Published in final edited form as:

J Biomech. 2015 June 1; 48(8): 1454–1460. doi:10.1016/j.jbiomech.2015.02.028.

An optimized transversely isotropic, hyper-poro-viscoelastic finite element model of the meniscus to evaluate mechanical degradation following traumatic loading

Benjamin B. Wheatley¹, Kristine M. Fischenich², Keith D. Button³, Roger C. Haut^{3,4}, and Tammy L. Haut Donahue^{1,2}

¹Department of Mechanical Engineering, Colorado State University, Fort Collins, CO USA

²School of Biomedical Engineering, Colorado State University, Fort Collins, CO USA

³Orthopaedic Biomechanics Laboratories, College of Osteopathic Medicine, Michigan State University, East Lansing, MI USA

⁴Department of Radiology, Michigan State University, East Lansing, MI USA

Abstract

Inverse finite element (FE) analysis is an effective method to predict material behavior, evaluate mechanical properties, and study differences in biological tissue function. The meniscus plays a key role in load distribution within the knee joint and meniscal degradation is commonly associated with the onset of osteoarthritis. In the current study, a novel transversely isotropic hyper-poro-viscoelastic constitutive formulation was incorporated in a FE model to evaluate changes in meniscal material properties following tibiofemoral joint impact. A non-linear optimization scheme was used to fit the model output to indentation relaxation experimental data. This study is the first to investigate rate of relaxation in healthy versus impacted menisci. Stiffness was found to be decreased ($p=0.003$), while the rate of tissue relaxation increased ($p=0.010$) at twelve weeks post impact. Total amount of relaxation, however, did not change in the impacted tissue ($p=0.513$).

Keywords

meniscus; knee

© 2015 Published by Elsevier Ltd.

*Corresponding Author. Tammy L. Haut Donahue, Department of Mechanical Engineering, Colorado State University, 1374 Campus Delivery, Fort Collins, CO 80523, Telephone: (970) 491-1319, Tammy.Donahue@ColoState.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of Interest Statement

The authors have no financial, personal, or other conflicts of interest to report.

1. Introduction

Menisci are wedge shaped semilunar biphasic tissues composed of approximately 70% fluid and 30% organic matter (Mow, 1993). Material testing can be performed on the meniscus to determine a number of properties including the compressive, tensile, and shear modulus, as well as Poisson's ratio and tissue permeability (Joshi et al., 1995; LeRoux and Setton, 2002; Martin Seitz et al., 2013; Moyer et al., 2012; Proctor et al., 1989). These material properties are governed by the arrangement and quantity of the various organic tissue components, including collagen, proteoglycans, elastin, and other glycoproteins (Mow, 1993). The matrix is predominantly type I collagen fibrils oriented in the circumferential direction that results in high tissue anisotropy (Neogi and Zhang, 2013; Proctor et al., 1989). Compressive loading from the femoral condyles is converted to tensile hoop stresses (Upton et al., 2006), which is supported by the circumferential collagen fibers. Proteoglycans help retain interstitial fluid during loading, which is important in load support and load distribution (MacConaill, 1950). However, these tensile and compressive properties are not fully independent (Sanchez-Adams et al., 2011), and characterizing the relationship between tissue structure and mechanical behavior is inherently important for understanding tissue function.

Identifying mechanical changes in meniscal tissue is of particular interest with respect to osteoarthritis (OA) research. OA is a degenerative disease that affects all tissues within the joint, and is one of the leading causes of adult joint pain and disability (Neogi and Zhang, 2013). Two critical components of OA research are developing models that mimic degradation in humans and characterizing changes to the tissue as a result of OA. Experimental animal models have been used extensively to simulate osteoarthritic changes within the knee, but very few have investigated meniscal changes (Adams et al., 1983; Fischenich et al., 2014a; Fischenich et al., 2014b; Hellio Le Graverand et al., 2001). The majority of these studies have used a traditional anterior cruciate ligament transection (ACLT) model. ACLT models have been shown to induce osteoarthritic type changes that appear to differ when compared to OA-type changes induced by traumatic loading (Killian et al., 2010). A traumatic loading model may more directly recapitulate the common jump landing injury (Levine et al., 2013; Meyer and Haut, 2005; Yeow et al., 2009), and joint injury has been shown to increase the risk of OA development (Blagojevic et al., 2010).

Directly evaluating mechanical properties from experimental data provides useful insight into tissue behavior, but often yields limited results such as elastic modulus (Fischenich et al., 2014a; Fischenich et al., 2014b; Proctor et al., 1989) and testing procedures can be destructive in nature (Mansour and Mow, 1976). Inverse finite element (FE) approaches are an effective method to evaluate a range of material properties through parameter optimization (Korhonen et al., 2002; Lei and Szeri, 2007; LeRoux and Setton, 2002) and can be utilized with non-destructive experimental analyses. Previous FE modeling efforts of the meniscus have employed a combination of a biphasic approach (Haemer et al., 2012; Proctor et al., 1989; Spilker et al., 1992), three dimensional geometry (Haut Donahue et al., 2002; LeRoux and Setton, 2002; Peña et al., 2006, 2005), and non-linear behavior (Haemer et al., 2012), in addition to known transverse isotropy (LeRoux and Setton, 2002; Proctor et al., 1989). Although these models are successful in studying the effect of particular changes

within the meniscus, they often fail to combine all aspects of tissue behavior. Viscoelasticity, for example, is seldom included in meniscal models, despite the studies that show the meniscus exhibits viscoelastic behavior in shear (Anderson et al., 1991; Zhu et al., 1994).

