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Modeling of long-term fatigue damage of soft tissue with stress softening and permanent set effects

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Abstract

One of the major failure modes of bioprosthetic heart valves is non-calcific structural deterioration due to fatigue of the tissue leaflets. Experimental methods to characterize tissue fatigue properties are complex and time-consuming. A constitutive fatigue model that could be calibrated by isolated material tests would be ideal for investigating the effects of more complex loading conditions. However, there is a lack of tissue fatigue damage models in the literature. To address these limitations, in this study, a phenomenological constitutive model was developed to describe the stress softening and permanent set effects of tissue subjected to long-term cyclic loading. The model was used to capture characteristic uniaxial fatigue data for glutaraldehyde-treated bovine pericardium and was then implemented into finite element software. The simulated fatigue response agreed well with the experimental data and thus demonstrates feasibility of this approach.

Keywords

Soft tissue fatigue model; Permanent set; Stress softening; Bioprosthetic heart valve

1 Introduction

Biologically derived and chemically treated collagenous tissues are extensively utilized in a broad spectrum of medical applications including cardiovascular grafts and bio-prosthetic heart valves (BHV), as well as ligament, tendon, cartilage, sclera, and hernia repair and replacement. However, despite their widespread use, fatigue-induced degradation, wear and tearing of collagenous tissue implants have not been well characterized. Fatigue-induced damage has been identified as a major problem associated with the some implant failures (Broom 1978; Vyavahare et al. 1999; Teoh 2000; Sacks 2001; Slaughter and Sacks 2001; Mirnajafi et al. 2010; Schoen and Levy 1999).

Fatigue is an especially critical issue for the application of BHVs. Today, the only effective, long-term treatment for valvular heart disease is open-chest cardiac valve repair or replacement surgery. BHVs fabricated from glutaraldehyde-treated bovine pericardium (GLBP) have been used to treat valvular disease for over four decades and continue to be one of the dominant replacement valve modalities, either as a conventional prosthetic valve design or more recently for minimally invasive percutaneous delivery (Munt and Webb 2006; Webb et al. 2007). BHVs display superior hemodynamics to mechanical valves, and they eliminate the need for anticoagulant therapy. Regardless of the specific design, long-term durability of the GLBP tissue leaflets is limited. Bioprosthetic valves often need to be

replaced within 10 years after implantation and in as soon as 5 years in younger patients (Schoen and Levy 1999). The two major failure mechanisms of BHVs are calcification and non-calcific structural deterioration due to fatigue of the GLBP leaflets (Schoen and Levy 1999). It is hypothesized that clinical BHV failure due to structural deterioration is caused by localized cuspal damage at stressed regions (Schoen and Levy 1999); yet, the mechanisms governing GLBP fatigue and BHV failure are incompletely understood.

There are many challenges associated with fatigue testing of BHV materials. The experimental methods can be very time-consuming and often involve complex testing instruments. The current FDA requirement mandates new BHV designs to be tested up to 200 million cycles using accelerated wear testers to evaluate the fatigue performance (Mirnajafi et al. 2010). Although accelerated wear testers can approximate the in vivo hemodynamics, it remains difficult to determine the specific effects of different fatigue modalities (tensile, compressive, bending, etc.) on the leaflet material properties when using this technique. To address this drawback, several studies have been conducted using isolated material tests in order to determine, for instance, the effects of uniaxial cyclic loading on GLBP material properties (Sun et al. 2004; Sellaro et al. 2007) and collagen fiber orientation (Sellaro et al. 2007). Others have investigated the effects of cyclic bending fatigue on the leaflet flexural rigidity (Mirnajafi et al. 2010). These studies, however, are limited to a moderate level of fatigue (i.e., less than 100 million cycles). A constitutive fatigue damage model for GLBP that can be calibrated from isolated material experiments would be ideal for investigating the effects of more complex loading conditions computationally on tissue durability for applications such as BHVs. However, there is a dearth of such models in the literature.

There is a limited number of constitutive models for describing the damage process in soft biological tissues, which can arise from the plastic deformation or fracture of the fibers or tearing of the matrix (Simo 1987; Rodríguez et al. 2006; Alastrué et al. 2007; Calvo et al. 2007; Pena 2011; Li and Robertson 2009). In 1987, Simo (Simo 1987) introduced the concept of a fully three-dimensional finite-strain viscoelastic damage model, based on irreversible thermodynamics with internal variables. This pioneering work served as the basis for several soft tissue damage models (Rodríguez et al. 2006; Alastrué et al. 2007; Calvo et al. 2007; Pena 2011). More recent models have been developed to apply both the stress softening and permanent set effects of damaged soft tissue (Pena 2011). Each of these models can be utilized to model damage induced by cyclic stretching with increasing magnitude; however, damage in these models is dependent only upon the strain history and not on the number of loading cycles. Under this assumption, a tissue specimen subjected to cyclic displacement control loading will only incur damage during the first cycle given the elastic limits of the tissue are exceeded. However, uniaxial tension fatigue experiments (Sun et al. 2004) show that the structural and mechanical properties of GLBP tissue are altered at the low fatigue state (30×10^6 loading cycles) and continue to change between low and moderate fatigue state (65×10^6 cycles) under displacement control loading. This limits the applicability of such models to study long-term fatigue damage in BHVs where the loading conditions are relatively constant throughout fatigue life. The inclusion of a continuous damage mechanism is necessary (Miehe 1995; Li and Robertson 2009).

