Effect of Arthroscopic Cartilage Defect Repair with Bone Marrow Derived Cells on the Lubricant Properties of Synovial Fluid

1Grissom M J; 2Temple-Wong M M; 1Adams M S; 1Schumacher B L; 2Fortier L A; 3Chu C R; +1Sah R L
1University of California-San Diego, La Jolla, CA, 2Cornell University, Ithaca, NY, 3Univeristy of Pittsburgh, Pittsburgh, PA
Senior author: rsah@ucsd.edu

Introduction: A variety of arthroscopic procedures for repair of articular cartilage defects appear promising but also lead to variable outcomes. Both traditional microfracture (MF) and application of minimally-processed bone marrow aspirate concentrate (BMC) attempt to stimulate repair with the initial formation of a bone- adherent clot at the defect site.¹ In healthy individuals, synovial fluid (SF) provides lubrication to articular cartilage through its high concentration of lubricant molecules proteoglycan-4 (PRG4) and hyaluronan (HA), individually and in combination.² After a variety of naturally-occurring joint injuries as well as experimental procedures performed via (mini-)arthroto¬my, the lubricant quality of SF is abnormal. However, the extent of such abnormality is unclear after surgery that is performed in an arthroscopic manner typical of the clinical situation and in the setting of cartilage defect repair. We tested the hypothesis that arthroscopic cartilage repair procedures, MF and BMC, lead to alterations in the lubrication quality of SF. The aims of this study were to determine whether treatment of full thickness chondral defects in equine stifles joints by arthroscopic (1) MF or (2) BMC injection modulate the lubricant function (friction) and lubricant molecules (concentration and structure) in equine synovial fluid (eSF) in a manner dependent on time after treatment.

Methods: With IACUC approval, experimental cartilage defects 15 mm in diameter extending down to, but not through, the subchondral bone were created bilaterally in the mid-lateral trochlear ridge of adult horses (n=12). For each horse, one stifle joint was treated with MF (n=12) while the other was treated with BMC injection (n=12). From each of these two joints, SF was aspirated at different times, at day 0 (the pre-injury state, 0d), and at 10 days (10d) and 3 months (3mo) following surgery. The eSF was clarified by centrifugation (3,000g, 30min, 4°C) and stored at −70°C before subsequent analysis. Friction Test of Boundary Lubrication: Portions of eSF were analyzed for start-up (static, μs) with pre-spin pause times, Tp=1, 2, 12, and 120s) and steady-state (kinetic, μk) coefficients of friction as measures of boundary lubrication function in a cartilage-on-cartilage articulation test.³ Lubricant solutions, as well as PBS controls, were supplemented with protease inhibitors and tested on substrates of normal bovine articular cartilage. Friction coefficients were determined in the boundary mode of lubrication at 18% compression and a sliding velocity of 0.3mm/s. Biochemical Analysis of Putative Boundary Lubricants. Other portions of eSF were assayed for the concentrations of HA (ELISA-like assay⁴), PRG4 (Western Blot and comparison to equine PRG4 standard), and total protein (BCA). Statistics. Data are expressed as mean ± SEM. Differences were assessed by repeated-measures ANOVA with treatment (BMC, MF) as the main effect and time (0d, 10d, 3mo) as the repeated factor. When time (but not treatment) had an effect, the effect of time (i.e., before or after repair treatment) was assessed using a 1-way ANOVA with Tukey post-hoc tests. Correlation of friction data with [HA] and [PRG4] was determined using linear regression.

Results: Kinetic (Fig 1A) and static (Fig 1B) friction coefficients of eSF varied significantly with time after surgery (each, p<0.001) but not between treatment groups (each, p>0.6). The kinetic friction coefficients at t=0d (before the repair procedures) averaged 0.303 and 0.031 in the knees used for MF and BMC, respectively. Relative to those values, the kinetic friction coefficients were 60% higher at t=10d (p=0.01, Fig 1B) but returned to baseline levels at t=3mo (p=0.9, Fig 1B). HA (Fig 2A), PRG4 (Fig 2B), and protein (Fig 2C) concentrations also varied with time (each, p<0.001) but not with treatment (p=0.9, 0.4, and 0.7, respectively). HA concentration was 73% lower in t=10d samples (p<0.01 Fig 2A) and 49% higher in t=3mo samples (p<0.01 Fig 2A) than t=0d samples. PRG4 and protein concentrations, on the other hand, were higher (510% and 93%, respectively) in t=10d samples than those at t=0d (each, p<0.01, Fig 2B and 2C) and returned to t=0d levels at t=3mo (p=0.2 and p=0.9, respectively, Fig 2B and 2C). Kinetic friction coefficients decreased linearly with increasing [HA] (Fig 3A, slope: p<0.01) and increased linearly with increasing [PRG4] (Fig 3B, slope: p<0.001).

Discussion: The finding that SF function and composition is modulated over time following surgical repair of a cartilage defect independent of the type of repair suggests a common local response that adversely affects joint lubrication post-operatively. On the other hand, systemic factors may also have contributed to the similar responses of the ipsilateral joints. Such abnormal lubrication, even for a short duration post-operatively, may lead to cartilage wear especially at the articular surface. If so, counteracting altered lubrication may be a target for intervention and also enhance cartilage repair strategies.

References: 1 Horas+; J Bone Joint Surg Am, ’03. 2 Schmidt+, Arthritis Rheum, ’07. 3 Fosang+, Matrix, ’90.
Acknowledgements: NIH, HHMI.