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Highly nonlinear stress-relaxation response of articular cartilage in indentation: Importance of collagen nonlinearity

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ABSTRACT

Modern fibril-reinforced computational models of articular cartilage can include inhomogeneous tissue composition and structure, and nonlinear mechanical behavior of collagen, proteoglycans and fluid. These models can capture well experimental single step creep and stress-relaxation tests or measurements under small strains in unconfined and confined compression. Yet, it is known that in indentation, especially at high strain velocities, cartilage can express highly nonlinear response.

Different fibril reinforced poroelastic and poroviscoelastic models were used to assess measured highly nonlinear stress-relaxation response of rabbit articular cartilage in indentation. Experimentally measured depth-dependent volume fractions of different tissue constituents and their mechanical nonlinearities were taken into account in the models. In particular, the collagen fibril network was modeled using eight separate models that implemented five different constitutive equations to describe the nonlinearity. These consisted of linear elastic, nonlinear viscoelastic and multiple nonlinear elastic representations.

The model incorporating the most nonlinearly increasing Young's modulus of collagen fibrils as a function of strain captured best the experimental data. Relative difference between the model and experiment was ~3%. Surprisingly, the difference in the peak forces between the experiment and the model with viscoelastic collagen fibrils was almost 20%. Implementation of the measured volume fractions did not improve the ability of the model to capture the measured mechanical data.

These results suggest that a highly nonlinear formulation for collagen fibrils is needed to replicate multi-step stress-relaxation response of rabbit articular cartilage in indentation with high strain rates.

1. Introduction

Articular cartilage function depends on its structural constituents. The extracellular matrix (ECM) consists mainly of interstitial fluid (60–85 % of the tissue weight), collagen type II (~50–80 % of dryweight) and proteoglycans (PGs) (~30 % of dryweight) (Buckwalter and Martin, 1995; Buckwalter and Mankin, 1998; Mow and Hayes, 1991; Mow et al., 1992). Collagen fibril matrix provides a durable network, resisting primarily tensile forces and dynamic forces in transient periods. This is needed under rapid impact loads, which cause rapid increases in the interstitial fluid pressure. In prolonged loading, the interstitial fluid flows out, leaving proteoglycans (PGs) primarily responsible for the equilibrium stiffness (Buckwalter and Martin, 1995; Buckwalter and Mankin, 1998).

Fibril-reinforced poroelastic finite element (FE) models of cartilage consist of fibrillar and non-fibrillar parts, describing the mechanical effects of collagen, PGs and fluid. The non-fibrillar part has usually been modeled as a linear elastic Hookean or nonlinear hyperelastic Neo-Hookean material, but for the collagen fibers in cartilage, several material models, *e.g.,* linear elastic, nonlinear elastic and nonlinear viscoelastic, have been presented (DiSilvestro and Suh, 2001; Julkunen et al., 2009b, 2013; Kiviranta et al., 2006; Li et al., 1999, 2001; Shirazi and Shirazi-Adl, 2005; Wilson et al., 2004, 2005a, 2005b, 2006). The modern fibril reinforced computational models of articular cartilage can also include inhomogeneous tissue composition and structure of articular cartilage. Implementing tissue nonlinear behavior, structure and volume fractions, *i.e.*, fluid fraction, proteoglycan content, collagen orientation and collagen content, should help to simulate cartilage nonlinear behavior (Julkunen et al., 2008a, 2008b, 2013; Korhonen et al., 2008; Mononen et al., 2012; Pierce et al., 2013, 2015; Rasanen et al., 2013; Saarakkala et al., 2010; Shirazi and Shirazi-Adl, 2008; Shirazi et al.,

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2008; Tanska et al., 2013; Wilson et al., 2006). These fibril reinforced biphasic models have served well in particular for single step creep and stress-relaxation protocols or under small strains in unconfined and confined compression geometries, yet in indentation cartilage may express more nonlinear mechanical response (DiSilvestro and Suh, 2001; Korhonen et al., 2002). The strength of indentation testing lies in the ability to test intact articular cartilage attached to its native bone. However, there are no studies in the literature showing thoroughly the importance of different depth-wise structural components and collagen nonlinearity on the experimentally measured highly nonlinear mechanical response of cartilage in multi-step indentation tests, especially under rapid loading conditions.

We hypothesize that realistic, sample-specific tissue structure and composition together with fibril reinforced biphasic constitutive models typically used for cartilage modeling are not enough to capture highly nonlinear cartilage response in indentation. Therefore, a new material formulation is needed. We applied FE modeling to replicate experimentally measured indentation stress-relaxation tests of rabbit articular cartilage in indentation. The effects of experimentally measured depth-dependent volume fractions were taken into account and the importance of the content and mechanics of different constituents on cartilage nonlinearities were studied.