In this study, we propose a phenomenological damage model to describe the overall fatigue damage of GLBP due to the strain history and number of loading cycles for the purpose of investigating the fatigue damage process of BHVs. The model incorporates descriptions of the fatigue-induced stress softening and permanent set of biological tissues. The damage model is implemented into ABAQUS via a user defined material (UMAT) in conjunction with the nonlinear orthotropic Fung-elastic model and is utilized in a tissue uniaxial fatigue loading simulation.

2 Methods

2.1 Unfatigued state tissue properties

Let Ω_0 and Ω be the fixed reference and deformed configurations of a continuous body, respectively. We consider the general mapping $\chi : \Omega_0 \rightarrow \mathbf{R}^3$, which transforms a material point $X \in \Omega_0$ to a position $x = \chi(X, t) \in \Omega$ in the deformed configuration at time t . Assuming that the stress at any point in the body Ω_0 depends only on the deformation surrounding that point, the deformation gradient, $\mathbf{F}$, can be written as

$$\mathbf{F}(X, t) = \frac{\partial_x (X, t)}{\partial X}. \quad (1)$$

The Green strain tensor, $\mathbf{E}$, can then be defined as a function of $\mathbf{F}$.

$$\mathbf{E} = \frac{1}{2} (\mathbf{F}^T \mathbf{F} - \mathbf{1}). \quad (2)$$

GLBP is assumed to be an incompressible ($\det \mathbf{F} = 1$), anisotropic, nonlinear, hyperelastic material (Sun and Sacks 2005), and the unfatigued strain energy, W^0 , can be expressed as a function of $\mathbf{E}$. Thus, the in-plane second Piola Kirchhoff stress at the unfatigued state ($\mathbf{S}^0$) can be computed by Eq. 3.

$$\mathbf{S}^0 = \frac{\partial W^0}{\partial \mathbf{E}} \quad (3)$$

The generalized Fung-type strain energy function for the planar biaxial response of soft biological tissues is given by (Fung 1993):

$$W^0 = \frac{c}{2} (e^Q - 1), \quad (4)$$

$$Q = A_1 E_{11}^2 + A_2 E_{22}^2 + 2A_3 E_{11} E_{22} + A_4 E_{12}^2 + 2A_5 E_{11} E_{12} + 2A_6 E_{22} E_{12}, \quad (5)$$

where c and A_{1-6} are material parameters.

2.2 Fatigued state tissue properties

The stress-strain response of collagenous soft tissues has 3 distinct regions: the toe region where the collagen fibrils extend, the quasi-linear region as the collagen fibrils uncrimp as they bear load causing the tissue stiffness to greatly increase, and the damage region as the strain exceeds a specific limit and collagen fibrils and interfibrillar bonds progressively break down, and the material stiffness decreases until the tissue fails (Natali et al. 2008). During the fatigue process, irreversible un-crimping of the collagen fibers induces a permanent set in the tissue (Sun et al. 2004; Sellaro et al. 2007).

2.2.1 Fatigued state tissue strain energy function—To incorporate changes to the material properties as a result of fatigue damage, the strain energy function, W , is enhanced with the addition of a stress softening parameter, D_s , and a permanent set parameter, $\mathbf{D}_{ps}$.

$$W = W(\mathbf{E}, D_s, \mathbf{D}_{ps}). \quad (6)$$

At the unfatigued state, both D_s and D_{ps} are inactive, i.e. $D_s = 0$ and $D_{ps} = 0$, thus W is only a function of $\mathbf{E}$,

$$W(\mathbf{E}, 0, 0) = W^0(\mathbf{E}). \quad (7)$$

The parameters D_s and D_{ps} become active with the onset of fatigue damage induced by cyclic loading, and the inclusion of these terms provides a means of changing the form of the strain energy function, which is no longer elastic. The fatigued strain energy function can be expressed as:

$$W(\mathbf{E}, D_s, D_{ps}) = (1 - D_s) W^0(\mathbf{E}) + W_{ps}(\mathbf{E}, D_s, D_{ps}), \quad (8)$$

where W_{ps} is the dissipated strain energy due to the permanent set and $D_s W^0$ represents the dissipated energy due to the unfatigued softening effect alone.

