Fluid Flow Properties Of Articular Cartilage Change Most In Very Early Osteoarthritis

Janne TA Mäkelä, MSc¹, Sang Kuy Han, PhD², Walter Herzog, PhD³, Rami Korhonen, PhD¹.
¹University of Eastern Finland, Kuopio, Finland, ²Korea Institute of Industrial Technology, Cheonan-si, Korea, Republic of, ³University of Calgary, Calgary, AB, Canada.

Disclosures: J.T. Mäkelä: None. S. Han: None. W. Herzog: None. R. Korhonen: None.

Introduction: Anterior cruciate ligament transection (ACLT) is a recognized method to produce osteoarthritic symptoms in rabbit knee joints. The earliest degenerative changes in the structure of rabbit cartilage have been reported to occur 4 weeks post surgery[1,2]. However, it is not known how the functional properties of cartilage constituents (collagen, proteoglycans, fluid) change in different locations in this animal model. Finite element (FE) modeling can distinguish the mechanical effects of collagen, proteoglycans (PGs) and fluid in loaded articular cartilage, and thus, can be used to study the role of these constituents in osteoarthritis. In this study, experimental indentation tests together with a fibril-reinforced poroviscoelastic (FRPVE) model were applied to assess the very early, location-specific changes in the mechanical properties of rabbit articular cartilage in normal and osteoarthritic cartilage, created experimentally by ACLT.

Methods: Skeletally mature, female New Zealand white rabbits were used. Unilateral ACLT was performed in eight rabbits and the contralateral joints were used for analysis as a contralateral (C-L) control group. A separate control (CTRL) group consisted of ten knee joints from five non-operated rabbits. Animals were sacrificed at four weeks after ACLT and cartilage-on-bone samples from femoral groove, medial and lateral femoral condyles, and tibial plateaus were harvested for the measurements (Fig. 1). All procedures were approved by the Animal Ethics committee at the University of Calgary and the guidelines of the Canadian Council on Animal Care were followed.

Our axisymmetric FRPVE model (Fig. 1) consisted of a viscoelastic fibrillar matrix and a biphasic, poroelastic, non-fibrillar matrix. In order to keep the modeling analysis independent of the structural analysis, no information of cartilage structure and composition was implemented into the FRPVE model. A stress-relaxation protocol in indentation geometry was used for biomechanical measurements (2x5% steps, 100%/s ramp rate, 15 min relaxation time after each step, 1 mm indenter diameter). The first step was considered as a pre-strain, thus the FRPVE model was fitted to the force curve of the second step by minimizing the mean absolute error between the experimental results and the model predictions. Three parameters were optimized: fibril network modulus (Ef), representing the collagen network; non-fibrillar matrix modulus (Enf), representing the PG matrix; and permeability (k)[3] (Fig. 2). Statistical comparisons for the model parameters between the groups were done using the Kruskal-Wallis (K-W) non-parametric ANOVA as animal specific variation was not significant.

Results: Apart from the non-fibrillar matrix modulus Enf, the experimentally determined mechanical parameters of the CTRL group illustrated significant variation between locations (p < 0.001) (Fig. 3). ACLT caused significant changes (p < 0.05) especially to the permeability k, but also to the fibril network modulus Ef and Enf (Fig. 3). The permeability k in the ACLT group (compared to the CTRL group) was significantly higher (p < 0.05) in all of the sites except for the medial tibial plateau. On the other hand, the non-fibrillar matrix modulus Enf in the ACLT group (compared to the CTRL group) was significantly lower (p < 0.05) in the lateral femoral condyle and Ef in the lateral and medial femoral condyles and in...
the femoral groove. In the C-L group (compared to the CTRL group), k was significantly higher and Ef significantly lower ($p < 0.05$) in all sites.

**Discussion:** ACLT modulated alterations in the mechanical properties of cartilage were noticed at all sites of rabbit knee joints. Changes were most severe in the permeability, but significant changes were also found in the fibril network and non-fibrillar matrix modulus. Higher permeability is related to an increase in water content in the tissue[4], yet changes in collagen and PGs also play a role as water has to flow through the pores of the tissue which are controlled by these constituents. In our previous study using ACLT rabbits[5], the amount of collagen in the superficial zone had decreased and the altered orientation angle of collagen fibrils extended deep into the tissue in the femoral groove, where changes in the permeability due to ACLT were largest. Furthermore, due to ACLT, the PG content was reduced most in the femoral condyles, where the non-fibrillar matrix modulus was observed to decrease. Significantly reduced collagen fibril network modulus may be related to collagen fibrillation (increased fibril orientation angle), as observed earlier by us in particular for the lateral femoral condyle and the femoral groove[5]. On the other hand, the FRPE model was able to identify functional changes in locations where biomechanical modulus values were not changed (for instance in the femoral groove). As incompressible water absorbs impact forces and can support $\sim 90\%$ of the loads, higher permeability increases fluid flow and decreases pressurization in the tissue. This leads to weaker resistance of cartilage to impact forces and faster tissue relaxation. On the other hand, lower fibrillar network strength leads to larger tissue deformations and also weaker ability of the tissue to withstand dynamic forces. Thus, a degenerated collagen network combined with higher permeability may expose articular cartilage to additional damage and OA progression via excessive strains.

**Significance:** We used computational modeling to identify the mechanical changes in very early OA, 4 weeks after ACLT. The model was effectively able to distinguish location-specific changes especially in fluid flow properties of cartilage due to ACLT. During joint loading, impairment of this novel parameter may (by reduced fluid pressurization and increased strain) lead to more severe OA without any intervention.
Fig 1: Measurement locations (marked with black dots) and the mesh of the finite element model. Analyzed locations were medial (left) and lateral (right) tibial plateaus (A), femoral condyles (B), and femoral groove (C). The axisymmetric finite element mesh from one cartilage sample (D) and the model swept 360° for illustrative purposes (E).
Fig 2: Representative experimental stress-relaxation responses and the optimized model predictions for ACLT, C-L (contralateral) and CTRL (non-operated control) group samples (tibial plateau).
Fig. 3: A column bar graph showing the average values (± 95% confidence intervals) of material parameters for each group. ACLIT = anterior cruciate ligament transection, C-L = contralateral, CTRL = non-operated control, EF = fibril network modulus, End = non-fibril network modulus, k = permeability, *p < 0.05, **p < 0.01, ***p < 0.001.

ORS 2015 Annual Meeting
Poster No: 0791