Conclusions: Our findings illustrate that a shoe design incorporating both a lateral wedge and variable-stiffness sole can significantly reduce parameters of medial knee joint load compared to a control walking shoe. Future research examining the effects of these shoes on pain, physical function and long term joint structural changes are warranted.

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THE RELATIONSHIP BETWEEN QUADRICEPS ANGLE DURING WALKING AND PATELLOFEMORAL OSTEOARTHRITIS IN OLDER ADULTS: THE MOST STUDY

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Purpose: A purported cause of patellofemoral (PF) joint damage in younger adults is lateral patellar maltracking brought about by an excessive quadriceps angle (Q-angle) during gait. However, the relationship between Q-angle during gait and PF radiographic OA (ROA) has not been studied in older adults. Challenges to such a study include between-person differences that can confound the association of Q-angle with PF ROA, but may be difficult to adequately measure or control for. The purpose of this study was to assess the cross-sectional relationship of Q-angle during walking with PF ROA in older adults using a within-person knee-matched design that eliminates confounding by unmeasured between-person differences.

Methods: Eligible subjects were participants in the 60-month Multicenter Osteoarthritis Study (MOST) exam with unilateral PF ROA. MOST includes subjects from Alabama and Iowa that have or are at risk for knee OA. Individuals for this study were selected as having knees discordant for PF ROA. Case knees met the OARSI criteria for definite PF ROA on lateral knee radiograph, as read by two musculoskeletal radiologists (inter-rater weighted kappa = 0.75 for joint space narrowing score). Control knees were the contralateral knee without PF ROA from the same subject. Using synchronized frontal and sagittal 60 Hz video recordings, a single trained physical therapist (intra-rater ICC= 0.64) measured Q-angle between a line connecting passive markers on the anterior superior iliac spine of the pelvis with the center of the patella, and a line connecting passive markers on the center of the patella with the tibial tuberosity at midstance during two self-paced walking trials. Categories of increasing Q-angle were formed using the sex-specific quintile distribution of Q-angle among case knees. With the lowest quintile as a reference group, conditional logistic regression estimated the relative odds of PF ROA in each category of increasing Q-angle while adjusting for the presence of tibiofemoral (TF) ROA (KL grade $\geq$ 2 on PA fixed flexion x-ray).

Results: 142 subjects had knees discordant for PF ROA. Mean +/- sd age, BMI, and walking speed was 68.9 +/- 7.6 yrs, 32.3 +/- 6.6 kg/m2, and 1.12 +/- 0.20 m/sec, respectively. 52.1% of subjects were female, 89.4% were white, and 47.9% were examined at the Alabama clinic site. Mean +/- sd Q-angle was greater among case knees than among control knees (7.7 +/- 6.4 degrees vs. 6.9 +/- 6.1 degrees, p = 0.19), and greater generally among women. After adjusting for the presence of TF ROA, the relative odds of PF ROA were greater in categories with increased Q-angle (p for linear trend $<$ 0.0001) (see Table). Among knees with the largest Q-angle ($>$ 14.4 degrees among women or $>$ 11.1 degrees among men) the odds of PF ROA was 2.3 (95% CI: 0.9, 5.7) times greater than among knees with the smallest Q-angle ($<$ 4.0 degrees among women or $<$ 0.5 degrees among men). When comparing all other knees (2nd - 5th quintile categories) to knees with the smallest Q-angle (1st quintile category), the odds of PF ROA was twice as great (adjusted OR = 2.0; 95% CI: 0.9, 4.3).

Conclusions: Increased Q-angle during walking is associated with an increased prevalence of PF ROA among older adults. These findings from a within-person knee-matched study are unlikely to be confounded by unmeasured between-person differences. The findings may have implications for the treatment of PF ROA using interventions that reduce Q-angle during walking.