2.2.2 Equivalent strain—In order to establish the law of tissue fatigue damage evolution, we first define an equivalent strain Ξ_t (Simo 1987), a scalar quantity proportional to the unfatigued strain energy at time t ,

$$\Xi_t(\mathbf{E}(t)) := \sqrt{2W^0(\mathbf{E}(t))}, \quad (9)$$

where $\mathbf{E}(t)$ is the Green strain tensor at time $t \in [0, T]$. Here, it is assumed that material damage is related to the maximum distortional energy, independent of hydrostatic pressure (Simo 1987). Furthermore, since the primary focus of this study is long-term tissue fatigue damage after millions of cycles of loading, the damage criteria were only evaluated at the peak of each sinusoidal loading cycle to reduce computational time. Therefore, we introduce a peak equivalent strain that is updated after each loading cycle and is equal to the max equivalent strain experienced during the loading portion of that cycle, given explicitly by:

$$\Xi_n^{\text{peak}} = \max_{t \in [\frac{n}{f}, \frac{n+1}{f}]} \sqrt{2W^0(\mathbf{E}(t))}, \quad (10)$$

$$n = 0, 1, 2, 3, \dots, n_{\text{tot}}$$

where f is the frequency and n is the number of loading cycles up to a maximum number, n_{tot} .

Remark 1: In the literature (Simo 1987; Rodríguez et al. 2006; Alastrué et al. 2007; Calvo et al. 2007; Pena 2011), the maximum value of $\Xi_t(\mathbf{E}(t))$ over the past history up to the current time T was used to evaluate damage evolution:

$$\Xi_t^{\text{max}} := \max_{0 \leq t \leq T} \sqrt{2W^0(\mathbf{E}(t))} \quad (11)$$

where Ξ_t and Ξ_t^{max} define a damage surface in the strain space given by

$$\varphi_d(\mathbf{E}(t), \Xi_t^{\text{max}}) := \Xi_t(\mathbf{E}) - \Xi_t^{\text{max}} = 0. \quad (12)$$

Based on these studies (Simo 1987; Rodríguez et al. 2006; Alastrué et al. 2007; Calvo et al. 2007; Pena 2011), a nonincreasing damage criterion in the strain space was defined by the condition $\varphi_d < 0$. However, it should be noted that such damage surface is not suitable for fatigue damage evolution because even if $\Xi_t(\mathbf{E})$ is smaller than Ξ_t^{max} , fatigue damage could still occur over continued cycling.

Remark 2: A continuous damage evolution parameter based on the accumulated equivalent strain has been presented in the literature (Miehe 1995; Li and Robertson 2009), where the accumulated equivalent strain, Ξ_t^{acc} , is given as:

$$\Xi_t^{\text{acc}}(t) = \int_0^t |d\sqrt{2W^0(\mathbf{E}(s))}/ds| ds. \quad (13)$$

The Ξ_t^{acc} term allows for fatigue damage evolution; however, this approach is computationally expensive for long-term applications.

2.2.3 Fatigue-induced stress softening—The stress softening caused by cyclic fatigue damage is considered as a function of both the equivalent strain and the number of loading cycles. Here, we introduce two parameters $\psi_{\min}$ and $\psi_{\max}$, to define the boundaries of the fatigue damage evolution zone. A specimen cyclically loaded to an equivalent strain of $\psi_{\max}$ will fail instantaneously during the first loading cycle. A specimen loaded to an equivalent strain of $\psi_{\min}$ will be able to endure a maximum number, $n_{\max}$, of loading cycles before complete failure. Therefore, $\psi_{\min}$ represents the minimum equivalent strain to elicit the accumulation of fatigue damage, while $\psi_{\max}$ represents the tissue maximum equivalent strain limit. Herein, we propose that the number of cycles until failure (n_{tot}) is given by the following equation:

$$n_{\text{tot}}(\Xi_n^{\text{peak}}) = \begin{cases} \infty & \text{if } \Xi_n^{\text{peak}} < \psi_{\min} \\ \frac{\beta(n_{\max}-1)}{\Xi_n^{\text{peak}} - \psi_{\min} + \beta} \left(\frac{1 - \exp^{\alpha(1 - \frac{\Xi_n^{\text{peak}}}{\psi_{\max}})}}{1 - \exp^{\alpha(1 - \frac{\psi_{\min}}{\psi_{\max}})}} \right) + 1 & \text{if } \psi_{\min} \leq \Xi_n^{\text{peak}} \leq \psi_{\max}, \\ 1 & \text{if } \Xi_n^{\text{peak}} > \psi_{\max} \end{cases} \quad (14)$$

where α and β are material constants governing the amount of damage incurred by a single cycle at Ξ_n^{peak} . These parameters are intrinsic of a material and should be measured from tissue fatigue tests conducted at different Ξ_n^{peak} values. The inclusion of fitted parameters α and β allows the model to capture a wide range of fatigued tissue responses. The effects of varying α and β in Eq. 14 on the number of cycles to failure, n_{tot} , are illustrated in Fig. 1a, c.