The goal of the current study was to develop and employ a finite element model of the meniscus which would utilize a novel constitutive model to predict tissue behavior under non-destructive indentation relaxation testing. The development of this model would be beneficial in multiple ways: (1) it would show the effectiveness of characterizing material behavior of the meniscus, (2) it could be used to evaluate potential changes in the material properties of healthy and traumatized menisci, and (3) it could provide a tool to further study how individual constituents affect the structural response of the menisci.

2. Methods

2.1 Mechanical Testing

Six skeletally mature Giant Flemish rabbits (5.7 ± 0.2 kg) were used in this study. Following anesthesia (2% isoflurane and oxygen), a 1.75 kg mass was dropped from 70 cm in height onto the distal femur with the right tibiofemoral joint at 90° flexion, causing ACL rupture and acute damage to surrounding tissues (Fischenich et al., 2014a; Fischenich et al., 2014b). Left limbs remained non-impacted as paired controls. Animals were euthanized twelve weeks post injury. This procedure was approved by Michigan State University and Colorado State University All-University Committees on Animal Use and Care. A licensed veterinary technician monitored the rabbits and administered buprenorphine (0.3 mL/KG-BW) for pain every 8 hours for 72 hours post impact.

Tissue harvest was performed immediately following euthanasia, and all samples were refrigerated (1.7° to 3.3° C) before testing within 18 hours of sacrifice. Each meniscus (lateral and medial for each joint) was sectioned into three regions: anterior, central, and posterior (Figure 1). A 1.59 mm diameter sphere indenter tip was displaced 0.25 mm normal to the tissue surface in ~1 second and then held for 900 seconds of relaxation. All testing was completed with specimens submerged in 0.9% phosphate buffered saline (PBS) using a servo-hydraulic testing system (MTS Corp, Eden Prairie, MN).

2.2 Constitutive Model

The constitutive model utilized in this study combined a strain energy density function, the interaction between the solid portion (matrix and fibers) and the saturating fluid through a poroelastic approach, and the inherent viscoelasticity of the solid portion of the tissue. Thus, the meniscus was modeled as hyper-poro-viscoelastic. As the meniscus has been shown to be anisotropic (LeRoux and Setton, 2002; Proctor et al., 1989), non-linear (Abraham et al., 2011; Danso et al., 2014), and highly compressible (Sweigart et al., 2004), a hyperelastic, transversely isotropic strain energy density (SED) function was developed and employed (Holzapfel, 2000) (Equation 1). In this expression $\frac{1}{J_1}$ and $\frac{1}{J_2}$ are the first and second modified invariants of the left Cauchy-Green deformation tensor B which characterize tension/compression and shear, respectively. J is the Jacobian or volume change ratio, and I_4

is a pseudo-invariant characterizing the transverse isotropy or circumferential fiber stiffness. This function incorporated both the volume-preserving ($\mathbf{I}_1, \mathbf{I}_2, \mathbf{I}_4$) and volume-changing (J) responses of the material. Thus, three parameters (a_2, b_2, d_2) were used to characterize the isochoric response of the solid, while a fourth parameter (c_2) was used to characterize compressibility.

$$\Psi = a_2 \left(\mathbf{I}_1 - 3 \right)^2 + b_2 \left(\mathbf{I}_2 - 3 \right)^2 + c_2 (J - 1)^2 + d_2 (\mathbf{I}_4 - 1)^2 \quad (1)$$

A three-term Prony series viscoelastic expansion was applied to the solid phase of the tissue (Equation 2), where $g_R(t)$ is the time dependent shear relaxation modulus, g_n are fractions of this shear modulus, and τ_n are time constants (Dassault Systèmes, 2012). The application of a three term series is common in studies incorporating the Prony method, as it provides a smooth curve shape without a large number of parameters (Kalyanam et al., 2009; Seifzadeh et al., 2012). The Prony series was applied to the constitutive relation at each increment (Equation 3, where τ and γ are shear stress and strain, respectively). Additionally, for the material to retain positive stiffness, all g_n terms must sum to less than one.

$$g_R(t) = 1 - \sum_{n=1}^3 g_n \left[1 - \exp \left(-\frac{t}{\tau_n} \right) \right] \quad (2)$$

$$\frac{\partial \tau}{\partial \gamma}(t, \tau) = \frac{\partial \tau}{\partial \gamma}(\gamma)^* g_R(t) \quad (3)$$

The inclusion of poroelasticity decoupled the total stress of a porous material (Equation 4) into the solid phase (where σ^{solid} is determined from Equations 1 and 3) and fluid phase (where p is the pressure of the fluid and $\mathbf{I}$ is the identity matrix). In the case of meniscus, these pores were assumed to be fully saturated with interstitial fluid. The pressure of the saturating fluid is a function of the permeability, as shown in Darcy's Law (Equation 5), where k is the permeability, ∇p is the pore pressure difference within regions the tissue (and is the same pressure as Equation 4), μ is the fluid viscosity, and q is the fluid flow per unit area through the tissue. The permeability controls how quickly the fluid pressure reaches equilibrium following loading, which manifests itself in the overall relaxation rate of the tissue.