Q-angle Category (sex-specific case-based quintiles)	Cases N=142 n (%)	Controls N=142 n (%)	Crude Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Lowest	27 (19.0)	34 (23.9)	1.0 (Reference)	1.0 (Reference)
2nd	29 (20.4)	29 (20.4)	1.4 (0.6, 3.2)	2.3 (0.9, 5.7)
3rd	29 (20.4)	34 (23.9)	1.3 (0.6, 2.9)	1.5 (0.6, 3.5)
4th	29 (20.4)	20 (14.1)	2.3 (0.9, 5.6)	2.5 (0.9, 6.8)
Highest	28 (19.7)	25 (17.6)	1.8 (0.7, 4.4)	2.3 (0.8, 6.4)
p for trend			0.13	$<$ 0.0001
Q-angle Category (dichotomized)				
Lowest	27 (19.0)	34 (23.9)	1.0 (Reference)	1.0 (Reference)
2nd - Highest	115 (81.0)	108 (76.1)	1.5 (0.8, 3.1)	2.0 (0.9, 4.3)

*Adjusted for presence of radiographic tibiofemoral OA

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ROTATIONAL KNEE LOAD PREDICTS CARTILAGE LOSS OVER 12 MONTHS IN KNEE OSTEOARTHRITIS

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Purpose: Walking biomechanics are recognized as important in the structural progression of knee osteoarthritis (OA). In this regard, much focus has been directed at the external knee adduction moment as a marker of knee joint load. However, other indices of knee joint loading may also be important influences in structural disease progression. Of relevance may be rotational forces applied to the knee. Many of the structural changes that occur in knee OA are plausible candidates of rotational load related damage. This study evaluated the relationship between the knee medial rotation moment (KRM) during walking and indices of structural progression assessed by magnetic resonance images (MRI), in people with medial knee OA.

Methods: Data from 143 (72%) individuals (80 females, age: 64.4 yrs, BMI: 28.6 m/kg^2) who participated in a clinical trial were analyzed. The clinical trial showed no significant effect of lateral wedge insoles on pain, function or joint structure compared to control insoles, thus data from treatment groups were pooled for this analysis. Baseline knee rotational load, expressed as an external moment during walking, was assessed by the peak KRM and KRM impulse obtained from three-dimensional biomechanical gait analyses. MRI at baseline and at 12 months was used to assess structural progression. Medial and lateral tibial cartilage volumes were defined by manual segmentation of the cartilage with subsequent three-dimensional rendering. Total tibial cartilage volume was defined by summing the medial and lateral volumes. Tibiofemoral cartilage defects and bone marrow lesions (BMLs) were scored using a validated semi-quantitative system. Multiple regressions with adjustment for covariates were used to assess the relationships between baseline rotational knee load parameters and annual change in medial, lateral and total tibial cartilage volume normalized to the respective tibial plateau area. Logistic regression was used for the dichotomous dependent variables of progression (yes/no) of medial and lateral tibiofemoral cartilage defects and BMLs.

Results: A higher baseline peak KRM was associated with greater loss of lateral and total tibial cartilage volume loss over 12 months (Table). A higher baseline KRM impulse was associated with greater medial, lateral and total tibial cartilage volume loss over 12 months (Table). No significant relationships were found between baseline rotational loading and progression of medial or lateral tibiofemoral cartilage defects or BMLs.

Conclusions: This study suggests that rotational knee loading may be a risk factor for loss of tibial cartilage volume. The medial/lateral location of the cartilage loss appears dependent on the rotational loading parameter evaluated (peak KRM vs. KRM impulse). As rotational knee load is modifiable [e.g. insoles], biomechanical treatments targeting rotational load may potentially modify the disease progression and warrant future investigation.