2. Methods

2.1. Biomechanical measurements and samples

Experimental stress-relaxation measurements were done using a custom made, high-precision material testing device (Korhonen et al., 2002) (resolution: 0.1 µm, 0.005 N) in indentation geometry using an indenter of 1 mm in diameter. After the initial contact of 0.02 N, 3 steps, each 5% of remaining thickness, were applied with 0.05 s ramp time and 15 min relaxation time after each step. Stress-relaxation data was gathered from eight skeletally mature New Zealand white rabbits (Oryctolagus cuniculus, age 14 months), prepared originally for our other study (Makela et al., 2014). All of the measurements showed a highly nonlinear mechanical response in particular for lateral femoral condyle cartilage. Thus, model testing was first conducted using this site, after which the simulation results with the optimal material model were compared with the measurements done in other sites of the knee joint: medial femoral condyle, lateral and medial tibial plateau, and femoral groove. Measurements from one animal were used for model optimization. The animal was chosen as its stress-relaxation response in lateral femoral condyle represented an average of all the measured samples of eight animals. Based on the microscopic measurements (Makela et al., 2015), thickness from surface to subchondral bone was 473 µm for the lateral femoral condyle cartilage and between 485 and 873 µm for the other locations. Width of the cartilage surface exceeded 10 mm in all locations.

2.2. Modeling and optimization

The used models were created using Abaqus 6.10 (Dassault Systèmes Simulia Corp., Providence, RI). Mechanical model parameters were acquired using an optimization process. The applied displacement of the indenter was based on the experimental displacements and the measured force experienced by the indenter was replicated using optimization of the model parameters. In order to obtain best match between the simulated and experimental data, mean squared relative error between the measured and simulated reaction forces with weight on the peak forces, δF_o, was minimized:

$$\delta F_o = \frac{1}{n}\sum_{i=1}^{n}\left(\frac{F_i^{\mathrm{sim}} - F_i^{\mathrm{exp}}}{F_i^{\mathrm{exp}}}\right)^2 + 100\frac{1}{k}\sum_{k=1}^{3}\left(\frac{F_k^{\mathrm{sim}} - F_k^{\mathrm{exp}}}{F_k^{\mathrm{exp}}}\right)^2, \tag{1}$$

where F_i^{sim} and F_i^{exp} are the forces of the simulated and experimental data at current time point i, respectively, and F_k^{sim} and F_k^{exp} are the peak force values of each step.

The latter part of the equation has been used earlier and its function is to give weight to the peak values thus emphasizing their effect in the relative error calculation (Seifzadeh et al., 2011). The weight factor (100) was based on extensive preliminary tests on multiple samples improving the correspondence between the models and experiments. The used sampling frequency in calculations was 100 Hz for the first 50 s of each step which was followed by a 10 Hz sampling frequency. Minimization of error was done using Matlab's built-in minimum search algorithm (fminsearch). The optimization results were verified by altering the initial values and obtaining always the same results. The same parameters as optimized here have also been successfully optimized in earlier studies (Julkunen et al., 2007; Wilson et al., 2004, 2005a, 2005b). Thus, unique material parameters should have been obtained from each optimization.

Cartilage thickness in each model was based on experiments and the radius of the samples in the model was set to constant 4 mm even though from microscopy the value was $>$ 5 mm (Makela et al., 2015). This was enough to eliminate any effects from the sample edges (Spilker et al., 1992). Convergence test for the FE mesh density was conducted in our earlier study (Makela et al., 2015). Here, the mesh was even denser with 960 linear axisymmetric pore pressure continuum elements (type CAX4P, Fig. 2). The following boundary conditions were applied: the cartilage-bone interface was fixed in all directions, the cartilage edge and free surface were assumed to be fully permeable, and the contact between the indenter and cartilage was assumed to be impermeable. At the axis of symmetry, lateral displacements were prevented and fluid was not allowed to penetrate this boundary.

Total of eight separate material models were tested for model optimization (Fig. 1). The first material to be tested was a Neo-Hookean porohyperelastic material without the fibrillar network (Model 1), with the following total Cauchy stress ($\boldsymbol{\sigma}_{\mathrm{t}}$):

$$\boldsymbol{\sigma}_{\mathrm{t}} = \boldsymbol{\sigma}_{\mathrm{nf}} - p\mathbf{I}, \tag{2}$$

where $\boldsymbol{\sigma}_{\mathrm{nf}}$ is the non-fibrillar matrix stress, p is the fluid pressure and $\mathbf{I}$ is the unit tensor.

The hyperelastic non-fibrillar matrix stress can be further expressed as follows:

$$\boldsymbol{\sigma}_{\mathbf{nf}} = \frac{1}{2}K\left(J - \frac{1}{J}\right)\mathbf{I} + \frac{G}{J}\left(\mathbf{B} - J^{2/3}\mathbf{I}\right), \tag{3}$$

where $\mathbf{B}$ is the left Cauchy Green deformation tensor, J is the elastic volume ratio, K is the bulk modulus and G is the shear modulus. The bulk and shear moduli can be expressed as a function of the non-fibrillar matrix modulus E_{nf} and the Poisson's ratio ν_{nf} as follows:

$$K = \frac{E_{\mathrm{nf}}}{3(1-2\nu_{\mathrm{nf}})}, \tag{4}$$

$$G = \frac{E_{\mathrm{nf}}}{2(1+\nu_{\mathrm{nf}})}. \tag{5}$$

The fluid flow in the non-fibrillar matrix was modeled according to Darcy's law:

$$q = -k\nabla P, \tag{6}$$

where q is the flow rate in the non-fibrillar matrix, k is the permeability and ∇P is the pressure gradient across the region. The