FIBRIL REINFORCED POROELASTIC MODEL PREDICTS MECHANICAL EFFECTS OF PROTEOGLYCAN AND COLLAGEN DEGRADATION IN ARTICULAR CARTILAGE

[+]Korhonen, R.K.; [*]Laasanen, M.S.; [+]Töyräs, J.; [*]Rieppo, J.; [*]Helminen, H.J.; [+#]Jurvelin, J.S.

[+]Department of Applied Physics, University of Kuopio, POB 1627, 70211 Kuopio, Finland
[*]Department of Anatomy, University of Kuopio, Kuopio, Finland
[#]Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland

INTRODUCTION: Loss of articular cartilage (AC) proteoglycans (PGs) and degradation of collagen fibril network are early signs of osteoarthrosis (OA) [1]. Experimental enzymatic treatments can simulate some tissue changes typical of OA. Mechanical, acoustic and MRI measurements, as well as microscopical analyses sensitively detect cartilage changes caused by chondroitinase ABC or collagenase [2,3]. Typically, PG depletion by chondroitinase ABC primarily affects the equilibrium (static) stiffness while experimental collagen degradation by collagenase reduces significantly the dynamic stiffness as well [3,4]. The objective of the present study was to model effects of PG depletion or collagen degradation on the stress-relaxation of AC in unconfined compression geometry using the fibril reinforced poroelastic (FRPE) finite element (FE) model [5]. Specifically, the mechanical effect of PG depletion was simulated in FRPE model by reducing the Young's modulus of the solid matrix while the effect of collagen network degradation was mimicked by reducing the modulus of the fibril network. The model predictions were then compared with the experimental results obtained after chondroitinase ABC or collagenase treatments of bovine cartilage.

MATERIALS AND METHODS: Cylindrical cartilage samples (∅=4 mm, thickness=1.48±0.32 mm) were harvested from the bovine patellae (n=12). Chondroitinase ABC (Seikagaku Co., Tokyo, Japan) was used for PG digestion (n=6) and collagenase type VII (C 0773, Sigma Chemical Co., St. Louis, MO, USA) for type II collagen degradation (n=6). The incubation time (in 37°C, 5% CO_2 atmosphere) for chondroitinase ABC (0.1 U/ml) and collagenase (30 U/ml) digestions was 44 h.

Stress-relaxation tests (12.5 kPa pre-stress, 10% strain, 2 mm/s ramp rate) were utilized to characterize time dependent behavior of cartilage in unconfined compression geometry. Samples were tested before (reference measurements) and after enzymatic digestions.

Mechanical behavior of two characteristic chondroitinase ABC and collagenase treated samples were simulated with a commercial FE package (Abaqus v.5.8, Hibbitt, Karlsson&Sorensen, Inc., Pawtucket, RI, USA). In the axially symmetric model, cartilage consisted of 8-node quadratic poroelastic elements (element type CAX8P). Collagen fibrils were modelled as nonlinear springs (element type SPRINGA), which resist tension only. The mesh included 12×18 poroelastic elements and spring elements were attached in the horizontal direction (Fig. 1). Symmetry boundary condition was applied by restricting the horizontal movement of the axial line. Values of material dimensions (∅=4 mm, thickness=1.43 and 1.51 mm) were the same as the values found from experimental tests. Modulus of fibril network, modulus of solid matrix, and permeability were adjusted in order to simulate the experimental data (Table 1). The Poisson's ratio of solid matrix (ν=0.42) was constant during simulations.

Table 1. Material parameters used in FE simulations.

