IDENTIFICATION OF NONLINEAR CONSTITUTIVE LAW PARAMETERS OF BREAST TISSUE

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INTRODUCTION

Breast pathology is manifested by changes in stiffness. A model capable of capturing large deformations characteristic of surgical and diagnostic procedures is needed for applications in elastography, tactile imaging, surgical simulation and planning. Several researchers have acquired *ex vivo* indentation data to 10% nominal strain on various pathologic breast tissue samples [1-3]. Although they all report a nonlinear force-displacement response, only Samoni et al [2] model the response using a nonlinear hyperelastic constitutive law in the form of a polynomial strain energy function. A more physically based model is needed to acquire the unique material parameters of breast tissue undergoing large strains (>30%) typical of medical manipulations [4]. Since the model reflects the tissue structure, we can identify how the specific contributions of the individual tissue constituents vary with mechanical response and pathologic state. In this abstract we present large strain indentation data from normal glandular and infiltrating ductal carcinoma breast tissue, and determine the parameters of a modified Arruda-Boyce hyperelastic model through an optimization technique.

METHODS

Test Apparatus and Experimental Procedure. A portable manually driven test instrument was used to acquire indentation force-displacement data in the operating room within 10 minutes after excision [3]. Data was collected from 4 mm and 6 mm diameter flat-ended cylindrical punches for one sample of normal glandular tissue (11x16x4.4 mm) and for three samples of infiltrating ductal carcinoma (10-19 mm diameter, 3.8-4.6 mm thick). The force and displacement data were filtered using a 30 Hz second-order low-pass butterworth filter. Maximum forces were used to determine the end of the loading period and the derivative of force with respect to displacement was plotted against force to determine the initial contact with the tissue for the first indentation. The data was divided into bins of quarter-percentile nominal strains to determine the mean loading curve from multiple loadings.

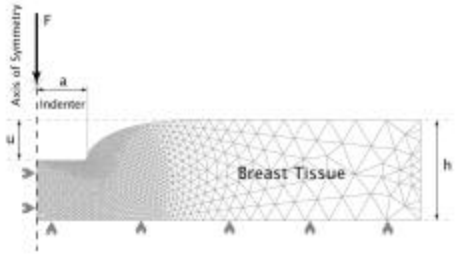

Figure 1: Mesh of axisymmetric indentation model, depicting tissue height *h*, indenter radius *a*, depth of indentation *u*, and applied force *F*.

Finite-element Modeling. Our indentation experiment is modeled as a two-dimensional, finite-deformation, axisymmetric problem, using commercial finite-element software (ABAQUS 6.4-1, HKS, Providence, RI). The mesh of the model consists of quadratic triangular elements (CAX6H), which were chosen over quadrilateral elements in order to improve the model's ability to deform to high nominal strains (Figure 1). The indenter, modeled as a rigid body with a flat-ended cylindrical shape and a 0.2 mm fillet radius with a frictionless contact, has a prescribed vertical displacement, and the corresponding reaction force is calculated. The bottom surface of the tissue is constrained in the vertical direction to account for testing on a hard substrate and has a frictionless boundary condition.

To model the large deformation behavior of breast tissue, a hyperelastic nonlinear constitutive model was chosen that accounts for the interactions among the various tissue constituent networks: collagen and elastin in parallel with a hydrated ground substance [5, 6]. In this study we focused on modeling the loading behavior of the material and neglected the dissipative component of the response. Thus, the nonlinear hyperelastic component of the model was used to capture the quasi-static loading response (50%/sec). Studies using the Arruda-Boyce hyperelastic model [1, 3], suggest that additional parameters are required to transform the 8-chain network model designed for polymers into one that can be used for biological tissues.

An initial state of zero stress in the fibrous network cannot be assumed due to tissue hydration. Similarly, the resistance to hydrostatic deformations needs to be accounted for. Thus in addition to the initial shear modulus (m) and the locking stretch (l_L), we have added an initial network stretch (l_0) to account for the pre-tensioned state of the fibrous network, and a bulk modulus (k) to account for three different mechanisms that contribute to changes in volume: resistance to flow from the interstitial fluid, resistance to osmotic pressure from the ECM network, and the inherent compressibility of the collagen network.

