Exploring Spatial Relationships of Macroscopic Tissue Degradation and Quantitative Sensory Testing of the Knee

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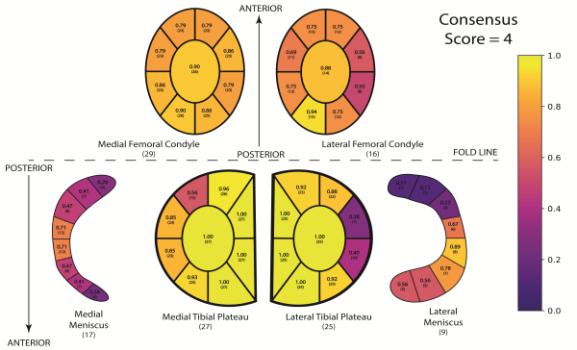
Disclosures: K. Allen: 8; Associate Editor for Osteoarthritis and Cartilage. Y. Cruz-Almeda: 8; Associate Editor for Journal of Pain. 9; (Treasurer of the US Association for the Study of Pain.INTRODUCTION: Discordance in somatosensory function – both painful and non-painful – is a well-documented phenomenon in individuals with osteoarthritis (OA). Clinical observations reveal substantial variability: some individuals with minimal joint degradation report intense pain, while others with extensive joint degradation report little to no pain. This discrepancy may be partly due to the limited spatial resolution of conventional grading systems, which typically assign a single score to an entire joint, potentially masking localized structural-clinical relationships. However, the relationship between joint degradation and non-painful sensory changes remains largely unexplored. In this study, we sought to enhance macroscopic grading by integrating spatial mapping of tissue degradation and comparing these spatially resolved data with site-specific vibratory detection thresholds.

METHODS: All procedures were approved by the UF institutional review board. Individuals scheduled for a total knee arthroplasty (TKA) provided informed consent to attend a preoperative testing visit, including vibratory detection thresholds at multiple superficial superior, medial, lateral, and patellar sites on the knee. Resected tissues were collected during surgery and brought to a dissection hood, where optical pictures were taken of the tissue from an elevated view prior to being dissected for histological and molecular analysis. These optical pictures of tissue were 'segmented' into sub-regions and reviewed by three orthopedic medical residents who graded the tissue individually and as a consensus according to modified Cooper/Outerbridge systems. These modified systems retain the original 0-4 grading scale but also assign sub-regions of highest degradation, introducing spatial resolution. Inter-rater reliability among the graders was evaluated using both Fleiss' kappa and intraclass correlation coefficients (ICC), with kappa values interpreted according to Landis and Koch (1977) criteria, and ICC values interpreted according to Koo and Li (2016). Mean vibratory detection thresholds measures were assessed as a function of tissue score and testing site using a Mann-Whitney correlation test and Spearman's rank tests. A linear mixed-effects model was fit to predict mean vibratory detection thresholds from participants with 'high' or 'low' damage defined by tissue score, including random intercepts for participant ID, vibratory detection threshold site, and tissue type.

RESULTS: Tissues from thirty-one participants undergoing TKA were collected and graded, including medial (n=31) and lateral menisci (n=28), medial (n=31) and lateral (n=31) femoral condyles, and medial (n=29) and lateral (n=28) tibial plateaus. Inter-rater reliability by Fleiss' kappa indicated moderate agreement ($\kappa = 0.475$, $p < 0.001$) while ICC analysis showed moderate reliability for individual raters (ICC_single r = 0.685) and good reliability when averaging across all graders (ICC_average r = 0.897). Figure 1, a heatmap of the degradation driving sub-regions for tissues scored as a 4 by the consensus grade, reveals the distribution of tissue sub-regions driving the score. In all tibial and femoral bone segments, the loading regions consistently showed the most frequent degradation while adjacent regions were less affected. In menisci, central sub-regions showed the greatest degradation while the proximal horns were relatively preserved. Across tissue types, medial compartments showed higher average total tissue degradation compared to lateral compartments. Figure 2 displays the vibratory detection thresholds against tissue score per tissue type and test location, where linear model fits through the data are represented. Spearman's correlation was fitted to these models, and Table 1 displays these correlation coefficients. A Mann-Whitney test showed that participants in the High score group (Score = 4, n = 411) had significantly higher vibratory detection thresholds ($W = 65442$, $p = 0.014$) when compared to those in the Low score group (Score < 4, n = 355). After accounting for repeated measures within participants and across testing sites, the mixed-effects model showed there was no evidence that tissue damage group (High vs Low) predicts differences in mean vibratory detection thresholds ($p = 0.957$).