$$\sigma^{total} = \sigma^{solid} + p\mathbf{I} \quad (4)$$

$$q = \frac{-k}{\mu} \nabla p \quad (5)$$

However, permeability is also dependent on the voids ratio of the material (Equation 6) where V_V is the volume of the voids space (in this case full saturation was assumed) and V_S is the volume of only the solid. Haemer et al., 2012 utilized a permeability function

(Equation 7) where the voids ratio is determined from the strain state of the material. In Equation 7, $k(e)$ is permeability as a function of voids ratio, k_0 is the permeability of the undeformed material, e_0 is the undeformed voids ratio, and η and M are unit-less material parameters (Haemer et al., 2012).

$$e = \frac{V_v}{V_s} \quad (6)$$

$$k(e) = k_0 \left(\frac{e}{e_0} \right)^\eta \exp \left\{ \frac{M}{2} \left[\left(\frac{1+e}{1+e_0} \right)^2 - 1 \right] \right\} \quad (7)$$

Table 1 summarizes all material parameters utilized in this complex formulation, including those fixed throughout the analysis and those that were varied.

2.3 Finite Element Model

A three dimensional coupled solid-fluid finite element model was developed in Abaqus 6.11 (Simulia Corp., Providence, RI) to simulate a region of the meniscus (Figure 2). The model consists of a solid meniscus region constructed of eight node linear hexahedral elements with three degrees of displacement freedom and one degree of pore pressure freedom (C3DRP) and an indenter tip constructed of rigid shell elements. The meniscus was modeled as porous and wedge shaped (a 5×4.5×3.2 mm triangle extruded 4 mm) and the indenter tip was modeled as a half sphere with a diameter of 1.6 mm. The meniscus dimensions were determined from the general size of segmented (anterior, central, and posterior) rabbit menisci. Mesh density (1644 elements total) was determined from a convergence study, which evaluated total strain energy at the loading peak and at equilibrium (Figure 3). A user subroutine (UANISOHYPER_INV) was written to incorporate the SED function from Equation 1, as this formulation was not available in the Abaqus material library. The indenter tip was displaced 0.25 mm over 1 second and held for 900 seconds of relaxation, similar to the experimental procedure. The final model output consisted of a force-time curve of the total reaction force at the indenter tip. The distal face of the meniscus (which contacts the tibial plateau) was set to encastre and no flow across the boundary as it was glued during experimental testing. All other faces had no displacement conditions and were set to free fluid draining across the boundary.

2.4 Parameter Optimization Procedure

A non-linear least squares Levenberg-Marquardt optimization procedure was employed in Matlab (The Mathworks, Inc., Natick, MA) with the “lsqnonlin” function (Holzapfel, 2001; Kauer et al., 2002; Kim and Srinivasan, 2005; Lei and Szeri, 2007; Martins et al., 2006) to vary model material properties to match experimental data. Experimental indentation relaxation testing showed a sharp peak, relaxation curve, and equilibrium response. However, the relaxation and equilibrium portions of the curve consisted of 900 seconds combined, while loading occurred over 1 second (Figure 4). Thus, additional weight was given to the peak response within the optimization procedure to ensure a proper fit. A simple method was employed in this study (Equation 8), where f is the total summed square of each

residual, n is the total number of data points, f_i is the residual at data point i , and f_{peak} is the residual at the peak response. In this case, the f_i data points are the difference between model force output and experimental force values at each time increment.

$$f(x) = \sum_{i=1}^n f_i(x)^2 + (f_{peak} * n)^2 \quad (8)$$

As shown in Table 1, there were a number of material parameters that could be varied to adjust the overall behavior of the FE model. However, with the limitation of a single stress relaxation curve, there was an inherent challenge in running a single optimization with eleven parameters. One goal of this optimization technique was to minimize the overall number of parameters to be varied such that each parameter had a distinct effect on the material behavior. Thus, the above constitutive equation terms which affected the whole model indentation relaxation behavior in a similar fashion were coupled together into optimizing parameters, as outlined below. Each sample was individually optimized. Following optimization, parameters were averaged for all control samples and compared to the average for the impacted samples.

The first parameters (a_2, b_2, d_2) control the non-linear isochoric stiffness of the solid, and were coupled together according to previous experimental investigations of tensile, shear, and transversely isotropic material properties of the menisci and represent the axial modulus (~ 20 MPa, a_2), shear modulus (~ 60 MPa, b_2), and circumferential modulus (~ 130 MPa, d_2) (Fithian et al., 1990; Haut Donahue et al., 2003; LeRoux and Setton, 2002; Skaggs et al., 1994; Tissakht and Ahmed, 1995; Whipple et al., 1984) (Equation 9). Here a grouping parameter α was utilized which controlled material stiffness. Each term was also scaled by multiple orders of magnitude to improve the optimization technique (Lei and Szeri, 2007).

$$a_2 = \frac{b_2}{3} = \frac{d_2}{6.5} = \alpha * 10^7 \quad (9)$$

The first three viscoelastic parameters g_1, g_2, g_3 controlled the total viscoelastic relaxation of the solid constituent, while the compressibility of the solid c_2 similarly controlled total relaxation as a result of fluid movement. Thus, these four parameters had a similar effect on the material behavior, and were also coupled together. Furthermore, all g_n terms were fixed relative to each other to produce a smooth relaxation curve shape. Again, a new term was provided (β) to represent these parameters as a whole, which controlled total relaxation (Equations 10 and 11).