Parameter Identification. An iterative FEM technique is used to solve the inverse problem of identifying the parameters of the constitutive law, such that a satisfactory correspondence between model and experiment is obtained. Identification of the parameters is an optimization problem in four-dimensional parameter space [l_0, l_L, m, K] where the objective function minimized is the mean squared error (MSE) between the modeled and experimental force vs. nominal strain curves. Since all of the parameters are directly related to physical constituents in the tissue, their upper and lower limits are well understood and a plausible parameter space can be defined [$1.0<l_0<1.5$, $1.0<l_L<2.0$, $10\ \text{Pa}<m<20\ \text{kPa}$, $100\ \text{kPa}<K<10\ \text{MPa}$]. Initially, this space is explored manually to estimate the sensitivity to each parameter and to obtain a physically feasible initial estimate for a given tissue type. A link between Matlab and ABAQUS environments carries out an iterative adjustment of material parameters, according to the Nelder-Mead simplex method. An iterative solution consisting of approximately 200 steps requires approximately 10 hours of computational time on a 3.0 GHz Pentium 4 machine with 2GB of RAM. The simplex method is seeded from three starting points to increase the likelihood of finding the global solution, rather than a local minimum. The optimization is carried out for both tissue types, with the termination conditions set to either a maximum of 1,000 iterations or the normalized simplex diameter smaller than $1\text{x}10^{-4}$.

RESULTS

The means and standard deviations of six indentations for the normal glandular tissue sample and 39 indentations for the IDC samples are shown in Figure 2. Also shown are the model responses reflecting the parameters obtained from the optimization using the initial set that produced the best fits (Table 1). The 5.5 and 4.5 fold increases in both initial shear and bulk moduli respectively and the decrease in the locking stretch, indicate that IDC is stiffer than normal glandular tissue. The small difference in the initial stretch suggests that this parameter is nearly independent of pathology.

DISCUSSION

This work is part of an ongoing effort in characterizing the nonlinear mechanical behavior of soft tissues. Here we show that a nonlinear hyperelastic constitutive model captures the effects of large strain (>30%) indentation on *ex vivo* breast tissues, and provides insight into the changes in tissue structure between pathologic states. We observed that large strains are needed not only to provide more realistic data for modeling medical manipulations but also to distinguish the differences in pathologic state.

The selected model serves to balance the swelling tendency of the hydrated ground substance with the tensile forces from the collagen network. Our exploration of the solution space demonstrated that the model's response was sensitive to changes in both the initial stretch and the locking stretch, and less sensitive to changes in the initial and bulk moduli. Since initial shear modulus is proportionally related to the bulk modulus and the stretches are inversely related, an increase in osmotic pressure should result in an increase in initial shear modulus

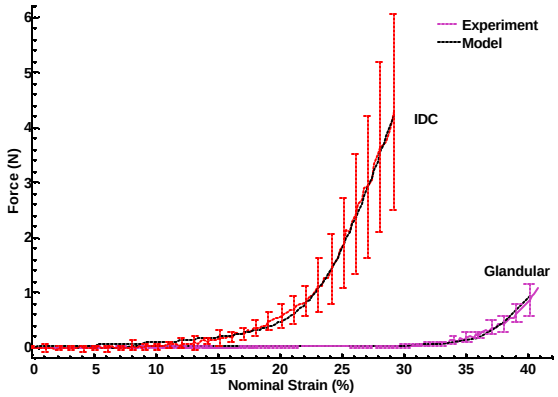

Figure 2: Loading curves (mean ± SD) and model fits for normal glandular and infiltrating ductal carcinoma tissue.

	l_0	l_L	m [Pa]	k [MPa]	MSE
Normal (n = 6, a/h = 0.5)	1.017	1.114	49.62	1.488	0.0013
IDC (n = 39, a/h = 0.6)	1.014	1.036	274.6	6.680	0.0073

Table 1: Material parameters for constitutive model.

as well as a decrease in both stretches. Our results show that the restructuring of breast tissue from the normal to pathologic state involves a decrease in tissue compressibility (increase in bulk modulus related to water content, pH, and ion concentration) balanced by an increase in initial shear modulus and a decrease in the maximum extensibility (increase in number of cross-links) of the collagen fibrils. The initial stretch appeared to be unaffected by pathology.

While our optimization results produced excellent fits between model and experimental data, the issues of global convergence and uniqueness of solution need to be addressed in future work. Our initial optimization trials suggest that convergence to a global minimum is strongly dependent on a good initial estimate, motivating the need for a dense sampling of the parameter space, which could be interpolated to determine the initial estimate for the simplex method. Additionally, dense sampling would provide an overall understanding of the parameter space and help address the issue of uniqueness of the parameters found.

Future work will incorporate these new optimization techniques on additional data from Wellman [3] to the current model. The data includes both loading and unloading responses of breast tissue in five pathologic states. Thus the viscous term of the model will be reintroduced as in [5] to capture the observed hysteresis.

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