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Use of a Poroelastic Model to Predict Intramuscular Pressure

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Abstract

Measurement of individual muscle tension in a clinical setting has yet to be achieved. Previous investigators have suggested that the tension in skeletal muscle, comprised of approximately 70% fluid, could be determined using interstitial muscle fluid pressure (IMP). A computational model is needed to aid in understanding IMP distribution in muscles of varying geometry and contractile states without exhaustive testing. The first aim of this study was to determine a set of transversely isotropic material properties (i.e., permeability, relaxed modulus, and drained Poisson's ratio) for excised skeletal muscle using inverse finite element analysis with a poroelastic constitutive formulation on tension data from either longitudinal or transverse uniaxial load-relaxation tests of skeletal muscle tissue. The second aim was to compare pore pressure estimated from a model to experimental pressure measurements to assess its ability to accurately predict IMP. Results of this study indicated that skeletal muscle was transversely isotropic under load-relaxation as demonstrated by significant differences in the drained Poisson's ratio. It was also noted that the drained Poisson's ratios under both longitudinal and transverse loading were negative in these tests of excised muscle tissue. Pore pressure calculated with this model provided a good prediction of the development of IMP. These results point to the benefit of using a poroelastic model of skeletal muscle to predict IMP.

INTRODUCTION

Evaluation of the force of a single *in situ* muscle is difficult to implement in a clinical setting. Intramuscular pressure (IMP), the pressure applied by muscle fibers on interstitial fluid, has been considered as a correlate for muscle force (Hill 1948). Numerous studies in animals (Hill 1948; Kirkebo and Wisnes 1982; Mazella 1954; Sutherland et al. 1977) and humans (Aratow et al. 1993; Hargens et al. 1982; Hussain and Magder 1991; Järvholm et al. 1989; Körner et al. 1984; Mubarak et al. 1976; Owen et al. 1977; Parker et al. 1984; Petrofsky and Hendershot 1984; Sejersted et al. 1984; Sylvest and Hvid 1959) have shown that an approximately linear relationship exists between IMP and muscle force. A microsensor has recently been developed that is accurate (Cottler et al. 2009; Kaufman et al. 2003), biocompatible (Yang et al. 2003), and, at <300 μm , appropriately sized for clinical

use. While muscle force and pressure have been shown to be correlates, challenges exist in the clinical application of this measure. IMP has been shown to be non-uniform within the muscle (Ameredes and Provenzano 1997; Crenshaw et al. 2000), varying with the depth of the recording catheter within the muscle, the shape of the muscle (Jarvholm et al. 1991; Sejersted et al. 1984), and the compliance of the surrounding tissue (Garfin et al. 1981). It would not be practicable to evaluate IMP distribution in muscle through empirical methods. Rather, computational modeling may provide the means to fully evaluate IMP generation in muscles of various shapes and operating conditions.

Computational models of skeletal muscle have been developed previously for use in applications ranging from tension prediction to calculation of strain distribution (Mazella 1954). Many of these models have been created based on the assumptions that skeletal muscle is hyperelastic, transversely isotropic (Blemker and Delp 2005; Morrow et al. 2010; Morrow et al. 2010), and isovolumetric (Elliott et al. 1963; Huxley 1969). These assumptions can all be incorporated into a single-phase solid mechanics model. However, no 3D model of skeletal muscle has been developed that predicts IMP. The goal of this study was to determine if a poroelastic description of muscle could be used to achieve IMP prediction.

Inverse finite element analysis can be used to determine material parameters for a given constitutive model of biological tissues that might be otherwise difficult to obtain directly. This type of analysis has been established for use in biological materials in previous studies on cartilage (Lei and Szeri 2007; Seifzadeh et al. 2012) and meniscus (LeRoux and Setton 2002), but not skeletal muscle. The first aim of this study was to determine poroelastic material properties of skeletal muscle from longitudinal and transverse load-relaxation tests. It was anticipated that the transverse isotropy previously observed in skeletal muscle would still be apparent in a poroelastic analysis. The second aim of this study was to use these poroelastic material properties in a computational model to assess the suitability of such a model to predict IMP.

MATERIALS AND METHODS

Load-Relaxation Tests

All animal experimentation was performed under institutional approval (IACUC A17308). Twenty tibialis anterior (TA) muscles from New Zealand White rabbits were obtained. Hind limbs were amputated mid-femur and TAs were dissected free of surrounding tissue, including all fascia. Testing was completed within two hours of sacrifice to prevent confounding effects of rigor mortis (Van Ee et al. 2000). Ten muscles each were used for load-relaxation tests in either longitudinal or transverse loading. The TA muscle was chosen for its low pennation angle (Lieber and Blevins 1989). Specimen samples were cut from the muscle midbelly using a razor tissue-punch. As the relaxed stress in muscles under load-relaxation has been shown to be strain-rate insensitive (Rehorn and Blemker 2010), all material tests were performed at a uniform rate of displacement. Tissues were elongated at a rate of 3.8 mm/sec, corresponding to 0.1 fiber-lengths/sec (Lieber and Blevins 1989).

