Stress distributions and material properties determined in articular cartilage from MRI-based finite strains

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Abstract

The noninvasive measurement of finite strains in biomaterials and tissues by magnetic resonance imaging (MRI) enables mathematical estimates of stress distributions and material properties. Such methods allow for non-contact and patient-specific modeling in a manner not possible with traditional mechanical testing or finite element techniques. Here, we employed three constitutive relations with known loading conditions and MRI-based finite strains to estimate stress patterns and material properties in the articular cartilage of tibiofemoral joints. Displacement-encoded MRI was used to determine two-dimensional finite strains in juvenile porcine joints, and an iterative technique estimated stress distributions and material properties with defined constitutive relations. Stress distributions were consistent across all relations, although the stress magnitudes varied. Material properties for femoral and tibial cartilage were found to be consistent with those reported in literature. Further, the stress estimates from Hookean and Neo-Hookean, but not Mooney-Rivlin, relations agreed with finite element-based simulations. A nonlinear Neo-Hookean relation provided the most appropriate model for the characterization of complex and spatially dependent stresses using two-dimensional MRI-based finite strain. These results demonstrate the feasibility of a new and computationally efficient technique incorporating MRI-based deformation with mathematical modeling to non-invasively evaluate the mechanical behavior of biological tissues and materials.

1. Introduction

Characterization of stress and strain patterns in load-bearing tissues such as articular cartilage is key to functionally evaluate the progression of tissue degeneration and treatment strategies for osteoarthritis, a disease affecting 27 million people in the United States (Lawrence et al., 2008). Moreover, knowledge of the structure–function relationships in cartilage provides a more comprehensive understanding of tissue integrity during degeneration and repair. By characterizing the properties of articular joint tissues and stress fields arising from applied loads, it may be further possible to predict failure or identify early markers of disease long before the joint otherwise shows signs of deterioration or declines in performance (Ea et al., 2011; Shirazi and Shirazi-Adl, 2009).

Articular cartilage is a complex material with behavior dominated by the interactions of cross-linked collagen networks, proteoglycans, and interstitial fluid (Mow et al., 1992). Characterizing the mechanical properties of the composite formed by these constituents in situ, however, is a difficult task. Cartilage deformations may be determined non-invasively by displacement-encoded magnetic resonance imaging (MRI; Chan et al., 2009b; Neu and Walton, 2008). Displacement-encoding with stimulated echoes (DENSE) and a fast spin echo (FSE) acquisition (Neu and Walton, 2008) has been used to determine in situ displacements and strains in tibiofemoral joints (Chan et al., 2009b). Based on measured strain fields in cartilage, stress patterns and intrinsic properties may be determined through further computational analysis.

MRI has been used to obtain joint geometry for use in finite element or mathematical analyses of the loading response, providing a patient-specific representation of the anatomy ( Fitzpatrick et al., 2010; Goslason et al., 2010; Pillai et al., 2007). A variety of constitutive models may be used in such modeling of joint mechanics. A linear elastic model, for example, provides a simple and straightforward relation between stress, strain, and material properties. Nonlinear models, in contrast, are more complex, yet far more descriptive of biomaterial behavior, including cartilage ( Federico and Herzog, 2008; Galle et al., 2007). However, while
the measurements of tissue mechanics \textit{ex vivo} for compression/tension (Julkunen et al., 2008), shear (Wong et al., 2008), or poroelasticity (Chin et al., 2011) test conditions are common, the results may not provide an accurate description of a living tissue’s response under normal loading conditions within an intact joint. Consequently, a given simulation may pair a highly accurate and specific geometry with a very broad estimate of material properties in order to model behavior (Anderson et al., 2010). Such methods may provide an estimate of joint response within a statistical range found in normal individuals, but have little application to diagnose or monitor individual patients.

In this work, we estimate stress fields and material properties based on displacement-encoded MRI within porcine knee cartilage. Three stress–strain relations (of increasing degrees of complexity) were employed, including linear relations described by Hooke’s Law as well as nonlinear Neo–Hookean and Mooney–Rivlin relations. Methods for estimating stresses using each of these constitutive relations, in combination with MRI-based strains, were developed and validated by finite element simulations. These methods were then applied using strains obtained from multiple intact porcine joints subjected to an externally applied load to model \textit{in situ} stresses.