For tissue long-term fatigue applications, since we are interested in the accumulated damage over millions of cycles, we assume that at a given equivalent strain, an equal amount of damage is accumulated during each loading cycle, representing a linear accumulation of damage over millions of cycles. Note that this assumption may be modified by introducing a nonlinear, time-dependent accumulation of damage, provided that experimental fatigue data are available at different time points for quantifying such nonlinear accumulations of damage. In this study, assuming the linear accumulation of damage, the total amount of damage due to stress softening, D_s , after n tensile loading cycles is given by

$$D_s(\Xi_n^{\text{peak}}) = \begin{cases} 0 & \text{if } \Xi_n^{\text{peak}} < \psi_{\min} \\ \sum_{n=0}^n \frac{n}{n_{\text{tot}}} & \text{if } \psi_{\min} \leq \Xi_n^{\text{peak}} \leq \psi_{\max} \\ 1 & \text{if } \Xi_n^{\text{peak}} > \psi_{\max} \end{cases} \quad (15)$$

It can be seen that an increase in α results in greater damage due to stress softening at low Ξ_n^{peak} values (Fig. 1b), whereas an increase in β has the converse effect (Fig. 1d). The degree

of stress softening is more sensitive to changes in β at low Ξ_n^{peak} values, but more sensitive to changes in α at high Ξ_n^{peak} values.

Remark 3: The n_{tot} function is analogous to the stress versus number of cycles (S–N) curve used to describe the fatigue behavior of traditional engineering materials. An equivalent strain-based formulation was employed to facilitate model calibration through displacement-controlled fatigue experiments where Ξ_n^{peak} is held relatively constant throughout loading. The n_{tot} function can be determined from a series of fatigue-to-failure experiments under different Ξ_n^{peak} values.

Remark 4: Since a BHV is deformed under pressure loading (i.e., a load-control condition), the Ξ_n^{peak} value will change (e.g. increase) from cycle to cycle as the tissue softens; thus, the n_{tot} will decrease, representing accelerated fatigue damage compared to the displacement control loading condition.

2.2.4 Fatigue-induced permanent set—Tissue damage is associated with irreversible tissue elasticity loss. Therefore, when the elastic limits of the tissue are exceeded, a permanent set is exhibited upon unloading. The magnitude of the permanent set, $\mathbf{D}_{\text{ps}}$, is related to the degree of softening in the tissue and thus is also a function of Ξ_n^{peak} . The permanent set upon complete tissue failure, $\mathbf{D}_{\text{psmax}}$, can be measured experimentally by quantifying the change in the specimen geometry before and after fatigue loading. For planar tissues, $\mathbf{D}_{\text{ps}}$ has components of D_{ps11} , D_{ps22} , and D_{ps12} . Similarly, for long-term fatigue applications, we assume that at a given equivalent strain, an equal amount of permanent set is accumulated during each loading cycle, representing a linear accumulation of permanent set over millions of cycles. For the purpose of this study, we assume that the $\mathbf{D}_{\text{ps}}$ expressed as a permanent Green strain can be determined from:

$$\mathbf{D}_{\text{ps}}(\Xi_n^{\text{peak}}) = \begin{cases} 0 & \text{if } \Xi_n^{\text{peak}} < \psi_{\min} \\ \sum_{n=0}^n \frac{n}{n_{\text{tot}}} \mathbf{D}_{\text{psmax}} & \text{if } \psi_{\min} \leq \Xi_n^{\text{peak}} \leq \psi_{\max} \\ \mathbf{D}_{\text{psmax}} & \text{if } \Xi_n^{\text{peak}} > \psi_{\max} \end{cases} \quad (16)$$

Note that $\mathbf{D}_{\text{ps}}$ is related to n_{tot} , as expected; thus, parameters α and β also govern the amount of permanent set caused by loading to Ξ_n^{peak} , see Fig. 2.

A negative stress at zero deformation is equivalent to a permanent set (deformation) at zero stress; therefore, we employ a plastic stress, $\mathbf{S}_{\text{p}}$, to ensure this condition (Dorfmann and Ogden 2004).

$$\mathbf{S}_{\text{p}} = - \left. \frac{\partial (1 - D_s) W^0}{\partial \mathbf{E}} \right|_{(\mathbf{E}=\mathbf{D}_{\text{ps}})} \quad (17)$$

The $\mathbf{S}_{\text{p}}$ contribution to the overall tissue response is governed by η in Eq. 18, which was modified from Dorfmann and Ogden's η function (Dorfmann and Ogden 2004) in order to accommodate for the dissipated equivalent strain associated with the permanent set, Ξ_{ps} , defined by Eq. 19

$$\eta = \frac{\Xi_t - \Xi_{\text{ps}}}{\Xi_n^{\text{peak}} - \Xi_{\text{ps}}}, \quad (18)$$

$$\Xi_{ps} := \sqrt{2W^0(E(t))} \Big|_{(E=D_{ps})}. \quad (19)$$

The magnitude of $\mathbf{S}_p$ depends on the magnitude of the permanent sets. The η term is a function of Ξ_t that modulates the transition of $\mathbf{S}_p$ from the inactive phase ($\eta = 1$) at peak loading, i.e. peak $\Xi = \Xi_n^{\text{peak}}$, to the fully active phase ($\eta = 0$) at the permanent set.

