Computational Modeling Holds the Potential for Estimating Knee Pain Intensity in Individuals with Knee Osteoarthritis During Different Functional Activities: An Exploratory Cross-Sectional Study

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INTRODUCTION: Understanding the intricate relationship between joint mechanics and clinical pain holds paramount significance, especially in the context of prevalent musculoskeletal disorders such as osteoarthritis (OA). OA is a degenerative joint disorder characterized by the deterioration of articular cartilage, and the hallmark symptom is chronic pain, which leads to reduced quality of life. Elucidating the potential association between joint mechanics and clinical pain could potentially help in developing personalized interventions, e.g., rehabilitation and gait modification which aim to restore joint function, reduce pain, and postpone OA. Despite extensive research, a direct link between mechanical loading and clinical pain severity is currently missing [1]. In this study, we investigated the associations between regional knee mechanics and experienced knee pain in individuals with knee OA (KOA) during different functional activities. We hypothesized there would be a positive correlation between the compressive joint contact force (JCF) and the KOA pain intensity, only within the regions with cartilage defects extending to the bone.

METHODS: 14 participants (8 females) with tibiofemoral KOA, with no record of knee injuries/surgeries, performed 17 different daily activities (e.g., walking, stair negotiation, etc.) and rehabilitation exercises (e.g., side-slide, forward-backward step, etc.) [2], during which we collected motion data (3D marker trajectories and grand reaction forces), electromyography (EMG, 8 muscles of the studied leg), and subject-reported knee pain location and score during exercises (visual analog scale, range from 0 to 100, "0": no pain, "100": worst pain imaginable). Magnetic resonance images (MRI) of the knees were acquired to create musculoskeletal (MSK) models and assess knee cartilage health. The Northern Savo Hospital District ethics committee approved all procedures (#750/2018), and written informed consent was obtained from all participants. A previously developed MSK modeling framework was used [3], in which the knee had 12 degrees of freedom, and articulating surfaces were modeled by an elastic foundation contact model (Young's modulus of 20 MPa, Poisson's ratio of 0.45). Within the MSK models, knee geometries (i.e., femoral, tibial, and patellar bones and cartilages) were updated based on participants' MRI, using an atlas-based method [2] (Figure 1). We conducted an EMG-assisted MSK analysis [3,4], in which knee kinematics, muscle activations, and knee contact pressures were estimated concurrently. We used Pearson rank correlation to investigate the association between the knee pain and loading-related parameters, i.e., maximum and the impulse of the muscle activations, total and regional knee JCF (anterior, central, and posterior regions, Figure 1), and knee varus-valgus moment within the femoral and tibial cartilages, separately for each participant. The impulse was the area under the curve (time series) of the related quantity.

RESULTS: 7 participants had full-depth cartilage defects. In 6 out of these 7 participants (Table 1, #1-3, #7, #9, and #13), we observed moderate to strong correlations ($\rho = 0.76 \pm 0.12$, $0.001 < \text{p-value} < 0.05$) between clinical pain and impulse of regional compressive JCF (i.e., the JCF passing through the knee region with full-depth cartilage defect). Of note, the most painful activity varied across participants. In 6 out of the 7 remaining participants (Table 1, #4-6, #10-11, and #14), clinical pain was experienced as arising from structures outside of the knee. In these subjects, we did not observe a significant and meaningful correlation between knee pain and loading. In the remaining participant (Table 1, #8), who did not have full-depth cartilage defects but had pain at the knee, we did not observe significant correlations between maximum or impulse of knee mechanics and pain. Overall, no significant correlations were observed between knee pain intensity and maximum or impulse of knee-crossing muscle activations, knee varus-valgus moment, and total knee JCF.

DISCUSSION: These results indicated moderate to strong correlations between knee pain and the impulse of compressive regional knee JCF in subjects with full-depth cartilage defects. We observed no association between knee pain and loading within knee regions without cartilage defects, suggesting that the link between clinical pain and biomechanics might only be prevalent in a subset of patients with OA. This was in line with our hypothesis, which assumed that heightened mechanical stimulus within the area with a full-depth cartilage defect would stimulate the nerves of the underlying bone resulting in pain sensations. Notably, one subject with a full-depth cartilage defect was an exception (Table 1, #12), which might be attributed to the coexistence of knee osteophytes and Baker cysts (as detected via the MRI evaluation), affecting the knee pain. We observed no discernible correlations between knee pain and muscle activations, knee moment, or total knee JCF, consistent with the literature [1,5]. In the future, we will extend our simulations to tissue-level analysis [2], to account for the knee mechanobiological responses (including inflammation) and investigate the mechanisms underlying knee mechanobiology and pain in patients with KOA.

SIGNIFICANCE/CLINICAL RELEVANCE: This exploratory study showed the potential to predict knee pain intensity by modeling-based knee mechanics during different activities of individuals with KOA. With varying painful activities among participants, our results suggest that physics-based modeling could enhance targeted interventions, e.g., personalized rehabilitation to restore joint function while reducing knee pain and avoiding excessive cartilage loading.

REFERENCES: [1] Wu W. et al., OA and Cart., v30(6), 2022. [2] Esrafilian et al., IEEE TBME, v69(9), 2022. [3] Lenhart et al., Annals of BioMed. Eng., 43(11), 2015. [4] Pizzolato C. et al., J. Biomechanics, v48, 2015. [5] Astephen Wilson J.L. et al., OA and Cart., v19(2), 2011.

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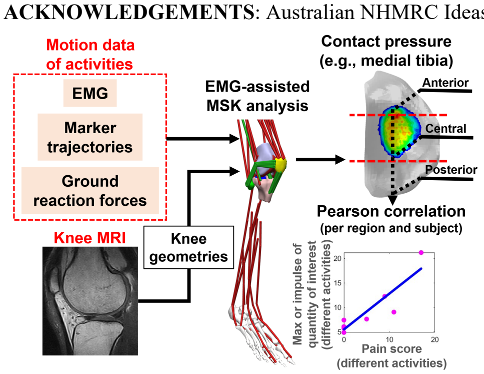

Figure 1. Workflow of the study.

# Subject	Impulse of regional JCF (ρ, p-value) Tibia	Femur	# Subject	Impulse of regional JCF (ρ, p-value) Tibia	Femur	# Subject	Impulse of regional JCF (ρ, p-value) Tibia	Femur
1	0.90, 0.001	0.88, 0.002	6	0.33, 0.35	0.40, 0.25	11	0.15, 0.67	0.08, 0.83
2	0.90, 0.001	0.91, 0.001	7	0.74, 0.015	0.64, 0.047	12	0.365, 0.3	0.286, 0.58
3	0.63, 0.061	0.722, 0.028	8	0.20, 0.68	0.22, 0.63	13	0.607, 0.042	0.488, 0.152
4	0.03, 0.93	0.095, 0.80	9	0.69, 0.039	0.62, 0.074	14	0.50, 0.14	-0.31, 0.38
5	0.15, 0.68	0.19, 0.60	10	-0.06, 0.87	-0.32, 0.23			

Table 1. Pearson correlation coefficients (ρ) and p-values between the impulse of JCF and knee pain during 17 functional activities performed by 14 participants. Subjects and locations with full-depth cartilage defects are highlighted. The red font indicates $p<0.05$.