2. Methods

2.1. Displacement-encoded MRI

Cartilage displacements and strains were determined using DENSE-FSE in juvenile porcine tibiofemoral joints \((n=7)\), as previously described (Chan et al., 2009b). The porcine legs (approximately 4 weeks old) were obtained freshly frozen from a local abattoir and remained frozen until use. Briefly, the intact joints were intermittently and cyclically compressed at one time body weight \((78 \text{ N} \times 0.3 \text{ s} \times 1.2 \text{ s ramp and total loading times, respectively})\) with a custom loading apparatus inside a 7.0 T MRI system (Bruker GMBH, Ettlingen, Germany) until a steady-state load–displacement response was considered to have been reached.

A steady-state load–displacement response was considered to have been reached when the linearly time-regressed slope of pneumatic cylinder displacement per 10 s cycle fell below a criterion of half the spatial resolution divided by the imaging time. A steady-state load–displacement response was achieved. Loading was applied to the joints via a double-acting pneumatic cylinder, computer-controlled by an electro-pneumatics system. A steady-state load–displacement response was considered to have been reached when the linearly time-regressed slope of pneumatic cylinder displacement per 10 s cycle fell below a criterion of half the spatial resolution divided by the imaging time, or 0.0163 \text{ mm/s} with a total imaging time of 128 min (Chan et al., 2009a; Neu and Hull, 2003). For each joint, displacement-encoded phase data from a single sagittal slice through the medial tibiofemoral joint was acquired (3000 ms repetition time, 21.6 ms echo time, 256 x 256 pixel matrix size, 64 x 64 mm\(^2\) field of view, 250 \text{ mm spatial resolution}, 1.5 mm slice thickness). Displacements in the loading \((y)\) and transverse \((x)\) directions within the femoral and tibial cartilage were calculated and smoothed for strain estimation using MATLAB software (The Mathworks, Natick, MA;Neu and Walton, 2008). Additionally, adjacent sagittal slices were imaged using conventional MRI (i.e. multi-slice two-dimensional FSE acquisitions) to record the anatomy of each joint and estimate the area of contact between the tibial and femoral cartilages.

2.2. Computational analysis of intact joints

Mathematical models of femoral and tibial cartilages representing a range of constitutive relations were developed and implemented in MATLAB. In these models, each pixel in the cartilage region of interest was treated as a separate isotropic unit cell. Stress values were computed at each pixel using stress–strain relations and strain data obtained from MRI.

For this study, stresses were analyzed in a cross section through the medial condyle. The 78 N load at the cartilage interface was assumed to act in proportion to the ratio of the contact area of the medial condyle to the overall contact area of the joint, as estimated by anatomical MRI. Considering the rapid (0.3 s) loading of the joint and the high water content of the cartilage, a nearly incompressible behavior (i.e. Poisson’s ratio of 0.49) was assumed. In addition, a plane stress assumption was used for all models. This assumption allows for deformation in the \(z\)-direction, a necessity to maintain incompressibility under loading.

A linearly elastic material was considered first in this analysis. Stresses were related to strain data in the \(x\), \(y\), and \(xy\)-directions by Hooke’s Law relations as follows:

\[
\sigma_{xx} = \frac{E}{(1+\nu)}(E_{xx} + \nu E_{yy})
\]

\[
\sigma_{yy} = \frac{E}{(1+\nu)}(E_{yy} + \nu E_{xx})
\]

\[
\sigma_{xy} = \frac{E}{(1+\nu)}2E_{xy}
\]

where \(\nu\) is Poisson’s ratio, \(E\) is Young’s Modulus, and \(E_{xx}\), \(E_{yy}\), and \(E_{xy}\) are the strains in the \(x\), \(y\), and \(xy\)-directions, respectively.