Remark 5: The purpose of the η function is to control the $\mathbf{S}_p$ contribution to the tissue response. For this reason, we chose a simple form for η . A more sophisticated functional form may be necessary for the accurate description of unloading cycles.

2.2.5 Fatigued tissue response—The overall fatigued response expressed as the second Piola–Kirchoff stress, $\mathbf{S}$, is given by:

$$\mathbf{S} = (1 - D_s) \frac{\partial W^0}{\partial \mathbf{E}} + \frac{\partial(1-D_s)}{\partial \mathbf{E}} W^0 + \frac{\partial W_{ps}}{\partial \mathbf{E}} + \frac{\partial W_{ps}}{\partial D_s} \frac{\partial D_s}{\partial \mathbf{E}} + \frac{\partial W_{ps}}{\partial D_{ps}} \frac{\partial D_{ps}}{\partial \mathbf{E}}. \quad (20)$$

It is assumed that D_s and D_{ps} are independent of $\mathbf{E}$, i.e. $\frac{\partial D_s}{\partial \mathbf{E}} = \frac{\partial D_{ps}}{\partial \mathbf{E}} = 0$, which is valid within a loading cycle because both are functions of Ξ_n^{peak} only and at a given cycle Ξ_n^{peak} is a constant value. The permanent set contribution is defined implicitly by Eq. 21 through Eqs. 8, and 16–19.

$$\frac{\partial W_{ps}}{\partial \mathbf{E}} = (1 - \eta) \mathbf{S}_p. \quad (21)$$

Thus, the second Piola–Kirchoff stress tensor may be expressed in the following reduced form:

$$\mathbf{S} = (1 - D_s) \frac{\partial W^0}{\partial \mathbf{E}} + (1 - \eta) \mathbf{S}_p. \quad (22)$$

Here, it can be seen that at peak loading, $\Xi = \Xi_n^{\text{peak}}$, $\mathbf{S}$ is reduced to Eq. 23 because $\eta = 1$, and at no load ($\mathbf{E} = \mathbf{D}_{ps}$ and $\eta = 0$) $\mathbf{S}$ is given by Eq. 24

$$\mathbf{S} = (1 - D_s) \frac{\partial W^0}{\partial \mathbf{E}}, \quad (23)$$

$$\mathbf{S} = (1 - D_s) \frac{\partial W^0}{\partial \mathbf{E}} + \mathbf{S}_p. \quad (24)$$

The elasticity tensor in the material description may be expressed in the following form:

$$\mathbf{C}(n) = \frac{\partial}{\partial \mathbf{E}} \left((1 - D_s) \frac{\partial W^0}{\partial \mathbf{E}} + (1 - \eta) \mathbf{S}_p \right). \quad (25)$$

Equation 25 can be expanded using the chain rule to Eq. 26

$$C(n) = \frac{-\partial D_s}{\partial \mathbf{E}} \frac{\partial W^0}{\partial \mathbf{E}} + (1 - D_s) \frac{\partial^2 W^0}{\partial \mathbf{E}^2} + \frac{-\partial \eta}{\partial \mathbf{E}} \mathbf{S}_p + (1 - \eta) \frac{\partial \mathbf{S}_p}{\partial \mathbf{E}}. \quad (26)$$

Again, because D_s and $\mathbf{S}_p$ are functions of only Ξ_n^{peak} , both values are constant throughout loading/unloading; thus, these terms do not affect the stiffness matrix. Thus, C can be reduced to

$$C(n) = (1 - D_s) \frac{\partial^2 W^0}{\partial \mathbf{E}^2} - \mathbf{S}_p \frac{\partial \eta}{\partial \mathbf{E}} \quad (27)$$

where $\frac{\partial \eta}{\partial \mathbf{E}}$ was solved by applying the chain rule as

$$\frac{\partial \eta}{\partial \mathbf{E}} = \frac{\partial \eta}{\partial \Xi_t} \frac{\partial \Xi_t}{\partial W^0} \frac{\partial W^0}{\partial \mathbf{E}}. \quad (28)$$

The exemplary effects of changing β on the fatigue damage due to both stress softening and permanent sets are illustrated in Fig. 3.

Remark 6: Residual strains in Pena (2011) are enforced by altering the strain invariants. This would be analogous to implementing the permanent set by shifting the Green strains in this formulation, i.e. $\mathbf{E}_n = \mathbf{E}^0 + \mathbf{D}_{ps}$. This permanent set may be more intuitive and would be easy to calibrate with experimental data. However, we chose to use a stress formulation to describe the permanent sets to facilitate the implementation into finite element (FE) software ABAQUS in which only the stress and stiffness tensors are defined explicitly and the strains approximated.

