Measurements of Local Strains Allows for Detection of Distinct Tribological Phenotypes of Arthritic Synovial Fluid and Efficacy of Viscosupplementation

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DISCUSSION: Patients with mild to moderate osteoarthritis have been treated with viscosupplementation using hyaluronic acid (HA) for decades as it functions to increase the viscosity of diseased synovial fluid and improve cartilage lubrication. Clinical efficacy of viscosupplementation has shown mixed results with some patients reporting reduced pain and function up to 6 months after injections and others reporting no change. It is unknown if there are different tribological phenotypes of arthritic synovial fluid, and if viscosupplementation may benefit specific disease states. Assessing friction coefficients of synovial fluid provides global measurements over the shear cycle, but does not account for temporal differences in static and kinetic friction. Few reports have investigated how static friction differs between pathologic human synovial fluid, and if temporal differences in static friction can explain observed strains through the tissue depth. The objective of this study was to investigate the effect of viscosupplementation on friction coefficients and shear strains in articular cartilage between inflammatory and non-inflammatory arthritic phenotypes of human synovial fluid, and identify any temporal differences in friction behavior.

METHODS: Diseased human synovial fluid samples were obtained with patient consent from the knee joints of 10 patients with osteoarthritis by Dr. Ramonda. Synovial fluid samples containing a white blood cell count greater than 2000 cells/mm³ and a polymorphonuclear neutrophil composition over 25% were classified as inflammatory arthritis (n=6), with the remaining samples classified as non-inflammatory arthritis (n=4). Cartilage was explanted from the femoral condyles of neonatal bovids and sectioned into 6x2mm cylinders. Samples were articulated against glass under 15% normal strain for 30 cycles at 1mm/s while bathed in either synovial fluid or a 1:1 mixture of synovial fluid with Hymovis, an HA viscosupplement. Friction coefficients were measured as described previously. In parallel, samples were bisected, fluorescently stained, and mounted onto a tissue deformation stage on an inverted confocal microscope. While bathed in a synovial fluid sample, cartilage plugs were axially compressed 15% then articulated against glass at a sliding speed of 1mm/s. Depth-dependent shear deformations were tracked by analyzing displacements of photobleached lines oriented perpendicular to the articular surface (Fig 1A). Local shear strains were calculated using a custom Matlab code. Following testing, the synovial fluid sample was mixed in a 1:1 ratio with Hymovis and the same test was performed on a new cartilage sample. The duration that the tissue spent in static friction (t_\text{static}) was calculated for each sample (Fig 1B). The ratio of time in static friction over one sliding cycle was calculated by dividing t_\text{static} by the period (t_\text{cycle}). This ratio was plotted against strains at three different depths in the tissue and fit using linear regression. Friction coefficients were compared using a t-test and shear strains were compared between inflammatory and non-inflammatory groups +/- Hymovis using a two-way repeated measures ANOVA.

RESULTS: Friction coefficients and shear strains in inflammatory synovial fluids were compared to non-inflammatory synovial fluids, but were not statistically significant (p=0.154 and p=0.091 respectively, Fig 2A). The addition of Hymovis to the inflammatory synovial fluid group significantly reduced the strains (p<0.05), but did not decrease tissue strains in the non-inflammatory synovial fluid group (p=0.989). Friction coefficients and ratio of time in static friction both showed positive correlations with tissue shear strains, but the ratio of time in static friction consistently explained more variability in shear strains than friction coefficients at all tissue depths (Fig 2B,CD). The amount of variability explained by the ratio t_\text{static}/t_\text{cycle} increased from 66% at the surface to over 75% at a depth of 225µm.

DISCUSSION: This study showed that there are arthritic phenotypes that have different tribological behavior resulting in different tissue strains under shear loading. For all synovial fluids, longer durations in static friction correlated with increased tissue strains under shear. Inflammatory synovial fluid samples showed higher shear strains and longer t_\text{static}/t_\text{cycle} ratios that were decreased with the addition of Hymovis while non-inflammatory samples showed no change. This suggests that viscosupplementation may be more effective for certain arthritic phenotypes. Regardless of arthritic phenotype, this study shows that time in static friction explains tissue shear strains better than the coefficient of friction. High shear strains have been linked to increased cell death and apoptosis, and therefore identifying how lubricants alter static friction may be important when understanding their efficacy in arthritis treatment.

SIGNIFICANCE: Our results describe distinct arthritic synovial fluid tribological phenotypes with inflammatory synovial fluid showing increased strains compared to non-inflammatory synovial fluid, and HA supplementation only improving lubrication in the inflammatory group. Time in static friction is a better predictor of tissue scale phenomena than friction coefficients for arthritic synovial fluid with or without viscosupplementation.