An initial Young’s Modulus was estimated and stresses were calculated at each unit cell. To determine whether this estimate was appropriate, the predicted load at the joint contact region was compared to the actual \((78 \text{ N})\) value of the applied load. Here the region of contact was defined as the locations along the joint surface where strains normal to the surface curvature were negative (Fig. 1). The forces along this region were estimated by first finding the component of stress acting in the loading direction at each pixel along the joint surface. The corresponding stress values were multiplied by the cross-sectional area of the unit cell to determine the force acting in the loading direction. The force values were then summed and compared to the known applied load. The value of Young’s Modulus was subsequently iterated until the error between calculated surface forces and the known load input fell to within a value of 0.1% of the applied load.

Second, an incompressible Neo-Hookean model was considered. Here, the strain energy density function was given by

\[
W = \frac{1}{2}I_2(J^{-1/2}-1) + c_1(J_1-3) - p(J_2-1)
\]

where \(I_2\) is the first invariant of the left Cauchy–Green tensor, \(C\), \(J\) is the determinant of the deformation gradient, \(c_1\) and \(p\) are material parameters, and \(p\) represents a hydrostatic pressure term included to enforce incompressibility. The Second Piola–Kirchoff stress tensor, \(S\), with the identity tensor, \(I\), was then determined by

\[
S = 2[c_1(J-I)^{-2/3}C^{-1}] - \frac{p}{2} (det C) C^{-1}
\]

Imposing the incompressibility assumption and neglecting the stress in the \(z\)-direction, consistent with the plane stress assumption, yields a relationship for the hydrostatic pressure.

\[
p = 3\frac{2(c_1-[1-(C^{-1})_{11}])}{(det C (C^{-1})_{13})}
\]

An initial value of \(c_1\) was estimated and iterated as before, until the error between estimated and known applied loads fell to within 0.1%.

The final model examined the case of an incompressible Mooney–Rivlin hyperelastic solid, given as

\[
W = c_1(J_1-3) + c_2(J_2-3) - p(J_2-1)
\]
where $c_1$ and $c_2$ are material parameters, $t_2$ is the second invariant of the Cauchy–Green tensor, and $p$ is hydrostatic pressure. The Second Piola–Kirchhoff stress was calculated as

$$S = 2\left\{c_1 I + c_2 [(tr C - C) - \frac{1}{2}(det C)C^{-1}] \right\}$$

(8)

Neo-Hookean solids are a specialized case of the Mooney–Rivlin model, and as such the same assumptions used in the incompressible Neo-Hookean model were repeated (i.e. a plane stress model with isotropic behavior). With stress in the $z$-direction assumed to be zero, the term for hydrostatic pressure can be written in terms of the parameters $c_1$ and $c_2$ as

$$p = \frac{2(c_1 + c_2(tr C - C_{33}))}{(det C)(C^{-1})_{33}}$$

(9)

An initial estimate for $c_1$ was determined from the value estimated in the incompressible Neo-Hookean case. This parameter was then varied across a range of $\pm$ 10% of the initial estimate of $c_1$, with a value of $c_2$ iterated for each increment of $c_1$. The combination of $c_1$ and $c_2$ that resulted in a minimum error between calculated and known loads was then used as estimates for the next iteration. For each subsequent iteration, the range and increment step was decreased to 10% that of the previous loop. This procedure was done to consecutively smaller ranges until the desired error of 0.1% was reached. Further, for each model, First Piola–Kirchhoff stresses, $P$, were calculated and plotted in accordance with the relation $P = FS$, where $F$ is the deformation gradient and $S$ is the Second Piola-Kirchhoff stress tensor.

For each material parameter, the mean across all joints and standard error of the mean was calculated. Shear forces along the surface of the articular region were also calculated and summed for each model. Because a healthy joint typically exhibits a low coefficient of friction at the surface to enable smooth articulation, we reasoned that a calculated lower surface shear implies a more realistic and physiologically relevant model. Consequently, the shear forces calculated along the contact surface were used as a method to directly compare relations.