		Modulus of fibril network, $E_f=E_f^{\varepsilon}\varepsilon_f+E_f^{0}$ (MPa)		Modulus of solid matrix (MPa)	Permeability, (10^{-15} m^4/Ns)
		E_f^{ε}	E_f^{0}	E_s	k
Sample 1 (chondroitinase ABC)	Before treatment	2250	0.9	0.35	0.82
	After treatment	2250	0.9	0.04	1.02
Sample 2 (collagenase)	Before treatment	2500	1.0	0.20	1.12
	After treatment	750	0.3	0.10	2.04

RESULTS: Experimentally, the equilibrium Young's modulus decreased significantly ($p<0.05$, Wilcoxon signed ranks test) after both chondroitinase ABC (0.39±0.15 MPa → 0.18±0.12 MPa) and collagenase treatments (0.29±0.19 MPa → 0.12±0.15 MPa). PG depletion by chondroitinase ABC typically reduced peak and equilibrium loads by 20% and 80%, respectively. For collagen degradation by collagenase, typical reductions in peak and equilibrium loads were 70% and 50%, respectively (Fig. 2). In FRPE model, pure PG depletion through uncalcified cartilage, *i.e.* decrease of the Young's modulus of solid matrix without change in fibril modulus, decreased cartilage equilibrium load significantly, whereas the peak load reduced minimally. Instead, pure collagen degradation, *i.e.* decrease of the Young's modulus of fibrillar network without change in solid matrix modulus, induced an inverse behavior, i.e. stronger effect on the peak than equilibrium load. However, to optimize the agreement of model prediction with the experimental observations after collagenase digestion, reduction of the modulus of solid matrix and increase of permeability were also incorporated into FE model (Table 1, Fig. 2).

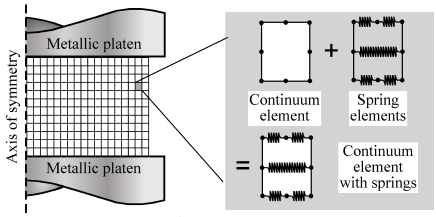

Figure 1. FE mesh in unconfined compression geometry. Nonlinear springs characterize the tangential collagenous network with high tensile stiffness in the horizontal direction.

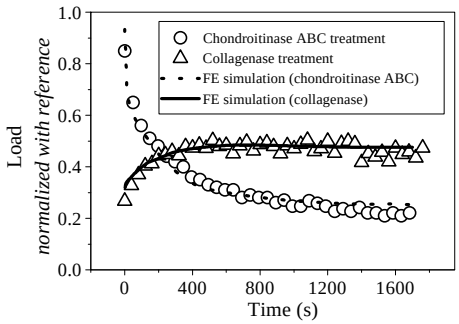

Figure 2. Experimental time dependent behavior of AC after chondroitinase and collagenase treatments, and numerical predictions with the FRPE model. The load is normalized with the reference measurement prior to enzymatic digestions.

DISCUSSION: Fibril reinforced poroelastic FE model predicted characteristic alterations in stress-relaxation behavior of AC, induced experimentally by enzymatic digestions. The model was found to be a good tool for the simulation of mechanical changes associated with early degeneration of AC. After chondroitinase ABC treatment, FE predictions matched with experimental cartilage behavior, provided that the modulus of solid matrix was decreased (PG depletion). After collagenase treatment, numerical analyses predicted experimental data most accurately when both Young's modulus of fibril network and solid matrix were reduced (collagen degradation and PG depletion). This was consistent with the microscopic finding on the secondary PG depletion after collagenase treatment.

The present results suggests that the compression-tension nonlinearity (*e.g.* FRPE) of the cartilage matrix [5,6,7] is necessary to capture realistically mechanical behavior of enzymatically modified articular cartilage.

ACKNOWLEDGEMENTS: Financial support from the Technology Development Center (TEKES), Finland; and the Finnish Graduate School for Musculoskeletal Diseases is acknowledged.

REFERENCES

[1]Helminen *et al*. J Bone Miner Metab **18**:245-57, 2000.
[2]Nieminen *et al*. Magn Reson Med **43**:676-81, 2000.
[3]Töyräs *et al*. Phys Med Biol **44**:2723-33, 1999.
[4]Laasanen *et al*. Biorheology, 2002 (in press).
[5]Li *et al*. Clin Biomech (Bristol, Avon) **14**:673-82, 1999.
[6]Cohen *et al*. J Biomech Eng **120**:491-6, 1998.
[7]Soltz *et al*. J Biomech Eng **122**:576-86, 2000.