A Parameterized Ultrasound-Based Finite Element Analysis of the Mechanical Environment of Pregnancy

Preterm birth is the leading cause of childhood mortality and can lead to health risks in survivors. The mechanical functions of the uterus, fetal membranes, and cervix have dynamic roles to protect the fetus during gestation. To understand their mechanical function and relation to preterm birth, we built a three-dimensional parameterized finite element model of pregnancy. This model is generated by an automated procedure that is informed by maternal ultrasound measurements. A baseline model at 25 weeks of gestation was characterized, and to visualize the impact of cervical structural parameters on tissue stretch, we evaluated the model sensitivity to (1) anterior uterocervical angle, (2) cervical length, (3) posterior cervical offset, and (4) cervical stiffness. We found that cervical tissue stretching is minimal when the cervical canal is aligned with the longitudinal uterine axis, and a softer cervix is more sensitive to changes in the geometric variables tested. [DOI: 10.1115/1.4036259]

1 Introduction

During pregnancy, the soft tissues surrounding the fetus must withstand mechanical forces to protect, support, and maintain the fetus in utero until term. As pregnancy progresses, the uterus and fetal membranes stretch to accommodate the growing fetus, placenta, and amniotic fluid. The cervix remains closed, acting as a mechanical barrier to the external environment. Then at term, in a reversal of roles, the uterus contracts and the cervix drastically deforms to allow for delivery of the fetus. The magnitudes of stress and stretch of these soft tissues are thought to control physiologic processes that regulate tissue growth, remodeling, contractility, and rupture, and it is generally hypothesized that these mechanical signals are clinical cues for normal labor, and when these signals occur prematurely, the result is often preterm birth [1,2]. Yet, the mechanical performance of these tissues during pregnancy remains poorly understood, preventing an understanding of the mechanisms that lead to normal term and preterm labor. In this study, we develop a finite element modeling platform to calculate and visualize the tissue stress and stretch of the pregnant uterus and cervix. We base this platform on parametric ultrasound measurements of maternal abdominal anatomy to create a fast and flexible analytical tool that has the potential to simulate how a pregnant uterus and cervix will function or dysfunction in pregnancy, and to identify those pregnancies that are at risk of spontaneous preterm birth (sPTB).

Preterm birth is defined as delivery between 20 and 37 weeks of gestation. It is a major public health problem with heavy emotional and financial consequences [3]. Preterm birth is the leading cause of childhood death [4], and for surviving infants, preterm birth is a leading cause of long-term disabilities [5,6]. Spontaneous preterm birth represents 70% of all preterm births and typically cannot be predicted, although the history of a prior sPTB is a major factor [7]. A current understanding is that sPTB is a premature activation of the common pathway of parturition, which is a complex continuum involving multiple and overlapping phenotypes [7–9]. Three of the major clinical phenotypes of sPTB include (1) premature cervical remodeling (i.e., cervical...
insufficiency), (2) premature preterm rupture of membranes, and (3) preterm labor (i.e., preterm onset of coordinated uterine contractions).

The mechanical function of the cervix, uterus, and fetal membranes and its relationship to these clinical phenotypes of sPTB are recognized clinically. The risk assessment and management of sPTB rely heavily on the serial ultrasound assessment of cervical length [10], where a sonographic short cervix is a risk factor for sPTB [11]. Studies on uterine smooth muscle cells have established a well-known electromechanical coupling [1], where stretch-activated calcium channels have been linked to the molecular pathways that promote contractility and labor. A recent study on monkeys found that uterine overdistention is associated with inflammatory pathways that lead to preterm contractions [2]. Clinically, uterine overdistention has been associated with sPTB. Multiple gestations [2,12,13] and patients with excessive amniotic fluid tend to delivery early [14]. Lastly, the integrity of the fetal membranes is essential for the maintenance of pregnancy, where its compliance is necessary to accommodate fetal growth. Yet, its rupture and fracture properties are required for normal term delivery [15].

Characterizing reproductive tissues in real time to understand these mechanical functions throughout gestation is challenging. Pregnancy is a protected environment and accessing organs to measure anatomical and tissue properties during this time is difficult. Hence, our driving engineering motivation is to create a finite element model of the mechanical environment of pregnancy based on the fewest and most minimally invasive clinical measurements possible. In a preliminary finite element study using maternal anatomy segmented from magnetic resonance imaging (MRI), we underscore the importance of capturing the interaction of the fetal membranes, uterus, and cervix and modeling the collagen architecture of these tissues [16]. Such a fully segmented computational model requires expert knowledge in anatomy and computer-aided design (CAD), which is not practical in a clinical setting, and the resulting finite element analysis is computationally expensive.