$$c_2 = \beta * 10^7 \quad (10)$$

$$g_n = \frac{g_n^{max}}{1+\beta}, g_n^{max} = 0.55, 0.3, 0.15 \quad (11)$$

The remaining parameters k_0 and τ_n impact the rate at which fluid flows throughout the tissue and the rate at which the solid viscoelastic constituent relaxes, respectively, thus each affected the overall rate of relaxation of the material. A similar framework for the relaxation parameter β was applied to these parameters (Equations 12 and 13, where γ_{H_2O} is the specific weight of water and is required as a FE input into Abaqus). Here the rate parameter was introduced (κ).

$$k_0 = \kappa^* \frac{10^{-9}}{\gamma_{H_2O}} \quad (12)$$

$$\tau_n = \frac{\tau_n^{max}}{1 + \kappa}, \tau_n^{max} = 20, 100, 200 \quad (13)$$

The specific relationships of Equations 9 through 13 were chosen as a result of varying these parameter values to obtain an acceptable fit to the maximum number of experimental specimens. An “acceptable” fit is defined below in *Statistical Analysis of Results*. For Equations 9, 10, and 12, the order of magnitude was varied to determine the optimal relationship between the hyperelastic and permeability terms and optimizing parameters, while a linear relationship was implemented for simplicity. The g_n^{max} terms in Equation 11 sum to a value of one by design, representing a maximum total relaxation of 100%. The specific g_n^{max} values were the result of varying the three terms from 0.35–0.8, 0–0.3, and 0–0.2, respectively. Equation 13 terms were initially chosen to be decade values of 10, 100, and 1000, respectively, similar to other viscoelasticity studies (Lucas et al., 2008; Troyer and Puttlitz, 2012, 2011). However, the above values were chosen after varying these terms a range of 5–100, 0–100, and 0–1000, respectively. The structure of Equations 11 and 13 were chosen to provide a maximum value for the viscoelastic terms and a minimum limit of zero (when the optimizing parameters approach infinity), while maintaining an inverse relationship between the viscoelastic terms and optimizing parameter. This inverse function was implemented to ensure that an increase in the optimizing parameters β and κ caused a decrease in total relaxation and an increase in relaxation rate, respectively, to be consistent with the effect of increases in compressibility and permeability.

The effect of these parameter couplings was a reduction in total optimization variables from eleven to three, greatly increasing the robustness of the optimization procedure. The initial parameter values were implemented as follows: $\alpha = 0.5$, $\beta = 0.05$, and $\kappa = 0.05$. These values, in addition to the values for Equations 9, 10, and 12 were obtained through analyzing the results of the optimization procedure with various initial parameter values, ranging up to four orders of magnitude. The goal of this procedure was to locate global minima (and thus an optimal fit) as opposed to local minima. However, with such a large amount of variability due to multiple parameter coupling (four hyperelastic parameters, permeability, and six viscoelastic parameters) this was inherently difficult. Equations 9 through 13 were thus implemented with the goals of evaluating differences between healthy and impacted menisci and developing a good agreement between the overall force response of the model and experimental data, not developing specific constitutive parameter values for the meniscus. It

should also be noted that while the constitutive model parameters have units (Table 1), the optimization parameters should be considered unit-less for simplicity.

2.5 Statistical Analysis of Results

Evaluation of fit was determined by analysis of the normalized mean square error (NMSE) (Equation 14), where *fit* is the NMSE goodness of fit parameter, which varied between negative infinity (worst fit) to 1 (perfect fit), y_i^m is the model force value at data point i , y_i^e is the experimental force value at the same data point. This was employed using the Matlab “goodnessOfFit” function. All *fit* parameters of 0.8 or greater were deemed an acceptable fit to experimental data, along with visual inspection of the curves.

$$fit = 1 - \sum_{i=1}^n \left[\frac{y_i^m - y_i^e}{y_i^m - \text{mean}(y_i^e)} \right]^2 \quad (14)$$

Paired t-tests were used to compare each of the three optimizing parameters (α, β, κ) between impacted and control limbs of the same animal with a significance level of $p < 0.05$.

3. Results

Eighteen paired specimens were optimized for the six rabbits, for a total of thirty-six optimizations. Some regions of the impacted menisci were either unable to be mechanically tested or were not present, as a result of tissue degradation. Five paired specimens from the lateral anterior, five from the lateral central, four from the lateral posterior, two from the medial anterior, and one each from the medial central and medial posterior regions were used. The data for all regions were averaged together into groups of impacted and control menisci. Any optimizations that failed to provide a sufficient fit were removed along with the paired specimen. The optimization procedure took roughly 1.5 hours per specimen.

The model showed an excellent fit to experimental data, as represented by both numerical analysis (Table 2) and visual inspection (Figure 5). The optimization procedure fit both the peak response and overall curve shape, as evidenced by low peak and mean percent error values and high *fit* terms. Optimizations that failed to accurately fit the relaxation curve were eliminated through a *fit* value of less than 0.8.

