

# Compression of the knee upon weight loading in healthy and osteoarthritis subjects as measured by MRI and X-ray

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**INTRODUCTION:** The ability to develop disease modifying drugs for osteoarthritis (OA) has been hampered by the inability to measure progression and treatment effects quickly in small cohorts. MRI with its soft-tissue contrast and 3D visualization was thought to be an obvious choice to replace X-ray for measuring OA progression in the knee. Despite its initial promise, measurements of cartilage morphology with MRI have, however, not been shown to be considerably more sensitive to disease progression than joint space width (JSW) measured from x-ray [1]. This may be partially a result of knee x-rays being acquired in standing position with the cartilage loaded by body weight while MRI is acquired supine with no load being applied to the knee. This study aims to investigate the impact of loading on JSW measured from x-ray and cartilage thickness measured from MRI and whether participants with knee OA encounter greater compression of knee cartilage under loading compared with healthy subjects.

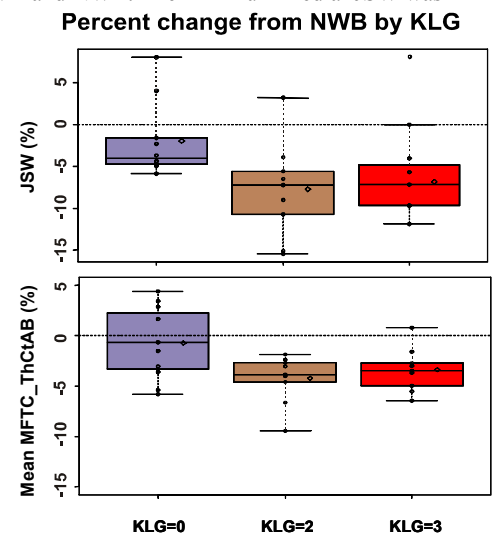
**METHODS:** Thirty-one women age 55 ( $\pm 6.0$ ) years and BMI 28 ( $\pm 2.4$ ) had x-rays and MRI of the knee in weight bearing (WB) and non weight-bearing (NWB) positions. Eleven subjects had no OA, Kellgren Lawrence grade (KLG) of 0. The other subjects had mild or moderate radiographic OA KLG 2 (n=10) and KLG 3 (n=10). Due to image quality or acquisition issues 1 KLG 0 and 2 KLG 3 subjects were excluded from JSW results and 1 KLG 3 was excluded from MRI cartilage results.

**X-ray Acquisition & Analysis:** Lyon-schuss x-rays were acquired of the knee using a Synaflexer (Synarc, San Francisco, USA) Plexiglas positioning frame. The WB x-ray was acquired with the subjects standing while the NWB x-ray was acquired with the subjects lying prone. Care was taken to insure the medial-tibial margins were aligned and the knee positioning was consistent between WB and NWB. The minimum medial JSW was measured using automated software (HOLYs, Lyon France) by an experienced reader blinded by subject and loading.

**MRI Acquisition & Analysis:** Subjects were positioned supine in the scanner on a custom-made MRI compatible loading device. The knee was positioned with 15° of flexion and 10° of external foot rotation approximating the positioning of the Synaflexer used for x-rays. Coronal, 3D water-excite SPGR images, were acquired on a 3.0T GE scanner using an 8-channel knee coil with TR = 23 ms, TE = 6.88 ms, flip angle = 18°, BW = 31.25 KHz, FOV = 14 cm, slice thickness = 1.5 mm, and matrix = 512x512. The sequence was first acquired with no loading (NWB) and then repeated with the leg pressing against a weight equal to half of the subjects body weight. The cartilage was manually segmented using proprietary software (Chondrometrics GmbH, Ainring, Germany) and the average thickness of the medial femoral tibial cartilage (MFTC\_ThCtAB) was calculated.

Values were reported as the % difference calculated as (WB – NWB)/NWB x 100%. Negative values indicate compression under loading. A linear model was fitted to assess the effect of KLG on the percent change from NWB in the endpoint and significance was determined, without multiplicity adjustment, at the  $p < 0.05$  level (two sided). Analysis was repeated after removal of outliers which were identified as their studentized residuals [2] being more than  $\pm 2$ .

**RESULTS:** The mean change for KLG 0 was -2.0% and -0.76% for JSW and MFTC\_ThCtAB respectively, neither were significantly different than zero. The mean change for the OA knees was greater than for the controls. For KLG 2 the mean change was -7.7% and -4.2% for JSW and MFTC\_ThCtAB and for KLG 3 the mean change was -4.9% (or -6.9% with the outlier removed) and -3.4% for JSW and MFTC\_ThCtAB, all OA measures were significantly different from zero. Figure 1 (top) shows the percent difference in JSW following loading as measured from the X-ray. Figure 1 (bottom) shows the percent difference in mean cartilage thickness from MRI.



**Figure 1** Box plots showing individual data (o), median values (middle bar) 25%-75% quartiles (colored box), mean ( $\diamond$ ), whiskers show data range excluding identified outliers. **Top:** %change in JSW from non-WB measured by x-ray. **Bottom:** %change in mean MFTC\_ThCtAB measured by MRI.

**DISCUSSION:** There was a significant decrease in JSW and mean cartilage thickness in MRI in the knees of subjects with OA under WB conditions. Healthy subjects had a smaller decrease which did not reach significance. It is possible that the increased compression in the joint space and cartilage seen in OA subjects may be a result of compositional and mechanical tissue degradation which is not apparent from morphological measurements made during NWB conditions. This was a small exploratory study. Additional studies will be required to assess the potential of this biomarker as a sensitive measure of longitudinal changes of the knee joint as a function of disease progression and its utility for drug development.

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**REFERENCES:** [1] Hellio Le Graverand, ARD 2008. [2] [http://en.wikipedia.org/wiki/Studentized\\_residual](http://en.wikipedia.org/wiki/Studentized_residual)