### 2.3. Finite element simulations

We validated the stress distributions generated by mathematical modeling using a finite element analysis with known stress and strain fields. Three models were created, representing material behavior governed by each of the aforementioned constitutive relations. A simple two-dimensional block measuring 5 cm square was created using the COMSOL Multiphysics software package (3.2 COMSOL AB, Stockholm, Sweden). Plane stress models with rectangular mesh elements arranged in a $256 \times 256$ grid were used, resulting in 65,536 total mesh elements and 526,338 degrees of freedom. The first model simulated material behavior in accordance with linearly elastic relations, with a Young’s Modulus of 12.5 MPa and Poisson’s ratio of 0.49. The second model used Neo–Hookean constitutive relations and a material parameter, $c_1$, of 12.5 MPa. The final model was a Mooney–Rivlin model with material parameters of 12.5 MPa for $c_1$, and 3.5 GPa for $c_2$. Homogeneous material assumptions were used for each model.

In each model the bottom boundary of the block was subjected to a distributed load of 39 N in the $y$-direction and 7.8 N in the $x$-direction, similar to values estimated from in situ cartilage loading. Constraints in the $x$- and $y$-directions were imposed on the top boundary of the block to restrict motion. After solutions for the simulation models were generated, the resulting strain fields and compressive load in the $y$-direction were used as inputs for the mathematical models. Error between the calculated stresses and those generated by finite element analysis was subsequently calculated as a means of comparison between models. For each analysis the root mean squared error was calculated between estimated and known stress fields, and was further normalized by the maximum value of the known stress field.

### 3. Results

#### 3.1. Displacement-encoded MRI

Based on the proportion of medial to total contact area determined by conventional MRI, the load applied to the medial compartment of each joint varied among samples (Table 1). Displacements from DENSE-FSE and computed strain patterns were heterogeneous (Fig. 2).
3.2. Computational analysis of intact joints

As expected, the models produced non-uniform stress distributions throughout the tibiofemoral cartilage. The calculated distributions for the linear elastic, Neo–Hookean, and Mooney–Rivlin relations showed similar stress patterns but differed in magnitude (Fig. 3). In these models, compressive stresses developed in the direction of loading with a region of positive stress in the loading direction at the cartilage–cartilage interface. A second tensile-stress region in the loading direction was also observed at the bone–cartilage interface.

The lowest mean surface shear values were found with the application of linear Hookean relations, followed closely by the Neo–Hookean and Mooney–Rivlin models. The mean Young’s Modulus for the seven joints was estimated by the linear model as 5.83 ± 2.44 MPa (Table 2). Material constants for nonlinear relations varied for the femur and tibia (Table 2).

3.3. Finite element simulations

The linear mathematical model correctly estimated a Young’s Modulus of 12.5 MPa for the linearly elastic finite element simulation, exactly matching the simulation input. Similarly the Neo-Hookean model converged to a value of 12.54 MPa for the parameter $c_1$, which was within 0.3% of the finite element simulation input of 12.5 MPa.

The Mooney–Rivlin model exhibited the largest discrepancy in estimates when compared to the parameter inputs of the finite element simulation. The Mooney–Rivlin model estimated values of...

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Table 2

<table>
<thead>
<tr>
<th>Force Type</th>
<th>Linear</th>
<th>Neo-Hookean</th>
<th>Mooney–Rivlin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Surface Shear Force (N)</td>
<td>13.25 ± 7.67</td>
<td>9.90 ± 5.08</td>
<td>12.21 ± 1.25</td>
</tr>
<tr>
<td>Femur</td>
<td>8.40 ± 6.58</td>
<td>12.15 ± 4.09</td>
<td>15.71 ± 3.15</td>
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<tr>
<td>Tibia</td>
<td>10.85 ± 6.93</td>
<td>11.03 ± 4.72</td>
<td>13.96 ± 2.40</td>
</tr>
<tr>
<td>Mean</td>
<td>5.99 ± 2.67</td>
<td>5.66 ± 2.41</td>
<td>5.83 ± 2.44</td>
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<tr>
<td>$E$ (MPa)</td>
<td>5.99 ± 2.67</td>
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<td></td>
</tr>
<tr>
<td>Femur</td>
<td>5.66 ± 2.41</td>
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</tr>
<tr>
<td>Tibia</td>
<td>5.66 ± 2.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>5.83 ± 2.44</td>
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<td></td>
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$C_1$ (MPa)