An analysis of the three optimizing parameters showed a significant change for the α and κ parameters between the control and impacted menisci ($p=0.003$ and 0.010 for α and κ , respectively), while the β parameter did not change ($p=0.513$) (Figure 6). The α decrease indicated a reduction in overall stiffness of the solid portion of the tissue, while increases in the κ parameter showed that relaxation occurred at a faster rate in impacted specimens versus control. No change in the β parameter suggested similar total relaxation between control and impacted menisci. Note that the importance of reporting parameter values is in comparing control to impacted specimen, and not in explicitly defining constitutive parameter values.

4. Discussion

4.1 Finite Element and Constitutive Models

To the authors' knowledge, this is the first FE model of the meniscus to be developed including both poroelasticity and viscoelasticity. FE analyses in the past have assumed the meniscus to be solely poroelastic (Haemer et al., 2012; Proctor et al., 1989; Spilker et al., 1992), while viscoelasticity is a common approach to evaluating experimental time dependent behavior of orthopedic tissues (Hayes and Mockros, 1971; Khodaei et al., 2013; Li et al., 2005; Troyer and Puttlitz, 2011). However, the inclusion of only one of these models provides an oversimplification of the physiological mechanisms that drive tissue mechanics. Prior work has shown the importance of both viscoelasticity and poroelasticity in biological materials such as cartilage (Mak, 1986), collagen gels (Chandran and Barocas, 2004), and passive muscle (Yang and Taber, 1991). As the meniscus is a porous, saturated, collagen rich tissue similar to these materials, it is likely that a comparable structure-function relationship exists.

The development of this model provided evidence that the hyper-poro-viscoelastic constitutive model is capable of capturing the behavior of menisci in an *in situ* setting. The ability of the model to fit experimental force-time data which differed by over an order of magnitude between specimens also highlighted the overall robustness of this approach. Furthermore, the model formulation provided an opportunity to tailor each component to account for degradation of certain constituents. Application of this model to an *in vitro* analysis holds great potential, as it could provide a method to study how each component of the constitutive model affects the native behavior of the meniscus and whole knee joint. While previous inverse FE analysis has been completed with experimental tensile data (LeRoux and Setton, 2002), our approach allowed an evaluation of mechanical behavior through *in situ* indentation testing, which was non-destructive thus allowing for subsequent histological analysis in addition to recapitulating the natural loading environment of the meniscus.

4.2 Parameter Optimization Procedure

This study presented a method in which a range of material parameters could be simplified to improve a non-linear optimization. Specifically, grouping together various parameters which have a similar effect on the material response can simplify an optimization analysis, clarify results, and provide a unique solution. In this particular case, three parameters each had a distinct effect on the shape of the indentation curve (Figure 7). The stiffness parameter α , which represented the hyperelastic terms a_2, b_2, d_2 , clearly impacted the overall magnitude of the reaction force in both peak and equilibrium response. The relaxation parameter β , which included the hyperelastic term c_2 and viscoelastic terms g_n , largely controls the equilibrium response. Finally, the rate of relaxation parameter κ , which controlled permeability k and viscoelastic terms τ_n , greatly influenced the shape of the relaxation curve. It should be noted that this rate parameter also increases or decreases the peak response, as both the viscoelastic and poroelastic relaxation responses occur at the onset of loading.

Another advantage of the reduction of material parameters is that this method produced a unique solution for each optimization. Take for example, the effect of viscoelastic relaxation rate (τ_n decrease, relaxation rate increases) and initial permeability (k_0 increases, relaxation rate increases). Without the coupling utilized in this study, these parameters could be varied relative to one another while producing an identical material response and a non-unique solution. Thus, the approach utilized in this work allowed for simple comparison between control and impacted specimens by the evaluation of any differences between the κ parameters for each group.

The disadvantage of this coupling approach is it remains unclear exactly what portions of the various mechanisms contribute to the observed changes. Future studies could delineate changes in the fluid flow properties or solid constituent specifically for their individual contribution to tissue degradation. Additionally, it remains unclear exactly how the optimization procedure could be improved by varying the coupling equations (Equations 9–13).

4.3 Optimization Results and Physiological Mechanisms

The primary purpose of fitting the model to experimental data in this case was to evaluate any changes between healthy and impacted menisci, with the goal of evaluating mechanical changes that may be indicative of a process leading to post-traumatic OA. The interpretation of the results might thus serve as a basis to investigate overall tissue changes, as opposed to specific material properties.

The observed decreases in the α (or stiffness) term from control to impacted menisci were not surprising, as the experimental data utilized for this study showed decreases in in meniscal instantaneous and equilibrium moduli (Fischenich et al., 2014a), while a similar study of an OA transection model also found decreased indentation stiffness (Fischenich et al., 2014b). Our results show that in addition to decreases in stiffness, the time dependent mechanical properties of the menisci were altered following tibiofemoral impact. Specifically, the rate at which the tissue reached equilibrium was decreased in impacted specimens, which also reduced the instantaneous stiffness of the tissue. While this result provides important insight into how tissue degradation manifests itself in mechanical behavior, the key to treatment is identifying how physiological changes alter the structure-function relationship of orthopedic tissues.