Load-relaxation tests were performed on an MTS 858 material test device (MTS, Eden Prairie, MN). Specimens were mounted using thin film clamps (Imada, Northbrook, IL). Longitudinal specimens were gripped and mounted to provide deformation along muscle fiber direction; transverse specimens were gripped in the clamp jaws such that applied extension occurred perpendicular to the fiber direction. Gage dimensions were taken under a pre-stress corresponding to 1% of the ultimate stress of the muscle by direction (Morrow et al. 2010). Material elongation was determined using crosshead displacement. Strain was reported using Green strain, the mechanical correlate to second Piola-Kirchoff stress, and calculated as:

$$e = \frac{1}{2} (\lambda^2 - 1) \quad (1)$$

where λ is the stretch ratio,

$$\lambda = \frac{l_i}{l_o} \quad (2)$$

where l_o is the original crosshead displacement and l_i is the current crosshead displacement. Samples underwent five cycles of load-relaxation in increments of approximately 3% strain and 300-second relaxation periods. Operating in this range ensured that tissue would not be strained to the point of creating damage or plastic deformation (Meyer et al. 2011). Force measurements were sampled at 20 Hz using a 1000-gf load cell (Transducer Techniques, Temecula, CA), and the second Piola-Kirchoff stress was calculated as the force divided by the initial cross-sectional area.

Finite element model

A finite element (FE) model was created in ABAQUS (Simulia Corp., Providence, RI) for each experimental muscle specimen using the gage measurements obtained during material testing. A rectangular mesh with 1350 nodes was populated by 8-noded elements with linear displacements and pore pressure degrees of freedom (C3D8P). Pressure was assumed to be zero at the nodes on the unclamped surfaces. Likewise, there were no flow restrictions placed on these nodes. Clamped surface nodes were restricted to have zero fluid flow. Displacement boundary conditions were defined as encastre at the stationary crosshead and $u_x = u_y = 0$, $u_z = d$ at the moving crosshead, where u_x , u_y , u_z represent displacement in the x, y, and z directions, respectively, and d represents the imposed displacement.

Material Parameter Optimization

Material parameters were found using a previously validated (Lei and Szeri 2007), non-linear least-squares optimization approach using the *lsqnonlin* routine in MATLAB (The Mathworks, Inc., Natick, MA). Parameters were estimated from the response of the first load-relaxation step response. Optimization was achieved through comparison of the experimental reaction force with the sum of the reaction forces from the corresponding nodes in the modeled specimen. Arbitrary initial parameter values were written to an ABAQUS input file that was run iteratively until the model converged to a minimal error value. Two-tailed t-tests were performed to test if the longitudinal permeability, drained

Poisson's ratio, and drained modulus determined by optimization were different from the corresponding transverse values. Significance for all tests was set at $p = 0.05$.

Intramuscular pressure load-relaxation tests

Four additional New Zealand White rabbit (TA) muscles were also tested to collect IMP data under longitudinal load-relaxation. Specimen preparation was similar to the procedure described above for material parameter testing. Specimens were subjected to a single load-relaxation test to avoid issues with allowing proper relaxation between trials. Specimens were strained to 20%, safely within the range where the material would be free from plastic deformation (Meyer et al. 2011). IMP measurements were obtained using a 250- μ m-diameter fiber-optic pressure sensor (Luna Innovations, Blacksburg, VA). The pressure microsensor was inserted into the central portion of the specimen using a 20-gauge hypodermic needle, which was withdrawn after sensor placement. IMP and displacement data were collected at 20 Hz through the MTS controller.

Intramuscular pressure finite element model

Finite element models of IMP trials were created in ABAQUS for each experimental muscle specimen using the procedure and boundary conditions described above. Model predicted pressure was reported as the pore pressure from a node located in the center of the model, representative of the IMP sensor head location during experiments. Model predicted pressures were graphically compared to experimental pressure values.

RESULTS

Material parameters

Representative optimizations for both longitudinal and transverse loading trials are shown in Figure 1. There was good agreement between experimental data and the poroelastic model for these uniaxial tests. Neither the permeability ($p=0.43$) nor the relaxed modulus ($p=0.45$) showed significant difference between longitudinal and transverse loading (see Table 1). Poisson's ratio did vary significantly between directions ($p=0.006$). While the Poisson's ratios were different, the common factor was that both values were negative (longitudinal: -0.56 ; transverse: -0.35).