To address the need for a fast, flexible, and affordable computational assessment of the soft tissue mechanics in pregnancy, we built a parametric finite element model that utilized ultrasound images of a pregnant abdomen at 25 weeks gestation. We scripted a user-friendly routine to convert these ultrasound parameters into a CAD model of the pregnant anatomy. This CAD model was used in finite element simulations to calculate the distribution of tissue stress and stretch at 25 weeks of gestation, where material parameters and loading and boundary conditions were informed or inferred by previously reported studies. Motivated by the clinical significance of cervical length and recent clinical trials of a biomedical device that angles the cervix away from a mechanical load in patients at high risk for sPTB [17–21], we investigate the effect of cervical structural parameters on the magnitude of tissue stretch at the cervical opening to the uterus (i.e., cervical internal os), which is the anatomical site of clinically observed cervical failure.

2 Methods

2.1 Ultrasound Measurements of Maternal Anatomy. Geometric dimensions of the uterus, cervix, and their position in reference to the symphysis pubis as a bony reference landmark were taken via ultrasound (GE Voluson E8, GE Healthcare, Port Washington, NY) (Fig. 1). All measurements were taken transabdominally or transperineally using the transabdominal probe (GE RAB4-8D, GE Healthcare, Port Washington, NY, real-time 4D volume, curved array transducer, 4–8.5 MHz). For the baseline
model, dimensions were measured from a 35-year-old patient with no prior pregnancies at 25 weeks gestation with an empty bladder. The patient subsequently delivered the neonate at 40 weeks.

Uterine diameters (UDs) were measured with the extended view imaging feature of the Voluson E8, which automatically registered adjacent ultrasound images as the probe was swept across the abdomen from the fundus to the pubic bone at a steady rate of 2 cm/s. With this sagittal view, we obtained measurements of uterine longitudinal diameter (UD1), anterior–posterior diameter (UD2 + UD3), and the offset of the cervical internal os from the uterine longitudinal diameter (posterior cervical offset (PCO)) (Fig. 1(a)). To measure the transverse uterine diameter (UD4) in an extended axial view, the transabdominal probe was swept from left to right across the midabdomen and the uterus measured at its widest point (Fig. 1(b)). Uterine wall thicknesses (UT1-5) were measured at multiple locations from the fundus to the lower uterine segment (LUS) with the transabdominal probe in a standard clinical resolution (Figs. 1(c) and 1(d)), and were considered the echogenic signal from the serosa to the decidua. Cervical length (CL), diameter (CD1), canal width (CD2), anterior uterocervical angle (AUCA), and angle with periosteum of the symphysis pubis (CA1) were assessed via transperineal scans (Figs. 1(e) and 1(f)).

### Table 1 Baseline ultrasound measurements. Note: UD—uterine diameter, PCO—posterior cervical offset, UT—uterine thickness, AUCA—anterior uterocervical angle, CA—cervical angle, CL—cervical length, and CD—cervical diameter.

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Measured value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UD1</td>
<td>192 mm</td>
</tr>
<tr>
<td>UD2</td>
<td>68 mm</td>
</tr>
<tr>
<td>UD3</td>
<td>55 mm</td>
</tr>
<tr>
<td>PCO</td>
<td>25 mm</td>
</tr>
<tr>
<td>UD4</td>
<td>215 mm</td>
</tr>
<tr>
<td>UT1</td>
<td>5 mm</td>
</tr>
<tr>
<td>UT2</td>
<td>6 mm</td>
</tr>
<tr>
<td>UT3</td>
<td>6 mm</td>
</tr>
<tr>
<td>UT4</td>
<td>6 mm</td>
</tr>
<tr>
<td>UT5</td>
<td>5 mm</td>
</tr>
<tr>
<td>AUCA</td>
<td>90 deg</td>
</tr>
<tr>
<td>CA1</td>
<td>15 deg</td>
</tr>
<tr>
<td>CL</td>
<td>30 mm</td>
</tr>
<tr>
<td>CD1</td>
<td>30 mm</td>
</tr>
<tr>
<td>CD2</td>
<td>4 mm</td>
</tr>
</tbody>
</table>

*Arbitrary value, not measured value.

### 2.2 Computer (CAD) Model of Pregnancy

The maternal ultrasonic parameters were converted into CAD geometries with a custom computer script (TRELIS PRO v15.1.3, csimsoft LLC, American Fork, UT). Geometries of the uterus, cervix, fetal membranes, vaginal canal, and abdomen were created with Boolean addition and subtraction of geometric primitives (Fig. 2). Dimensions for the baseline model are given in Table 1. For this initial model, the uterus was built by transforming two spherical shells into ellipsoids. The interior uterus was scaled to the diameters obtained during ultrasound (UD1-4) and rotated in relation to the reference angle of the symphysis pubis (CA1). The current iteration of this model does not have CA1 as a measured value from the patient. Instead, it uses an arbitrary value of 15 deg. The influence of CA1 will be the topic of a future study. The outer shell was then scaled, translated, and rotated to accommodate differences in uterine wall thickness (UT1-5) in the anterior–posterior, superior–inferior, and left–right directions.

The cervix was built by creating a cylinder representing the diameter of the inner canal (CD2) and subtracting that volume from a larger cylinder representing the outer cervical diameter (CD1) and cervical length (CL). The resultant hollow cylinder was then moved and rotated according to posterior cervical offset (PCO) and AUCA. The cylinder was rounded at its corners to match the anatomical rounding of the uterocervical junction and to replicate the roundness of the most exterior end of the cervix (i.e., external os).