<table>
<thead>
<tr>
<th>Force Type</th>
<th>Femur</th>
<th>Neo-Hookean</th>
<th>Mooney–Rivlin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>0.68 ± 0.40</td>
<td>0.66 ± 0.42</td>
<td>0.66 ± 0.42</td>
</tr>
<tr>
<td>Tibia</td>
<td>0.66 ± 0.42</td>
<td>0.67 ± 0.46</td>
<td>0.66 ± 0.42</td>
</tr>
<tr>
<td>Mean</td>
<td>0.67 ± 0.39</td>
<td>0.66 ± 0.42</td>
<td>0.66 ± 0.42</td>
</tr>
</tbody>
</table>

$C_2$ (MPa)

<table>
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<tr>
<th>Force Type</th>
<th>Femur</th>
<th>Neo-Hookean</th>
<th>Mooney–Rivlin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>0.32 ± 0.29</td>
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<td></td>
</tr>
<tr>
<td>Tibia</td>
<td>0.18 ± 0.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.25 ± 0.22</td>
<td></td>
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</tbody>
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Fig. 3. Heterogeneous stress fields were estimated and plotted for each computational model. For the joint in this representative image, the linear model estimated Young’s Modulus values of 3.54 MPa and 4.21 MPa for the femur and tibia, respectively. Similarly, the Neo-Hookean model estimated $c_1$ parameter values of 0.25 MPa and 0.25 MPa, and $c_2$ values of 15.52 kPa and 5.00 kPa, for the femur and tibia, respectively. Stresses estimated by modeling the joint with nonlinear Neo–Hookean relations are similar in distribution to that of the linear case, but exhibit lower peak stresses. Although stresses produced by the model developed with Mooney–Rivlin relations showed similar distributions to the other models in the loading and transverse directions, shear stresses were substantially lower throughout the cartilage regions.
31.8% for gest error at 8.67% (Table 3). In the respecti\-ves, while the Mooney–Rivlin model produced the lar-

models and the known stress field was calculated for each set as the root mean square deviation, normalized by the value of maximum stress of the known stress field.

The stresses calculated by the models for each set of strains were then compared to the known simulated stresses. The error between the stress values estimated by the models and the known stress field was calculated for each set as the root mean square deviation, normalized by the value of maximum stress of the known stress field.

The stress distribution estimates for the porcine tibiofemoral joint were largely consistent across models. Further, the mean modulus values determined from the linear analysis (5.99 MPa and 5.66 MPa for the femur and tibia, respectively) both fall within the range reported for dynamic modulus of porcine cartilage (Nissi et al., 2007). Given the cyclic nature and rapid application of the load experienced by the joints, it is reasonable that estimates would approach dynamic, rather than equilibrium, values as the analysis essentially considers one section of a dynamic loading cycle in a nonlinear material. Interestingly, the mathematical models predicted tensile stresses in the loading (x) direction and in shear, respectively. It is possible that the larger errors seen in the Mooney-Rivlin model may be caused by the fact that strains found with DENSE-FSE in these regions were near zero, causing the constitutive relations to be dominated by the larger tensile strains in the transverse (y) direction.

When the models were implemented using finite element-based strain fields, material parameters were correctly estimated within 1% for the linear and Neo–Hookean models and within 32% for the Mooney–Rivlin model. Further, all models were found to closely approximate the stress distributions and magnitudes in the y-direction or the direction of primary loading. Here the linear and Neo–Hookean models were within 2.5% of the known stresses, and the Mooney–Rivlin model correctly predicted stresses to within 9%. The linear and Neo-Hookean models also performed well in the estimation of stresses in the x-direction and in shear, where errors were within 1% for both models. In contrast, the Mooney-Rivlin model produced errors of 102% and 201% in the x-direction and in shear, respectively. It is possible that the larger errors seen in the Mooney-Rivlin model may be attributed to the number of simplifying assumptions necessary here to reach a determinate system.