Intramuscular pressure

IMP levels dropped significantly at the onset of relaxation, falling to -14 mmHg in under 1.8 seconds (Figure 2A). With continuing relaxation, IMP was observed to rise and reach an equilibrium value of approximately -8 mmHg. Results of the model simulations showed a similar overall trend (Figure 2B). The initial response in the simulation was slower, with minimum pressures reached in over 2.5 seconds, and stabilization occurring later as well. The most significant difference between the experimental results and model was that the poroelastic model relaxed completely, without the residual pressure observed experimentally.

Incorporation of a non-zero residual pressure in the model resulted in pressure predictions more in line with experimental results. A simulation was run with a residual pressure of -9

mmHg at the geometry surface nodes. The resulting pore pressure was plotted along with the corresponding experimental data in Figure 3. The poroelastic model incorporating this residual pressure more closely represents the trend of the IMP observed during load relaxation in skeletal muscle.

DISCUSSION

The relaxed moduli did not differ significantly by loading direction. This may have contrasted with previous reports indicating that skeletal muscle had higher instantaneous modulus under longitudinal extension than under transverse extension (Morrow et al. 2010). Since the permeability did not differ by direction either, one may infer that the statistically significant differences in the drained Poisson's ratio values must contribute to the anisotropy of skeletal muscle.

Drained Poisson's ratios were found to be negative for both directions of loading. The converged values for Poisson's ratio were reached regardless of the initial values used in the optimization indicating the robustness of the solution. The validity of the finding of negative drained Poisson's ratios was supported by findings from other tests by Abraham, et al. (Abraham et al. 2012) which likewise found similar values using optical measurement methods with sectioned muscle under longitudinal load-relaxation.

The largest discrepancy between the poroelastic model pressure response and the experimental data was the level of the stabilized pressure response. Regardless of the level of the instantaneous pressure, the model pressure stabilized to 0 mmHg (Figure 2B). This should be expected, as there were no constraining residual pressures imposed on the model. In the absence of a check to the flow, a poroelastic model will inevitably stabilize to a zero-pressure level. Zero-pressure stabilization was not witnessed empirically. A non-zero pressure was consistently observed in all experiments (Figure 2A). A limitation of the current study was the absence of a rationale for this residual pressure. Additional studies to define the nature of the movement of interstitial fluid are needed to precisely understand this phenomenon and create physiological relevant boundary conditions.

CONCLUSION

An inverse finite element method coupled with optimization has been used to determine poroelastic material properties of skeletal muscle under uniaxial tension for longitudinal and transverse loading.

Even with a simple elastic model as a base material, the poroelastic model was able to fit reaction forces from load-relaxation experiments. This model provided a good estimation of the initial pressure generated in the muscle. However, there is a residual muscle pressure during relaxation not represented by the model. The transverse isotropy of skeletal muscle was reflected significant differences in the drained Poisson's ratio, which varied by test direction and was observed to be negative for these cut specimens. Future work will focus on modelling the residual pressure.

A poroelastic representation of skeletal muscle, characterized from reaction forces developed during load-relaxation testing, is capable of predicting the instantaneous intramuscular pressure response of skeletal muscle. A mechanism for implementing a residual pressure in the model exists, which would allow for complete prediction of the relaxation of pressure. Additional studies of interstitial fluid flow may provide a biological rationale to incorporate this observed phenomenon.

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Figure 1. Representative constitutive model curve-fits (blue) and experimental data (red) for the relaxation phase of load-relaxation under longitudinal (A) and transverse (B) strains.

Figure 2.

Mean (dark line) $\pm$ one standard deviation (light lines) of relaxation phase of experimental IMP (A) and model predicted pressure (B). Both plots show immediate decrease in pressure immediately after the onset of relaxation followed by sudden reversal with pressure relaxing to stabilization.

Figure 3. Pressure prediction vs experimental measurement for relaxation of muscle strained to 20%. The incorporation of residual pressure in the simulation creates better agreement between the model and experimental data.

Table 1

Optimized parameters for permeability, modulus, and drained Poisson's ratio for longitudinal and transverse loading (SE). Only Poisson's ratio demonstrated significant differences ($p=0.0006$).

	Permeability (mm/sec)	Drained Modulus (kPa)	Drained Poisson's Ratio
Longitudinal	9.84E-5 (5.95E-6)	8.00 (0.41)	* -0.56 (0.01)
Transverse	1.38E-4 (1.57E-5)	6.62 (0.42)	* -0.35 (0.02)

* Indicates significant difference between directions.