Relationships between baseline rotational knee loading and changes in cartilage volume over 1 year

Annual cartilage volume loss	Univariate analysis		Multivariate analysis†	
	Regression coefficient (95% CI)	P	Regression coefficient (95% CI)	P
Medial tibial cartilage volume (mm^3)				
Peak KRM (Nm/BW*HT%)	-0.21 (-0.49 to 0.07)	0.145	-0.20 (-0.48 to 0.09)	0.178
KRM angular impulse (Nm.s/BW*HT%)	-0.92 (-1.8 to -0.03)	0.042	-1.05 (-1.98 to -0.12)	0.027
Lateral tibial cartilage volume (mm^3)				
Peak KRM (Nm/BW*HT%)	-0.99 (-1.83 to -0.17)	0.019	-1.07 (-1.89 to -0.24)	0.012
KRM angular impulse (Nm.s/BW*HT%)	-2.53 (-5.18 to 0.11)	0.060	-3.18 (-6.11 to -0.76)	0.012
Total tibial cartilage volume (mm^3)				
Peak KRM (Nm/BW*HT%)	-0.34 (-0.59 to -0.08)	0.010	-0.35 (-0.60 to -0.09)	0.008
KRM angular impulse (Nm.s/BW*HT%)	-1.02 (-1.83 to -0.21)	0.014	-1.29 (-2.11 to -0.47)	0.002

† Adjusted for age, gender, body mass index, static knee alignment, baseline value, MRI machine and treatment group

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MALDI IMAGING MASS SPECTROMETRY REVEALS A DIFFERENT PROTEIN DISTRIBUTION IN HUMAN CONTROL AND OA CARTILAGE

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Purpose: The knowledge of the distribution and the modulation of proteins in the osteoarthritis (OA) is necessary to understand the changes in the cartilage during the development of the disease. Matrix assisted laser desorption ionization (MALDI) imaging mass spectrometry (IMS) allows us to study the spatial distribution of different proteins with a high resolution in a section of tissue. In this study, we have studied the location and the abundance of OA-related proteins in different areas of normal and osteoarthritic (OA) human cartilage by MALDI IMS.

Methods: Human control and OA cartilage samples were cut by triplicate obtaining 10 μm thick sections and being deposited in indium tin oxide (ITO) high conductivity slides. Samples were washed and digested. Spots of trypsin were deposited by a high-accuracy position automatic chemical inkjet printer. Alpha-Cyano-4-hydroxycinnamic acid matrix (HCCA) was deposited by a vibrational sprayer system. Synapt HDMS MALDI-Q-TOF was used to perform the imaging-MS experiments with a spatial resolution of 150 μm. To perform the peptide identification, Mascot algorithm was employed after profiling MS/MS and imaging-MS/MS experiments. Biomap software was used to study the location and to quantify the intensity of the different peptides. Inmunohistochemistry analyses were used to validate the results. Hematoxylin-eosin staining complemented the spatial information. Principal Component Analysis (PCA) and Discriminant Analysis (DA) were used for data interpretation.

Results: We have previously described a higher presence of Fibronectin, Cartilage intermediate layer protein 1 (CILP1), Cartilage oligomeric matrix protein (COMP) and other possible biomarkers in the human OA cartilage by MALDI-IMS. Using Biomap software we have quantified the differences in OA vs. control samples, observing that the abundance of the peptides related to Fibronectin (m/z 1349.7, m/z 1401.7, m/z 1593.7, m/z 1431.7, m/z 1323.7) and COMP (m/z 1613.8, m/z 2256.1) increased in OA respect to normal samples but also with a clear difference between the deep and the superficial areas (table) [Deep OA vs. Deep Normal, $P^*<0.05$; Superficial OA vs. Superficial Normal, $P\&<0.05$]. We also plotted the number of pixels vs. the average intensity observed for two of these OA-related peaks (m/z 1349.7 and m/z 2373.7). The maximum intensity reached in the OA samples for the Fibronectin related peptide 1349.7, and for the hypothetical biomarker m/z 2373.7, was higher than the maximum intensity observed in the control cartilages (0.3 and 0.25 vs. 0.08 and 0.04 respectively). Moreover, in the OA spectra we could distinguish two different distributions: the first one with a low intensity (but higher than the intensities of the control distribution) and the second one with a high average intensity, showing the heterogeneity of the protein distribution that we can find in the human OA cartilage. We also validated the results of Fibronectin distribution by inmunohistochemistry, observing again a higher presence in the deep area of OA than in normal samples (0.2±0.0% normal vs. 0.71±0.32% OA; n=3, $P^*<0.05$).