The damage induced by fatigue is a non-reversible, non-decreasing quantity. Therefore, the following conditions must be satisfied:

$$\frac{\partial D_s}{\partial t} \geq 0, \frac{\partial \mathbf{D}_{ps}}{\partial t} \geq 0. \quad (29)$$

These conditions make this model distinct from models to capture the Mullin's effect in rubbers. For the Mullin's effect, D_s and $\mathbf{D}_{ps}$ become inactive during reloading (even after the material has been damaged), and the material response follows the primary loading curve once the previous maximum strain has been exceeded. Additional damage is only realized when the material is unloaded again. For the purpose of modeling long-term fatigue damage, viscoelastic effects are ignored and each reloading curve follows the previous unloading curve. In this case, the incremental damage over one cycle is very small, and therefore, the loading and subsequent unloading curve may be nearly identical. In this application, damage was evaluated at the peak of each loading cycle, at which point the stress and stiffness matrices were updated. The unloading curve then reflected the updated fatigue response. The following loading cycle lies along the unloading response until damage is reevaluated at the peak load.

3 Applications

3.1 Determination of fatigue model parameters

3.1.1 Experimental observation—The fatigue damage model was calibrated to the experimental fatigue data of GLBP subjected to cyclic uniaxial testing reported previously by Sun et al. (2004). In the experiment, it was shown that GLBP exhibited stiffening after fatigue loading with a mean permanent set of 7.1% in the loading direction (LD), with little change to the stiffness in the cross-loading direction (XD) but with a mean permanent set of −7.7%. Therefore, the sample became longer along the loading axis and narrower along the cross-loading axis as expected. Figure 4a illustrates the apparent tissue stiffening along the LD due to cyclic fatigue loading when the permanent set is not included. However, when the permanent set is included, it can be seen that the tissue stiffness has indeed degraded as a result of fatigue loading (Fig. 4b). This effect is likely due to the reorientation of collagen fibers and loss of collagen crimp (Sun et al. 2004; Sellaro et al. 2007).

3.1.2 Fatigue modeling: The unfatigued GLBP specimen biaxial data (Sun et al. 2004) was fitted in the least-squares sense to determine the unfatigued state Fung model parameters (Eq. 2). The equi-biaxial testing data of a GLBP specimen is illustrated in Fig. 5a. The maximum number of cycles to failure, $n_{\max}$, as well as the damage criterion, $\psi_{\min}$ and $\psi_{\max}$, was assumed to be a known constant. The maximum number of loading cycles, $n_{\max}$, was set to 368 million cycles, which corresponds to approximately 10 patient years assuming a heart rate of 70bpm. However, to reduce computational cost, in the simulation, $n_{\max}$, was proportionally scaled from 368 million to 368 cycles, representing an accelerated

accumulation of damage. The value $\psi_{\min} = 4.67 \frac{\sqrt{kN}}{m}$ was determined from a BHV

simulation reported previously (Sun et al. 2005a). The value $4.67 \frac{\sqrt{kN}}{m}$ is the maximum equivalent strain exhibited by the leaflets during closure and under an imposed pressure of approximately 120mmHg. Thus, our assumption is that under the peak equivalent strain of

$4.67 \frac{\sqrt{kN}}{m}$, this particular BHV will fail after 10 patient years. The equivalent strain limit

$\psi_{\max}$ was determined through uniaxial failure tests (Fig. 6) with $\psi_{\max} = 4.32 \times 10^5 \frac{\sqrt{kN}}{m}$ corresponding to a failure strain of approximately 0.45. The contour plot of equivalent strain

with $\psi = 4.67 \frac{\sqrt{kN}}{m}$ and $\psi_{\max} = 4.32 \times 10^5 \frac{\sqrt{kN}}{m}$ marking the damage evolution region is illustrated in Fig. 5b.

Due to a lack of experimental fatigue data under different loading conditions (i.e., Ξ_n^{peak} values), the true values for α and β of Eq. 12 for GLBP are unknown. For this study, α was assumed to be 1.0 and β was determined to be 0.58, to reflect the known degree of softening and permanent sets after 30×10^6 cycles of uniaxial loading. The complete list of parameters is presented in Table 1.

3.2 Uniaxial fatigue loading simulation

3.2.1 FE model setup: The fatigue damage model of Eq. 19 was incorporated in the finite element software ABAQUS via the user subroutine (UMAT). Details of the constitutive model implementation into ABAQUS have been previously presented (Sun and Sacks 2005; Sun et al. 2008). To evaluate the ability of the model to capture the fatigue response of GLBP, a uniaxial fatigue simulation was developed to mimic the experimental protocol in Sun et al. (2004). The simulated test specimen was modified from a previously developed

