Synovium-Cartilage Crosstalk in Facet Joint Osteoarthritis and Correlations with Adjacent Disc Degeneration

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INTRODUCTION: Low back pain (LBP) affects up to 85% of individuals and is the leading cause of disability worldwide, often stemming from degeneration of the spinal motion segment[1]. The facet joints (FJs) are synovial articulations posterior to the intervertebral disc (IVD) that play a critical role in load transmission and constrain range of motion in the spine (**Fig 1A**)[2]. These joints gradually undergo degenerative changes characterized by cartilage erosion, subchondral sclerosis, and synovial remodelling compounded by inflammatory responses and biochemical alterations that stimulate nociceptive pathways ultimately leading to chronic pain[3]. This pathology is called facet joint osteoarthritis (FOA), and contributes to back pain in 15-41%[4] of patients. In other synovial joints such as the knee and hip, synovitis is tightly linked to symptoms and structural progression of osteoarthritis (OA)[5], yet the contribution of the synovium to osteoarthritic changes in the facet joint and degeneration of the adjacent intervertebral disc remains poorly understood. ***We hypothesized that FJ synovium pathology initiates and drives inflammatory and catabolic changes in FOA and severity of FOA correlates with adjacent IVD degeneration.***

METHODS: *Cadaveric spine acquisition:* Five lumbar spines (2 male, 3 female, 27-70yo), were obtained from human cadavers (Science Care and NDRI). *IVD qMRI*: To assess disc degenerative changes, 3T MRI with sagittal T2 mapping (resolution = 0.5 mm, TEs = 13, 26, 39, 52, 71 ms) were obtained for disc Pfirmann grading[6], and to quantify nucleus pulposus (NP) T2 relaxation times[7]. Spinal motions segments (n = 22) were dissected into discs and facet joints. One facet joint from each spinal level was left intact, and its contralateral joint was disarticulated. *Facet cartilage creep indentation:* The articular surface was indented using a 2 mm spherical indenter (0.1 N creep load for 15 minutes at four locations per surface)[8]. *Facet qMRI and histopathology*: Following mechanical testing, T2 mapping of the facet articular cartilage was performed on a 4.7T preclinical MRI scanner (resolution = 117µm, TE = 15ms, 10 echoes). Evaluation of cartilage damage[9] and synovial inflammation and damage [10] was performed on paraffin embedded axial sections of intact facets (**Fig1B**). *Imaging mass cytometry (IMC)*: Additional axial sections underwent heat-mediated antigen retrieval and overnight incubation with a basic immune cell panel to delineate myeloid and lymphoid cells generally (CD3, CD20, CD45, CD68), a myeloid subset panel (CD11b, CD11c, CD14, CD66b, CD163, HLA-DR) and a tissue architecture panel (fibronectin, Col1, αSMA, VEGF) of metal-conjugated antibodies. This was followed by incubation with Intercalator-Ir nuclear stain, and imaging using a Hyperion Imaging System. *Statistical analysis:* Differences in quantitative outcomes stratified by OARSI score were assessed via a student's t-test ($p<0.05$). Principal component analysis (PCA) biplots were generated in Python.

RESULTS: Facet cartilage mechanical testing demonstrated that increased OARSI scores were accompanied by increased cartilage permeability and reduced tensile and compressive moduli **(Fig1 C, D, E**). Although synovial inflammation, synovial damage, and cartilage T2 values did not differ significantly when stratified by OARSI score, PCA biplots (**Fig 2**) demonstrated that more degenerative facet cartilage (higher OARSI scores and macroscopic grades) and higher synovial damage scores were associated with reduced IVD NP T2 values indicating more extensive disc degeneration. Synovial inflammation was not correlated with synovial damage but was inversely correlated with facet cartilage mechanical properties. PCA analysis revealed distinct phenotypes: healthy, hydrated IVDs with little facet pathology (cluster C); concomitant disc degeneration and facet synovium damage (cluster B); facet synovial inflammation with minimal disc and facet degeneration (cluster A), and severely degenerated discs and facets marked by high synovial inflammation, and compromised cartilage mechanics (cluster D). IMC demonstrated strong expression of collagen I, fibronectin, αSMA, and VEGF, as well as abundant immune and myeloid lineage cells within the facet synovium **(Fig 3**).