Conclusions: We have observed a high presence of OA-related proteins and possible candidates in the deep area of the cartilage by MALDI-IMS. This fact could help us to understand the role of the deep area in the joint remodelling that characterizes the OA pathology.

Quantitation of OA specific peptides

m/z	Superficial Normal	Deep Normal	Superficial OA	Deep OA
1349.7	0.16±0.12	0.19±0.12	1.58±0.77&	2.45±1.37*
1401.7	0.16±0.10	0.17±0.10	0.45±0.11	0.64±0.13*
1593.7	0.09±0.04	0.11±0.05	0.63±0.34&	1.14±0.75*
1431.7	0.25±0.12	0.29±0.15	0.66±0.22	0.99±0.33
1323.7	0.10±0.07	0.13±0.08	0.79±0.56	1.87±1.49*
1613.8	0.20±0.15	0.23±0.18	0.55±0.21	0.87±0.30
2256.1	0.11±0.06	0.12±0.06	0.20±0.07	0.29±0.11
2377.3	0.05±0.03	0.05±0.03	0.46±0.34	0.71±0.54*

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NON-INVASIVE SODIUM MR IMAGING AND QUANTIFICATION OF IN-VIVO ARTICULAR CARTILAGE AT 1.5 TESLA

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Purpose: Osteoarthritis (OA) can be characterised by the gradual loss of articular cartilage (AC). At the very early stages, the loss of proteoglycan from the extracellular matrix of articular cartilage has been associated with the onset of OA. Sodium magnetic resonance imaging has been shown to be sensitive in detecting small changes in proteoglycan content of articular cartilage at high field (>4Tesla) MR systems. This work aims to investigate the possibility of imaging and quantification of local sodium content of articular cartilage using sodium MRI at 1.5Tesla clinical MR system.

Methods: A dual tuned knee coil equipped with proton (1H) and sodium (23Na) channels tuned at 63.6 MHz and 16.8 MHz respectively is used to scan phantoms and human subjects. All the scans were performed using a 1.5T clinical MR system (Siemens Medical Solutions, Erlangen, Germany). Prior to human subjects, scanning was performed on phantoms. Sodium imaging of knee and phantoms were performed using 3D Gradient Echo sequence (TR/TE = 11.4/4.0 ms, flip angle = 62°, isotropic resolution = 2.81 x 2.81 x 8 mm3, and total acquisition time ~30 min). For the absolute measurement of sodium content in AC, a calibration marker (plastic tube with 300mmol/kg sodium concentration) was placed next to the human knee as sodium reference. In addition to sodium imaging, proton imaging was also performed using MEDIC 3D sequence (TR/TE = 37/20 ms, flip angle = 8°, isotropic resolution = 0.47 x 0.51 x 1.5mm3, and total acquisition time ~5 min). Sodium concentration was determined in the AC ([Na]AC) region of 23Na MRI images as ratio of the mean 23Na signal intensities (SNa) in cartilage region to the sodium signal from reference marker (SNa,ref) of 300mmol/L sodium concentration ([Na]ref) using the Equation 1:

$$[\mathrm{Na}]\mathrm{AC} = (\mathrm{SNa}/\mathrm{SNa,ref}) * [\mathrm{Na}]\mathrm{ref} \quad (1)$$

Results: High resolution proton images of phantom and human knee were acquired as shown in Figure 1a and 1b respectively, while the corresponding sodium images are shown in Figure 1c and 1d. The mean sodium signal intensities calculated from the sodium reference (see arrow in Figure 1e) and articular cartilage (Figure 1f) in sodium MRI image are 199 and 168 for 22 and 81 pixels respectively, representing homogeneous and intense sodium signal in both reference and AC . The estimated sodium concentration in AC region from sodium image is 253mmol/L, which correspond to values reported for the normal AC.