DISCUSSION: This study introduces a spatially resolved approach to macroscopic grading of knee tissues and demonstrates that degradation is not uniformly distributed across joint structures. Instead, this study provides empirical evidence that tissue degradation is region-specific, with load-bearing areas of bone regions and central meniscal zones most frequently affected, aligning with biomechanical predictions. Associations between tissue score and vibratory detection thresholds were generally weak and inconsistent across testing locations, supporting the mixed effects finding that the apparent group difference observed likely reflects within-subject clustering rather than a consistent effect across participants. Future studies will integrate histological and molecular correlations to macroscopic and other somatosensory function tests, providing further mechanistic insights. These findings emphasize the need for multidimensional assessments of OA that integrate structural, molecular, and sensory data rather than relying solely on gross joint tissue grading to explain pain outcomes.

SIGNIFICANCE/CLINICAL RELEVANCE: This work highlights the importance of spatially resolved grading in assessing tissue degeneration. By refining grading methods and linking them with site-specific measures, this approach may improve our understanding of the disconnect between structural changes and pain in osteoarthritis, ultimately informing targeted interventions and diagnostics.



	Inferior to Patella	Lateral Joint Lining	Lateral Patella Fat Pad	Medial Joint Lining	Medial Patella Fat pad	Superior to Patella
Lateral Femur	-0.446	0.21	-0.06	-0.003	0.045	-0.82
Lateral Meniscus		-0.02	-0.22	0.094	-0.088	-0.581
Lateral Tibia	-0.632	0.137	-0.076	-0.14	0.033	-0.63
Medial Femur	-0.028	-0.108	-0.171	-0.176	-0.267	0.036
Medial Meniscus	-0.675	-0.102	-0.232	-0.153	-0.053	-0.691
Medial Tibia	0.006	0.027	-0.09	-0.119	0.02	-0.352

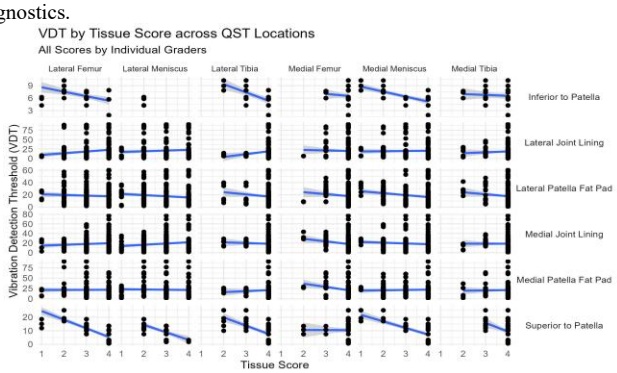


Figure 1 (upper left) displays a heatmap of regions of highest degradation for all tissues which received a score of 4 by consensus. Color in the region indicates the frequency of the region being selected, normalized by the total number of tissues with score 4 for that tissue type.

Figure 2 (upper right) displays the vibration detection thresholds on the left y-axis versus tissue score organized in rows by vibration detection threshold site and in columns by tissue type.

Table 1 (lower left) displays the Spearman's rank coefficients for vibration detection threshold versus total tissue score for specific VDT location sites and tissue types.