DISCUSSION: Our data revealed distinct phenotypes of spinal disease, with synovial damage and inflammation driving disparate phenotypes of degeneration, consistent with knee OA[10]. The presence of elevated synovial inflammation in samples with only modest structural damage suggests that synovial inflammatory signaling may contribute to subsequent tissue breakdown. These findings parallel knee OA where inflammatory cells can drive articular extracellular matrix degradation, pain and progression of disease[5]. The negative correlation between NP T2, synovial damage and cartilage degeneration provides evidence for facet–disc crosstalk, however, the biological mechanisms driving this relationship remain unclear and warrant further investigation. IMC further revealed ECM remodeling proteins (collagen I, fibronectin), myofibroblast activation (αSMA), angiogenic factors (VEGF), and immune cell infiltration, features consistent with synovial remodeling in knee OA, where fibroblast activation and neovascularization sustain inflammation and nociception[5]. Ongoing IMC analyses will quantify changes in tissue architecture and synovial cell populations as FOA progresses and will be compared to healthy facets to define molecular and cellular signatures of disease.

SIGNIFICANCE: Together, these results highlight the contribution of synovial inflammation and damage to FOA progression and adjacent disc degeneration, positioning the synovium as both a driver of pathological changes and a potential therapeutic target for low back pain.

REFERENCES:[1] Shahidi+ J Orthop Res., 2017, [2] Jaumard + J Biomech Eng., 2011, [3] Gelhorne + Nat Rev Rheumatol., 2013, [4] Du + J Pain Res., 2022, [5] Scanzello + Bone., 2012, [6] Pfirrmann + Spine (Phila Pa 1976)., 2001, [7] Martin + J Orthop Res., 2015 [8] Gupta + J Orthop Res., 2023 [9] Pritzker + Osteoarthritis Cartilage., 2006 [10] Philpott + Osteoarthritis Cartilage., 2024.

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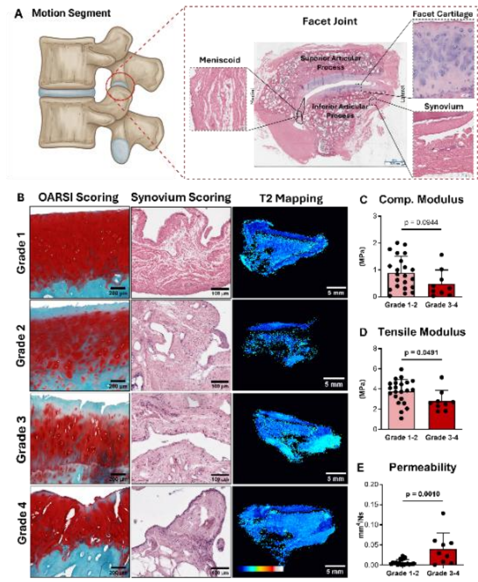

Fig 1: A) Facet Joint location and Anatomy. **B**) Facet cartilage, synovium scoring and T2 maps stratified by OARSI scores. Facet Cartilage Mechanical Properties stratified by OARSI score, **C)** Compressive Modulus, **D)** Tensile Modulus, **E)** Permeability.

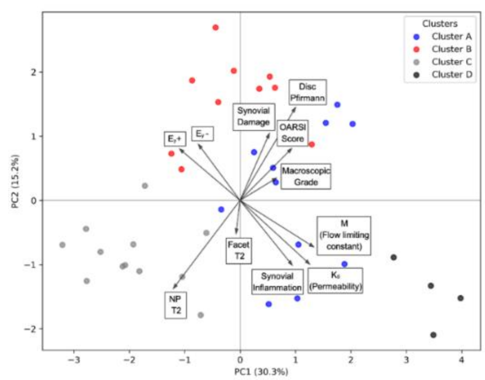

Fig 2: PCA biplot showing relationships between FJ cartilage properties, IVD structure, and FJ synovial pathology. Arrows in the same direction = direct correlation, arrows in opposite directions = inverse correlation, arrows at 90 degrees = no correlation.

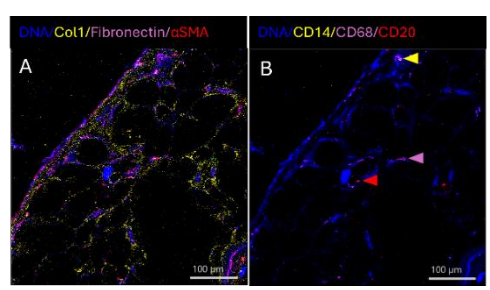

Fig 3: IMC of Facet Joint Synovium. A) tissue architectural markers in FJ synovium, **B)** Immune cell markers in FJ synovium.