The saturating fluid within the meniscus plays a key role in mechanical function, as it acts to disperse loads throughout the tissue (Haemer et al., 2012) without causing large strains in the solid phase. The behavior of this fluid is controlled largely by proteoglycans with glycosaminoglycan (GAG) chains. These GAG chains contribute to the overall time dependent and stiffness behavior of the tissue, in addition to the fluid viscosity (Fithian et al., 1990; Sanchez-Adams et al., 2011). Changes to the GAG content could therefore disrupt tissue permeability. Previous work shows a decrease in GAG content in menisci at twelve weeks post injury (Fischenich et al., 2014a; Fischenich et al., 2014b). Increases in permeability could lead to an overloading of the solid matrix and fibers, resulting in further degradation of these solid constituents. Thus, the observed changes in material properties suggested that this level of tibiofemoral impact resulted in damage to the solid phase of the

meniscus twelve weeks post impact. To the authors' knowledge this was the first investigation of how the rate of relaxation (either through permeability or inherent viscoelasticity of the solid phase) may be affected by a tibiofemoral impact.

5. Conclusions

This novel model of the meniscus, along with *in situ* experimental testing, holds great potential in monitoring the development post-traumatic OA in a lapine model. These analyses may then be utilized to understand how pathophysiological changes occur within the menisci following trauma. The employed constitutive model could also be incorporated into analyses under a wide range of conditions, which could benefit a broad variety of OA studies.

Acknowledgements

This study was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health under Award Number R21 AR060464.

References

- Abraham AC, Edwards CR, Odegard GM, Donahue TLH. Regional and fiber orientation dependent shear properties and anisotropy of bovine meniscus. *J. Mech. Behav. Biomed. Mater.* 2011; 4:2024–2030. [PubMed: 22098902]
- Adams ME, Billingham ME, Muir H. The glycosaminoglycans in menisci in experimental and natural osteoarthritis. *Arthritis Rheum.* 1983; 26:69–76. [PubMed: 6401994]
- Anderson DR, Woo SL, Kwan MK, Gershuni DH. Viscoelastic shear properties of the equine medial meniscus. *J. Orthop. Res.* 1991; 9:550–558. [PubMed: 2045982]
- Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage.* 2010; 18:24–33. [PubMed: 19751691]
- Chandran, PL.; Barocas, VH. *J. Biomech. Eng.* Vol. 126. IUTAM Bookseries; 2004. Microstructural Mechanics of Collagen Gels in Confined Compression: Poroelasticity, Viscoelasticity, and Collapse; p. 152
- Danso EK, Honkanen JTJ, Saarakkala S, Korhonen RK. Comparison of nonlinear mechanical properties of bovine articular cartilage and meniscus. *J. Biomech.* 2014; 47:200–206. [PubMed: 24182695]
- Dassault Systèmes. Volume III: Materials. Abaqus Analysis User's Manual. 2012
- Fischenich KM, Button KD, Coatney GA, Fajardo RS, Leikert KM, Haut RC, Haut Donahue TL. Chronic Changes in the articular cartilage and meniscus following traumatic impact to the lapine knee. *J. Biomech.* 2014; 48:246–253. [PubMed: 25523754]
- Fischenich KM, Coatney GA, Haverkamp JH, Button KD, DeCamp C, Haut RC, Haut Donahue TL. Evaluation of meniscal mechanics and proteoglycan content in a modified anterior cruciate ligament transection model. *J. Biomech. Eng.* 2014; 136:1–8.
- Fithian DC, Kelly MA, Mow VC. Material properties and structure-function relationships in the menisci. *Clin. Orthop. Relat. Res.* 1990:19–31. [PubMed: 2406069]
- Haemer JM, Carter DR, Giori NJ. The low permeability of healthy meniscus and labrum limit articular cartilage consolidation and maintain fluid load support in the knee and hip. *J. Biomech.* 2012; 45:1450–1456. [PubMed: 22391467]
- Haut Donahue TL, Hull ML, Rashid MM, Jacobs CR. A finite element model of the human knee joint for the study of tibio-femoral contact. *J. Biomech. Eng.* 2002; 124:273. [PubMed: 12071261]

