:** Chronic knee pain is a common feature of osteoarthritis (OA); the pain may be associated with different risk factors and may have various etiologies

**OBJECTIVE:** The purpose of this work was to determine which MR imaging characteristics can be used as risk factors - or imaging biomarkers - for the subsequent development of symptomatic knee pain

**METHODS:** Right knees from an Osteoarthritis Initiative (OAI) cohort with untreated right knee pain were examined. This medication free cohort had right knee pain symptoms recorded as "Pain most days of a month in past 12m" (RKSX=2) on observations later than the 12 month visit (V01). At the screening visit (P1), the 12 month visit (V01) control subjects had lower symptomatic scores (RKSX<2). A control group with no right knee pain was matched for age, BMI, gender and no therapy. Only subjects with DESS MRI images were analyzed. The MRI DESS analysis was done by Qmetrics Technologies software that automatically segmented the femoral, tibial and patellar cartilage into several regions of interest (ROI): femur, tibia, patella, central medial femur, central lateral femur, medial tibia, lateral tibia, medial trochlea, lateral trochlea, medial patella, lateral patella (Figure 1a). Automated segmentations that failed to correctly segment cartilage tissue were removed from the analysis. Each ROI was quantitated for volume, area, thickness, curvature and DESS signal contrast properties : Figure 1(b) and (c). ROI Statistical descriptors were computed for thickness, curvature and contrast. Using the control subjects, all measurements were adjusted for BMI, age and gender differences. The measurements then were z-transformed using the rank inverse normal transform. Finally, all measurements were categorized as low-control-quartile ( $p < 0.25$ ), mid-control-range ( $0.25 < p < 0.75$ ) and top-control-quartile ( $p > 0.75$ ). The time to pain event (RKSX>1) on cases and the time of last observation were used in Cox-Survival-Models. A bootstrapped-step-wise feature selection algorithm based on the Integrated Discrimination Improvement (IDI) was used to extract a robust multivariate COX-survival model from the 12 month observation (V01). The COX-model categorized subjects into high risk and low risk to develop future knee pain. All models were internally validated using a 10-fold cross-validation. Furthermore, the risk model was tested in the baseline observation and the 24 month observation



**Figure 1:** (a) ROIs definitions at the femur. (b) curvature map of the femur. (c) axial, coronal and sagittal MRI DESS slices of an OA patient. Inflammation process and tissue degradation affect the contrast between cartilage tissue and adjacent anatomical structures.

**RESULTS:** 80 cases qMRI (39:41 Males:Females), with successful right knee segmentations were included. 194 qMRI analysis (87:107 Males:Females) were used as controls. The total population had an average age of  $62.9 \pm 9.5$  years and BMI of  $27.0 \pm 4.4$ . There was no statistical difference between study subjects and controls for BMI and age. Table 1 shows the six MRI features that separate subjects into high/low risk for the development of chronic pain at the three starting points. The femur curvature was a consistent risk factor: Odds ratio (OR) 1.92 (1.5 to 2.5). Also constant predictive was the bone-cartilage signal contrast of the lateral femur: 2.42 (2.0 to 2.85). Figure 2 shows the Kaplan-Meier plots of the Baseline, 12 Month and 24 Month visits.

**CONCLUSIONS:** Abnormal curvature of the femur and low DESS signal contrast at the lateral femur articular surface are risk factors for the development of knee pain. Although the casual relationship of these findings with the evolution of OA still has to be established, this fact may be used to make clinical and treatment decisions for the prevention of symptomatic knee pain.

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Table 1: qMRI Features that predict which subjects are at higher risk of developing chronic knee pain during the next six years

Feature	Cases	Control	One Year Odds Ratio (95 CI)	Baseline Odds Ratio (95 CI)	Two Year Odds Ratio (95 CI)
	mean (std)	mean (std)			
Femur Curvature (Trimmed)	0.040 (0.006)	0.041 (0.006)	<b>1.92 (1.51 to 2.50) (-)</b>	<b>1.64 (1.26 to 2.13)</b>	<b>1.36 (1.13 to 1.69)</b>
cLF Superficial Contrast (5%)	-3.710 (1.236)	-3.918 (1.185)	<b>2.42 (2.02 to 2.85)</b>	<b>1.74 (1.38 to 2.25)</b>	<b>1.89 (1.58 to 2.30)</b>
Tibia Deep Layer Contrast (std)	1.154 (0.129)	1.116 (0.113)	<b>0.52 (0.27 to 0.89) (+)</b>	0.95 (0.60 to 1.60)	1.19 (0.60 to 2.16)
Lateral Trochlea Curvature (Trimmed)	0.029 (0.007)	0.029 (0.005)	<b>1.73 (1.40 to 2.18) (+)</b>	<b>1.34 (1.09 to 1.65)</b>	<b>1.36 (1.11 to 1.71)</b>
Femur Superficial Contrast (Mean)	2.281 (0.665)	2.607 (0.614)	<b>3.27 (1.92 to 5.61)</b>	2.07 (0.86 to 5.08)	1.23 (0.62 to 2.31)
Femur Curvature (Mean)	0.030 (0.005)	0.032 (0.005)	<b>0.21 (0.09 to 0.49)</b>	0.76 (0.39 to 1.37)	0.60 (0.26 to 1.22)

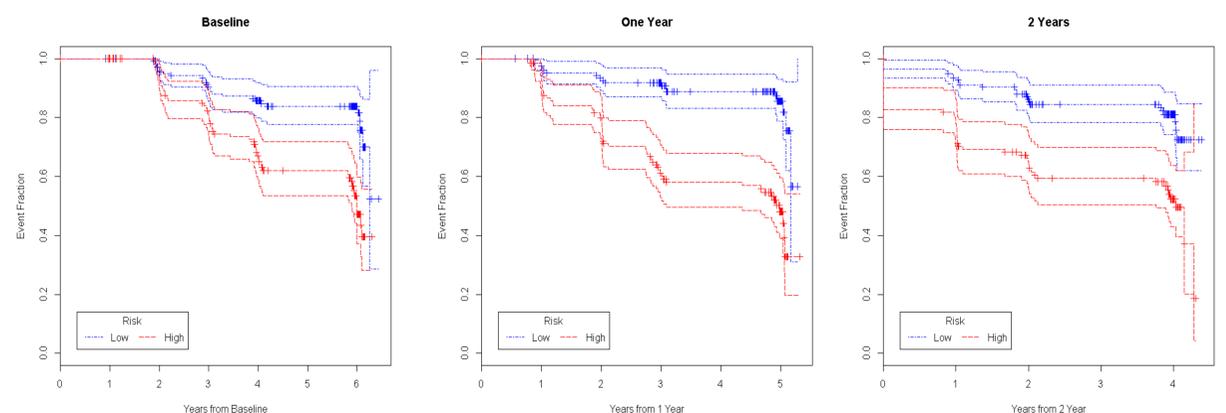


Figure 2 Kaplan-Meier plots with 95% CI of the one year multivariate model divided by high low risk categories. Left, the model observed at the 1 year observation is used to predict the pain event fraction. Middle, the one year model shows the rate of pain events in the high risk group. Right, the model found at the one year, applied to the two year observation still predicts that the high risk group show higher pain events than the low risk group.