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A continuous fiber distribution material model for human cervical tissue

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A B S T R A C T

The uterine cervix during pregnancy is the vital mechanical barrier which resists compressive and tensile loads generated from a growing fetus. Premature cervical remodeling and softening is hypothesized to result in the shortening of the cervix, which is known to increase a woman's risk of preterm birth. To understand the role of cervical material properties in preventing preterm birth, we derive a cervical material model based on previous mechanical, biochemical and histological experiments conducted on nonpregnant and pregnant human hysterectomy cervical tissue samples. In this study we present a three-dimensional fiber composite model that captures the equilibrium material behavior of the tissue in tension and compression. Cervical tissue is modeled as a fibrous composite material, where a single family of preferentially aligned and continuously distributed collagen fibers are embedded in a compressible neo-Hookean ground substance. The total stress in the collagen solid network is calculated by integrating the fiber stresses. The shape of the fiber distribution is described by an ellipsoid where semi-principal axis lengths are fit to optical coherence tomography measurements. The composite material model is fit to averaged mechanical testing data from uni-axial compression and tension experiments, and averaged material parameters are reported for nonpregnant and term pregnant human cervical tissue. The model is then evaluated by investigating the stress and strain state of a uniform thick-walled cylinder under a compressive stress with collagen fibers preferentially aligned in the circumferential direction. This material modeling framework for the equilibrium behavior of human cervical tissue serves as a basis to determine the role of preferentially-aligned cervical collagen fibers in preventing cervical deformation during pregnancy.

1. Introduction

During pregnancy, a closed firm cervix is required to maintain the developing fetus *in utero*. Towards the end of gestation, a normal cervix significantly deforms, dilates and shortens in preparation for delivery. An early onset of cervical shortening, hypothesized to be caused by premature cervical remodeling, is known to put pregnant patients at risk for preterm birth (PTB) (Iams et al., 2011). The true causes of preterm birth remain to be determined, but the mechanical failure of the cervix is a final common pathway for multiple etiologies (Gravett et al., 2010; Solomon and Iams, 2014). The overall research goal of our work is to quantify the mechanical environment of pregnancy and to determine how the cervix functions as a resistive barrier to prevent PTB. The objectives of this study are to present an equilibrium constitutive material model that captures the tension/compression nonlinearity of previously published uni-axial data of human cervical tissue samples (Myers et al., 2008, 2010) and to describe how to incorporate directionality and dispersion parameters measured by optical coherence tomography (OCT) (Gan et al., 2014) into this material model. The purpose of this paper is to report fiber composite material properties for human cervical tissue and initiate a starting point for a 3-dimensional material model that can capture the salient nonlinear features of the cervical material behavior while accounting for its collagen fiber directionality.

The *in vivo* 3-dimensional (3D) deformation and stress state of the cervix during pregnancy is complex due to patient-specific pelvic geometry, pelvic tissue material properties, passive and active external loading, and the contact and boundary conditions between organs (House et al., 2009, 2012, 2013; Mahmoud et al., 2013; Fernandez et al., 2015). The stress state of the cervix has been

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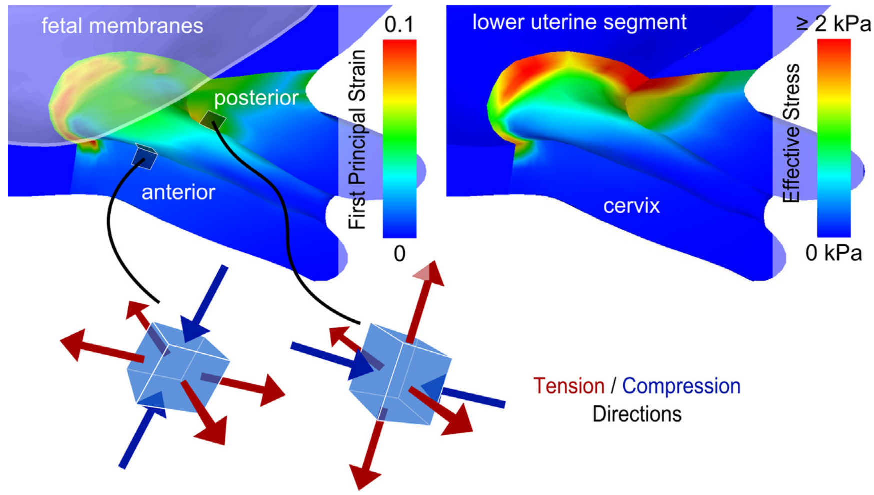

Fig. 1. Representative principal strain and stress directions depicted for a pregnant patient at 22 weeks of gestation. The intrauterine pressure of 8.6 kPa was applied to the inner surface of the fetal membranes, which are adhered to the lower uterine segment (Fernandez et al., 2015). The mechanical deformation state of the human cervix is a mix of tension and compression. Depending on the placement of the cervix within the pelvis, regions of the cervix experience a longitudinal compressive stress.