Based on a comparison of the overall stress distributions, shear values developed along the contact surface of the joint for each model, as well as a comparison of the models using finite element-based strain fields, we concluded that the incompressible

<table>
<thead>
<tr>
<th>Model</th>
<th>σxx (%)</th>
<th>σyy (%)</th>
<th>σxy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear</td>
<td>0.00</td>
<td>0.60</td>
<td>102.01</td>
</tr>
<tr>
<td>Neo–Hookean</td>
<td>0.00</td>
<td>2.25</td>
<td>8.67</td>
</tr>
<tr>
<td>Mooney–Rivlin</td>
<td>0.00</td>
<td>0.33</td>
<td>201.10</td>
</tr>
</tbody>
</table>

4. Discussion

The present work developed and verified a mathematical method to characterize the mechanical behavior of articular cartilage non-invasively using MRI-based strains, and to identify the set of constitutive relations that produced the most consistent results. When the methods were applied to intact joints under known (e.g. cyclic compressive) loading conditions there was good inter-model agreement of stress distributions, and modulus values estimated were within published ranges. Further, the methods described here were found to produce estimates of material properties that agreed closely with controlled finite element simulations.

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When the methods were applied to intact joints under known (e.g. cyclic compressive) loading conditions there was good inter-model agreement of stress distributions, and modulus values estimated were within published ranges. Further, the methods described here were found to produce estimates of material properties that agreed closely with controlled finite element simulations.
Neo–Hookean relation provided the best estimates of the stress state of the tissue. Both the linear model and Neo–Hookean model resulted in near-identical shear forces at the surface of the joints, with values lower than those estimated using Mooney– Rivlin relations. However, the linear model consistently predicted large peaks in stress that did not occur in either nonlinear method. It is accepted that cartilage behaves as a nonlinear viscoelastic solid (Mow et al., 1992), and it is likely that the dramatic shifts in stress predicted by the linear model are a result of the limitations of a purely elastic assumption with the large strains calculated at the joints. From this, it follows that the Neo–Hookean hyperelastic relations with incompressibility assumptions provided the most appropriate model for the characterization of stresses using two-dimensional MRI-based displacements.

Assumptions necessary in this analysis may introduce error in the models. Isotropic, homogeneous behavior of the cartilage, for example, was assumed in order to arrive at a determinate system for the cartilage based upon the available knowledge of deformation and loading conditions. Future work will consider nonhomogeneous behavior of the tissue. The inclusion of anisotropic constitutive relations (Nagel and Kelly, 2010), depth-dependent properties (Owen and Wayne, 2010), or mixture theory (Görke et al., 2009) may further enhance the accuracy of the method. In addition, expansion of the analysis to include three-dimensional displacement data should provide sufficient information to completely characterize the hyperelastic behavior of the tissue across a broad range of models with additional degrees of complexity. Estimation of load distribution throughout the volume of the joint may lead to additional refinement of results (Guess et al., 2010; Vaziri et al., 2008).

In conclusion, this study presents a new and novel method for assessing stresses and material properties of intact articular cartilage non-invasively through the use of displacement-encoded imaging and mathematical modeling. Of the models developed here, the utilization of Neo-Hookean relations with known two-dimensional strains was found to produce the best estimation of stresses within a body under an applied load. Displacement-encoded MRI, combined with refined mathematical visualization of stresses and strains within tissues, has potential for use in clinical environments, where tissue deformations and, more importantly, stress distributions in the joint may be markers for the early stages of degenerative disease like osteoarthritis. Patient-specific modeling in particular may find benefit in the growth of such techniques to model in situ mechanical behavior within a joint. Moreover, the methods detailed here are not limited only to the analysis of articular cartilage. With knowledge of strain and appropriate boundary conditions these methods can be extended to a variety of biological tissues and biomaterials, including performance analysis of tissue implants. Development of such techniques, coupled with appropriate material relationships, will allow for the non-invasive description of mechanical behavior across a broad range of applications.

Conflict of interest statement

The authors have no conflict of interest.

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References