- Haut Donahue TL, Hull ML, Rashid MM, Jacobs CR. How the stiffness of meniscal attachments and meniscal material properties affect tibio-femoral contact pressure computed using a validated finite element model of the human knee joint. *J. Biomech.* 2003; 36:19–34. [PubMed: 12485635]
- Hayes WC, Mockros LF. Viscoelastic properties of human articular cartilage. *J. Appl. Physiol.* 1971; 31:562–568. [PubMed: 5111002]
- Hellio Le Graverand MP, Vignon E, Otterness IG, Hart Da. Early changes in lapine menisci during osteoarthritis development: Part I: cellular and matrix alterations. *Osteoarthritis Cartilage.* 2001; 9:56–64. [PubMed: 11178948]
- Holzapfel, GA. *Nonlinear Solid Mechanics*. Chichester, West Sussex, England: Wiley; 2000.
- Holzapfel GA. Biomechanics of soft tissue. *The Handbook of Materials Behavior Models*. 2001:1049–1063.
- Joshi MD, Suh JK, Marui T, Woo SL. Interspecies variation of compressive biomechanical properties of the meniscus. *J. Biomed. Mater. Res.* 1995; 29:823–828. [PubMed: 7593020]
- Kalyanam S, Yapp RD, Insana MF. Poro-viscoelastic behavior of gelatin hydrogels under compression-implications for bioelasticity imaging. *J. Biomech. Eng.* 2009; 131:081005. [PubMed: 19604017]
- Kauer M, Vuskovic V, Dual J, Szekely G, Bajka M. Inverse finite element characterization of soft tissues. *Med. Image Anal.* 2002; 6:275–287. [PubMed: 12270232]
- Khodaei H, Mostofizadeh S, Brodin K, Johansson H, Osth J. Simulation of active skeletal muscle tissue with a transversely isotropic viscohyperelastic continuum material model. *Proc. Inst. Mech. Eng. H.* 2013; 227:571–580. [PubMed: 23637267]
- Killian ML, Isaac DI, Haut RC, Déjardin LM, Leetun D, Donahue TLH. Traumatic anterior cruciate ligament tear and its implications on meniscal degradation: a preliminary novel lapine osteoarthritis model. *J. Surg. Res.* 2010; 164:234–241. [PubMed: 19577765]
- Kim, J.; Srinivasan, MA. *Med. Image Comput. Comput. Assist. Interv. Vol. 8. Lecture Notes in Computer Science*; 2005. Characterization of viscoelastic soft tissue properties from in vivo animal experiments and inverse FE parameter estimation; p. 599-606.
- Korhonen R, Wong M, Arokoski J, Lindgren R, Helminen H, Hunziker E, Jurvelin J. Importance of the superficial tissue layer for the indentation stiffness of articular cartilage. *Med. Eng. Phys.* 2002; 24:99–108. [PubMed: 11886828]
- Lei F, Szeri aZ. Inverse analysis of constitutive models: biological soft tissues. *J. Biomech.* 2007; 40:936–940. [PubMed: 16730739]
- LeRoux, Ma; Setton, La. Experimental and Biphase FEM Determinations of the Material Properties and Hydraulic Permeability of the Meniscus in Tension. *J. Biomech. Eng.* 2002; 124:315. [PubMed: 12071267]
- Levine JW, Kiapour AM, Quatman CE, Wordeman SC, Goel VK, Hewett TE, Demetropoulos CK. Clinically relevant injury patterns after an anterior cruciate ligament injury provide insight into injury mechanisms. *Am. J. Sports Med.* 2013; 41:385–395. [PubMed: 23144366]
- Li LP, Herzog W, Korhonen RK, Jurvelin JS. The role of viscoelasticity of collagen fibers in articular cartilage: axial tension versus compression. *Med. Eng. Phys.* 2005; 27:51–57. [PubMed: 15604004]
- Lucas SR, Bass CR, Salzar RS, Oyen ML, Planchak C, Ziemba A, Shender BS, Paskoff G. Viscoelastic properties of the cervical spinal ligaments under fast strain-rate deformations. *Acta Biomater.* 2008; 4:117–125. [PubMed: 17923449]
- MacConaill MA. The movements of bones and joints; the synovial fluid and its assistants. *J. Bone Joint Surg. Br.* 1950; 32-B:244–252. [PubMed: 15422026]
- Mak AF. The Apparent Viscoelastic Behavior of Articular Cartilage—The Contributions From the Intrinsic Matrix Viscoelasticity and Interstitial Fluid Flows. *J. Biomech. Eng.* 1986; 108:123. [PubMed: 3724099]
- Mansour JM, Mow VC. The permeability of articular cartilage under compressive strain and at high pressures. *J. Bone Joint Surg. Am.* 1976; 58:509–516. [PubMed: 1270471]
- Martin Seitz A, Galbusera F, Kraus C, Ignatius A, Dürselen L. Stress-relaxation response of human menisci under confined compression conditions. *J. Mech. Behav. Biomed. Mater.* 2013; 26:68–80. [PubMed: 23811278]