biaxial test specimen model (Sun et al. 2005b) so that the top and bottom rows of elements act as the grips used to secure the tissue specimen in the experimental set-up. Therefore, damage was not considered in those elements (Fig. 7a). The test specimen model consisted of 400 plane stress elements to allow for a test specimen geometry of 25 mm $\times$ 25 mm $\times$ 0.4 mm. The simulation of 3 steps: (1) unfatigued state biaxial tension under load control imposed by evenly spaced nodal forces along both axes to apply a stress ratio of $S_{LD} : S_{XD} = 1 : 0.1$ to the specimen, similar to the corresponding biaxial test protocol (Sun et al. 2004), (2) 30 cycles of uniaxial tension to a peak strain of 16% imposed by a uniform displacement applied to the top and bottom row of elements, which corresponds to 30×10^6 cycles in real time, and (3) at the 30×10^6 state, biaxial tension with identical loading as in step 1. The damage criteria were evaluated at the peak displacement of each loading cycle. Fatigue damage accumulation was only considered in step (2). The biaxial tension tests in steps (1) and (3) were simply to facilitate comparison between the simulation results and the experimental fatigue data in Sun et al. (2004).

3.2.2 Simulation results: The uniaxial fatigue simulation demonstrated the altered geometry and mechanical properties of the tissue specimen in response to cyclic loading. As illustrated in Fig. 7b–d, the test specimen becomes clearly distorted throughout cyclic loading as a result of accumulating permanent sets. The specimen became elongated in the LD and narrowed along the XD, as observed experimentally. During the uniaxial loading in step 2, the specimen narrowed in the middle up to 20×10^6 cycles of fatigue loading (Fig. 7b). When cycled beyond this point, the specimen began to bulge in the middle at the zero LD displacement position (Fig. 7c). In the experimental set-up, the tissue will buckle upon unloading once the permanent set in the LD has reached some critical value. Because this simulation is planar, this buckling effect cannot be visualized, instead the specimen is compressed back to its unfatigued LD dimension, causing the specimen to bulge in the middle to satisfy the incompressibility constraint. The specimen geometry change after 30×10^6 fatigue cycles is evident in the stress-free state (Fig. 7d). The total permanent sets accumulated after 30×10^6 simulated fatigue cycles presented as the average Green strains at the zero stress-state in the central 16 elements were -0.0327 in the XD, 0.0693 in the LD, and 0.0149 in shear which agree well with the experimentally observed values (Sun et al. 2004). Damage was highest near the sides of the tissue along the LD axis, with a maximum stress softening factor of 0.803 . The stress softening factor throughout the center of the specimen was approximately 0.646 .

The change in the specimen mechanical properties is demonstrated by the altered stress–strain response. The mean stress–strain responses were extracted from the central 16 elements of the model where the stress and strain were nearly uniform. Figure 8a illustrates the changing stress–strain response under cyclic tension in step 2 of the simulation. As expected, the peak stress to achieve the maximum strain is reduced over fatigue life. In Fig. 8b the stress–strain response was extracted from the same elements during steps 1 and 3 of the simulation and were plotted against the experimental fatigue data from Sun et al. (2004). The simulation results agree well with the experimental data for both the 0 cycle (unfatigued) state and the 30×10^6 cycle state. In Fig. 8b a non-zero strain of approximately 0.0693 at zero stress is shown for the 30×10^6 cycle state response.

4 Discussion

In this study, we developed a theoretical and computational framework to model soft tissue fatigue that incorporates the long-term fatigue-induced stress softening and permanent set phenomena exhibited by biological tissues under cyclic loading. We demonstrate the feasibility of this approach by simulating tissue fatigue damage under cyclic uniaxial loading conditions.

In the uniaxial fatigue simulation, the model was able to capture the permanent set and experimental fatigue behavior of GLBP quite well along the loading direction. The model also captured the permanent set in the XD; however, the model as described cannot capture the fatigued stress–strain behavior along the XD. In previous experimental uniaxial fatigue studies of GLBP (Sun et al. 2004; Sellaro et al. 2007), it was reported that the LD becomes stiffer and XD becomes more extensible when referencing the current cycle state in response to fatigue, thus neglecting the permanent set. However, when referencing the unfatigued state, the peak stretches are higher in the LD and lower in the XD in response to cyclic loading (Sun et al. 2004). It has been hypothesized (Sun et al. 2004; Sellaro et al. 2007) that this loading condition may reorient the collagen fibers in the GLBP tissue toward the LD. This fiber reorientation may be responsible for narrowing the tissue and reducing the extensibility in the XD. The fatigue damage model presented here cannot accurately capture this phenomenon, because D_s is a positive increasing value marking the percent reduction of the tissue modulus. A structural-based constitutive model where the collagen fiber orientations are defined by functions of the loading history may be necessary to capture the stiffening effect observed in the XD. The presented formulation will be more appropriate for modeling changes induced by fatigue where the primary loading mode in both directions is tensile, and the peak stress values along the principal directions are similar, leading to stress softening in both directions.