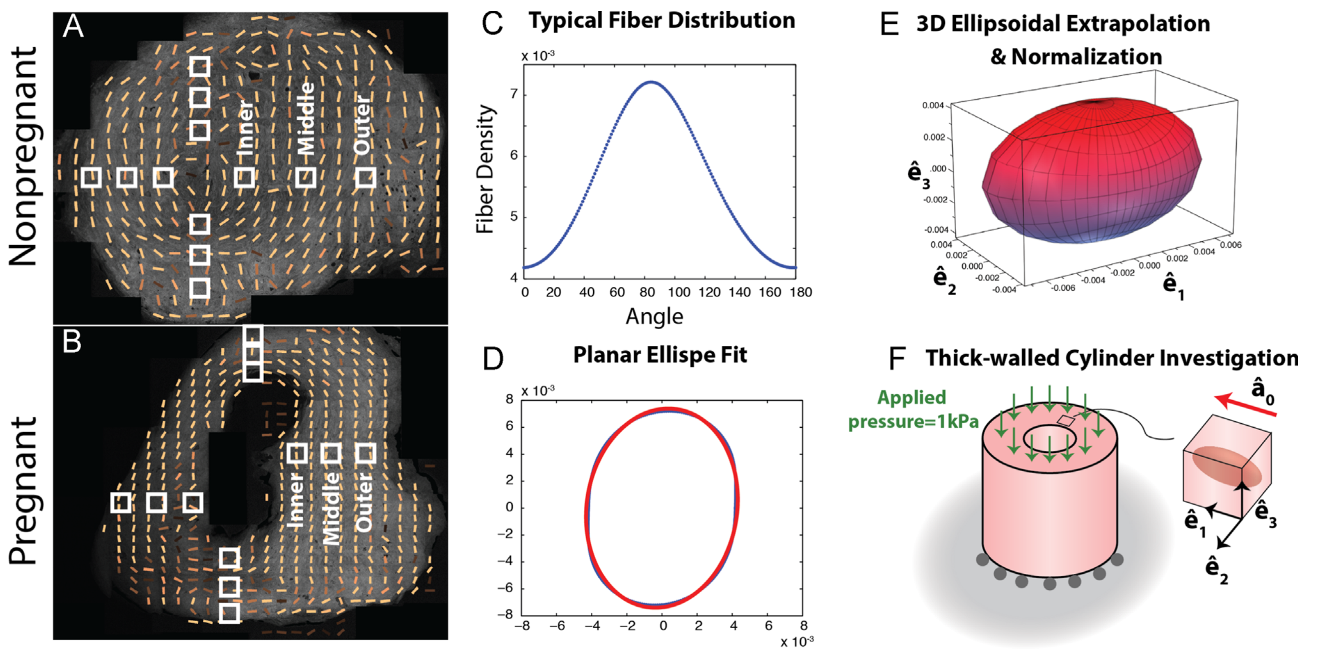

Fig. 2. Optical coherence tomography (OCT) fiber orientation maps and measurement locations for an axial slice of (A) a nonpregnant and (B) a pregnant human cervix (Gan et al., 2014). (C) A typical shape of the fiber distribution for a 1 mm × 1 mm zone. (D) A planar ellipse fit to the fiber distribution shown in C. (E) An extrapolation and normalization (Eq. (7)) of the planar ellipse into a 3D ellipsoid where it is assumed that the minor radii are equal. (F) Thick-walled cylinder loading condition, with sliding boundary conditions on the bottom and stress-free conditions on the outer walls and inner canal.

studied using CAD-based (House et al., 2012; Mahmoud et al., 2013) and patient-specific MRI-based (Fernandez et al., 2015) finite element models of the pregnant pelvis. Simulation results reveal that under a constant intrauterine pressure the stress state of the cervix is a combination of tension and compression (Fig. 1), where the magnitude and directionality of the principal stress and strain highly depend on the placement of the cervix within the pelvis, material characteristics of the cervix, and the interactions between the amniotic sac, the lower uterine segment, and the internal os (e.g. the opening of the cervix into the uterus) (House et al., 2012; Fernandez et al., 2015). Generally, there is a principal compressive stress in the longitudinal axis of the cervix, parallel to the inner canal, caused by the amniotic sac pushing on the internal os. This compressive stress translates into prominent tensile principal strains in the circumferential and radial directions. Taken together these forces cause the cervix to expand radially and shorten, similar to a thick-walled cylinder resisting a compressive axial stress.

The collagen ultrastructure of the cervix plays a crucial role to withstand the circumferential, radial, and longitudinal stresses throughout the tissue. A traditional view of the preferred directionality of the collagen was elucidated by X-ray diffraction techniques by Aspden from an average of eight nonpregnant human cervices (Aspden, 1988). This view details three seamless zones of aligned collagen with an inner and outer zone of longitudinal fibers and a middle zone of circumferential fibers. Additionally, this study reports a level of dispersion around the main fiber direction. More recently, second harmonic generation (SHG) (Feltovich et al., 2012) and OCT data (Gan et al., 2014, 2015) of human cervical tissue specimens reveal a large band of circumferential fibers that extend to the outer radial edges of the cervix (Fig. 2A). From these ultrastructure studies,