- Martins PALS, Natal Jorge RM, Ferreira AJM. A Comparative Study of Several Material Models for Prediction of Hyperelastic Properties: Application to Silicone-Rubber and Soft Tissues. *Strain*. 2006; 42:135–147.
- Meyer EG, Haut RC. Excessive compression of the human tibio-femoral joint causes ACL rupture. *J. Biomech*. 2005; 38:2311–2316. [PubMed: 16154419]
- Mow, V. *Knee Meniscus: Basic and Clinical Foundations*, Annals of the rheumatic diseases. Raven Press; 1993.
- Moyer JT, Abraham AC, Haut Donahue TL. Nanoindentation of human meniscal surfaces. *J. Biomech*. 2012; 45:2230–2235. [PubMed: 22789734]
- Neogi T, Zhang Y. Epidemiology of osteoarthritis. *Rheum. Dis. Clin. North Am*. 2013; 39:1–19. [PubMed: 23312408]
- Peña E, Calvo B, Martínez MA, Doblaré M. A three-dimensional finite element analysis of the combined behavior of ligaments and menisci in the healthy human knee joint. *J. Biomech*. 2006; 39:1686–1701. [PubMed: 15993414]
- Peña E, Calvo B, Martínez MA, Palanca D, Doblaré M. Finite element analysis of the effect of meniscal tears and meniscectomies on human knee biomechanics. *Clin. Biomech. (Bristol, Avon)*. 2005; 20:498–507.
- Proctor CS, Schmidt MB, Whipple RR, Kelly Ma, Mow VC. Material properties of the normal medial bovine meniscus. *J. Orthop. Res*. 1989; 7:771–782. [PubMed: 2677284]
- Sanchez-Adams J, Willard VP, Athanasiou KA. Regional variation in the mechanical role of knee meniscus glycosaminoglycans. *J. Appl. Physiol*. 2011; 111:1590–1596. [PubMed: 21903884]
- Seifzadeh, a; Oguamanam, DCD.; Trutiak, N.; Hurtig, M.; Papini, M. Determination of nonlinear fibre-reinforced biphasic poroviscoelastic constitutive parameters of articular cartilage using stress relaxation indentation testing and an optimizing finite element analysis. *Comput. Methods Programs Biomed*. 2012; 107:315–326. [PubMed: 21802762]
- Skaggs DL, Warden WH, Mow VC. Radial tie fibers influence the tensile properties of the bovine medial meniscus. *J. Orthop. Res*. 1994; 12:176–185. [PubMed: 8164089]
- Spilker RL, Donzelli PS, Mow VC. A transversely isotropic biphasic finite element model of the meniscus. *J. Biomech*. 1992; 25:1027–1045. [PubMed: 1517263]
- Sweigart, Ma; Zhu, CF.; Burt, DM.; DeHoll, PD.; Agrawal, CM.; Clanton, TO.; Athanasiou, Ka. Intraspecies and interspecies comparison of the compressive properties of the medial meniscus. *Ann. Biomed. Eng*. 2004; 32:1569–1579. [PubMed: 15636116]
- Tissakht M, Ahmed AM. Tensile stress-strain characteristics of the human meniscal material. *J. Biomech*. 1995; 28:411–422. [PubMed: 7738050]
- Troyer KL, Puttlitz CM. Human cervical spine ligaments exhibit fully nonlinear viscoelastic behavior. *Acta Biomater*. 2011; 7:700–709. [PubMed: 20831909]
- Troyer KL, Puttlitz CM. Nonlinear viscoelasticity plays an essential role in the functional behavior of spinal ligaments. *J. Biomech*. 2012; 45:684–691. [PubMed: 22236525]
- Upton ML, Hennerbichler A, Fermor B, Guilak F, Weinberg JB, Setton La. Biaxial strain effects on cells from the inner and outer regions of the meniscus. *Connect. Tissue Res*. 2006; 47:207–214. [PubMed: 16987752]
- Whipple R, Wirth C, Mow V. Mechanical Properties of the Meniscus. *ASME Advances in Bioengineering*. 1984:32–33.
- Yang M, Taber LA. The possible role of poroelasticity in the apparent viscoelastic behavior of passive cardiac muscle. *J. Biomech*. 1991; 24:587–597. [PubMed: 1880142]
- Yeow CH, Ng KS, Cheong CH, Lee PVS, Goh JCH. Repeated application of incremental landing impact loads to intact knee joints induces anterior cruciate ligament failure and tibiofemoral cartilage deformation and damage: A preliminary cadaveric investigation. *J. Biomech*. 2009; 42:972–981. [PubMed: 19380143]
- Zhu W, Chern KY, Mow VC. Anisotropic viscoelastic shear properties of bovine meniscus. *Clin. Orthop. Relat. Res*. 1994:34–45. [PubMed: 8070209]

Figure 1.

Schematic of how experimental samples were sectioned from menisci. Each limb yielded six specimens, three lateral (anterior, central, and posterior) and three medial (similarly).

Figure 2.

FE model of a posterior to anterior rotated meniscus and indenter tip. The tip was displaced 0.25 mm into the tissue. Boundary conditions are shown on the figure.

Figure 3.

FE model convergence study. There was no difference in strain energy between a model of 1644 elements and 2441 elements in both peak and equilibrium responses.

Figure 4.

Representative force-time plot of indentation stress relaxation data, where the loading portion of the graph consists of 1 second while the relaxation and equilibrium portions are 900 seconds combined.

Figure 5.

Visual model fit to experimental data for a single paired specimen (one of eighteen pairs), showing agreement with both control (A) and impacted (B) specimen data throughout the whole curve. Note the control specimen has a stiffer response. Each individual specimen was optimized and the parameter values were averaged (Figure 6).

Figure 6. Comparisons between parameter values for control and impacted specimens (mean $\pm$ standard error). * denotes significance ($p < 0.05$).

Figure 7.

Effect of each parameter on curve shape. (A) An α parameter decrease yields a decrease in peak response of 17.4% and 13.6% at equilibrium. (B) A β parameter decrease yields a decrease in peak response of 8.4%, while the relaxation response experiences an 89.2% decrease. (C) A κ parameter increase yields a decrease in peak response of 19.2% and a decrease of 44.9%, but only a 0.02 N force difference, at 900s (at which equilibrium has not been reached for $\kappa = 0.005$), and a drastic change to the shape of the relaxation curve.

Table 3

Material parameters, including both fixed vales and those that were varied.

Model	SED Function				Prony Series				Darcy's Law & Permeability			
Parameter	a ₂	b ₂	c ₂	d ₂	g _n (n=3)	τ _n (n=3)	k ₀	μ	e ₀	κ	M	
Value	Varied				Varied		Varied	981	3	0.0848	4.638	
Units	Pa				Unit-less		m ⁴ /N-s	Pa-s	Unit-less			

Table 4

Numerical results highlighting the agreement between experimental data and model output for all specimens (goodness of fit value, mean % error of each time point, and the error between peak responses).

Fit Metric	NMSE Fit	Total % Error	Peak % Error
Mean	0.937	5.3	-0.0172
Standard Error	0.0069	0.44	0.017