The distinguishing characteristic of our approach with respect to that of others (Simo 1987; Rodríguez et al. 2006; Alastrué et al. 2007; Calvo et al. 2007; Li and Robertson 2009) is that our focus is on long-term fatigue effects. Unlike previous damage models for fiber-reinforced composites (Simo 1987; Rodríguez et al. 2006; Alastrué et al. 2007; Calvo et al. 2007), we considered an incremental accumulation of damage at a set equivalent strain, whereas other models considered an accumulation of damage only when the previous maximum equivalent strain had been exceeded. Our approach was also unique to other models that consider fatigue-induced permanent set (Dorfmann and Ogden 2004; Pena 2011; Zhang et al. 2011), because our focus was not to model the hysteresis effect of each unloading cycle, rather the progressive permanent change in specimen geometry due to long-term cyclic loading, and thus, our D_s and D_{ps} functions are active during both loading and unloading cycles at the onset of damage. Therefore, our framework is not intended for the accurate fitting of each loading and unloading curve, rather we assume uniform damage accumulation to model the transition from an unfatigued state to a fatigued state with long-term (100+ million) loading cycles. The inclusion of permanent set allows for investigation of changes to the degree of leaflet coaptation in the fatigued BHV. This is of importance because as the leaflets become stretched out, there may be wrinkling of the leaflets during leaflet coaptation. This leaflet wrinkling and “pinwheeling” may increase the stresses in the leaflets and accelerate the rate of damage (Sun et al. 2010).

4.1 Limitations of this study

In this study, we assume a linear progression of the stress softening and permanent set parameters at a given equivalent strain as a function of the number of loading cycles, whereas both values may evolve faster during the initial cycles. Furthermore, to give the model more flexibility, the functional form of the permanent set should be independent of the loading condition. As presented, the permanent sets are functions of the maximum permanent sets along the principal axes, where the maximum permanent sets can be experimentally determined for a specific loading condition. Also, the dependence of the peak equivalent strain on the fatigue-induced parameters, damage and permanent set, is unknown. The fatigue damage model parameters were fit to experimental data at one set peak equivalent strain. The experiment in Sun et al. (2004) would have to be repeated for different values of uniaxial strain for a more comprehensive data set. Therefore, the model

parameters used in this simulation may not be representative of the true fatigued response of GLBP. However, this fatigue model may serve as a guideline to direct future experimental tissue fatigue studies. Future work includes incorporation of the fatigue damage model presented here into a structurally based strain energy function to describe the distinct damages of the fiber and matrix components. Inherent numerical instabilities due to the inclusion of damage effects in finite element analysis should also be addressed in the future.

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Fig. 1.

Illustration of the effects of α on the (a) number of cycles to failure, and the (b) degree of stress softening accrued during one loading cycle. The effects of β on the (c) number of cycles to failure, (d) and the amount of stress softening during one loading cycle

Fig. 2. Illustration of the effects of (a and c) alpha and (b and d) beta on the permanent set accrued in the principal directions during one loading cycle

Fig. 3.

Illustration of the effects of β on the stress-strain response (only the 11 direction is shown for clarity) at different cycle levels up to $n = 50 \times 10^6$

Fig. 4. Uniaxial response of GLBP in the LD at different fatigue states with (a) no permanent set included and with (b) permanent set included

Fig. 5.

(a) Equi-biaxial response of GLBP specimen at the unfatigued state (Sun et al. 2004). (b)

Contour plot of equivalent strain with $\psi_{\min} = 4.67 \frac{\sqrt{\text{kN}}}{\text{m}}$ and $\psi_{\max} = 4.32 \times 10^5 \frac{\sqrt{\text{kN}}}{\text{m}}$ marking the damage evolution region

Fig. 6. Uniaxial failure test data for 5 GLBP specimens with a mean failure strain of approximately 0.45 corresponding to $\psi_{\max} = 4.32 \times 10^5 \frac{\sqrt{\text{kN}}}{\text{m}}$

Fig. 7.

The simulated uniaxial fatigue specimen with a contour plot of the stress softening factor, D_s , after (a) 0 cycles (unfatigued state), (b) 20×10^6 cycles, (c) 30×10^6 cycles at zero LD displacement, and (d) 30×10^6 cycles at the stress-free state

Fig. 8.

(a) The simulated stress–strain response during the cyclic uniaxial displacement control loading (only cycles 1×10^6 , 5×10^6 , 10×10^6 , 15×10^6 , 20×10^6 , 25×10^6 and 30×10^6 are shown for clarity). (b) The 1-0.1 protocol biaxial stress–strain response of the simulated specimen compared to the actual specimen at the 0 state and the 30×10^6 cycle state

Table 1

Model parameters at the unfatigued and fatigued state

<i>0-State Fung parameters</i>						
C (kPa)	A ₁	A ₂	A ₃	A ₄	A ₅	A ₆
1.00	56.19	175.00	-18.02	50.90	-9.67	0.17
<i>Fatigue damage parameters</i>						
$\psi_{\min}(\sqrt{\text{kN}} / \text{m})$	$\psi_{\max}(\sqrt{\text{kN}} / \text{m})$	$n_{\max}$	D_{psmax11}	D_{psmax12}	D_{psmax22}	α
4.67	431,840.00	368.00	-0.05	0.02	0.11	1.00
						0.58