For purpose of tissue loading analysis, the cervix was then separated into three different regions: an upper portion, a lower portion, and the internal os region (Fig. 2). First, the cylindrical representation of the cervix was cut by a plane normal to the external os at a fixed distance of 15 mm from the internal os. Second, the top portion of the cervix was then separated by a surface extended from a smaller cylinder with a diameter that was twice of the cervical inner canal. Lastly, the vaginal canal was built by fitting a spline to three vertices located at the outside edges of the external os and one vertex at the approximate location of the vaginal introitus, and the fetal membrane was generated with uniform thickness based on the contours of the inner uterine wall.

### Table 2 Mesh properties for baseline model

<table>
<thead>
<tr>
<th>Element type</th>
<th>Total</th>
<th>Uterus</th>
<th>Membrane</th>
<th>Abdomen</th>
<th>Upper cervix</th>
<th>Lower cervix</th>
<th>Internal os region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Element count</td>
<td>180,735</td>
<td>35,246</td>
<td>9600</td>
<td>39,933</td>
<td>51,239</td>
<td>27,422</td>
<td>17,295</td>
</tr>
<tr>
<td>Average element volume (mm³)</td>
<td>—</td>
<td>16.3</td>
<td>0.994</td>
<td>0.236</td>
<td>0.344</td>
<td>0.131</td>
<td></td>
</tr>
</tbody>
</table>
uterus and cervix shared a boundary with the abdomen volume, those boundaries were also node-tied. The lower cervix was not tied to the interior vaginal canal, but floated freely inside the vaginal fornix.

The mesh density of the cervix was set to the finest setting by the inherent TRELIS element density function, in order to yield the most accurate deformation results for our analysis.

2.4 Material Properties. The cervix and uterus materials were treated as continuously distributed fiber composites with a compressible neo-Hookean ground substance. This hyperelastic solid model was developed to describe the tension-compression nonlinearity in human [22] and mouse [23] cervical tissue. Considering not much is known about the multiaxial material behavior of these tissues during pregnancy, we investigated the full range of possible properties, where term pregnant (PG) tissue was considered the remodeled tissue and nonpregnant (NP) tissue represented the not remodeled tissue.

The total Helmholtz free energy density $\Psi^{\TOT}$ for the uterine and cervical materials was given by

$$\Psi^{\TOT}(\mathbf{F}) = \Psi^{\GS}(\mathbf{F}) + \Psi^{\COL}(\mathbf{F})$$

where $\mathbf{F}$ is the deformation gradient. The free energy density of the ground substance $\Psi^{\GS}$ is given by a standard isotropic, compressible neo-Hookean relation

$$\Psi^{\GS} = \frac{1}{2} \mu(\mathbf{I} - 3) - \mu \ln J + \frac{\lambda}{2} (\ln J)^2$$

where $\mathbf{I}$ is the first invariant of the right Cauchy–Green tensor $\mathbf{C} = (\mathbf{F})^T \mathbf{F}$, and $J = \det \mathbf{F}$ is the Jacobian. $\mu$ and $\lambda$ are the standard Lamé constants. These Lamé constants combine to form the Young’s modulus $E^{\GS} = \mu(3 + (2\mu/\lambda))/(1 + (\mu/\lambda))$ and Poisson’s ratio $\nu^{\GS} = 1/(2(1 + (\mu/\lambda)))$, respectively. The strain energy density for the continuously distributed collagen fiber network is given by

$$\Psi^{\COL} = \frac{1}{4\pi} \int_0^{2\pi} \int_0^z H(I_3 - 1) \Psi^{\fiber}(I_3) \sin \phi d\phi d\theta$$

where the Heaviside step function $H$ ensures fibers hold only tension, and $[\theta, \phi]$ are the polar and azimuthal angles in a spherical coordinate system. $I_3 = n_0 \cdot C \cdot n_0$ is the square of the fiber stretch, where $n_0 = \cos \theta \sin \phi e_1 + \sin \theta \sin \phi e_2 + \cos \phi e_3$ in a local Cartesian basis $\{e_1, e_2, e_3\}$. $\Psi^{\fiber}$ is the strain energy density of a collagen fiber bundle given by

$$\Psi^{\fiber} = \frac{\varepsilon}{\beta} (I_3 - 1)^\beta$$

where $\varepsilon$ represents the collagen fiber stiffness with units of stress, and $\beta > 2$ is the dimensionless parameter that controls the shape of the fiber bundle stiffness curve. (Here, the fiber strain energy density is cast in a different form than the model presented for the human cervical tissue [22]; hence, direct comparison can be made by considering the $1/\beta$ prefactor here.)

To focus this study on the model sensitivity to maternal anatomy and collagen fiber stiffness parameters and not on the collagen ultrastructure, ground substance, or time-dependent properties, we made simplifying adjustments. Both material model fits were conducted on the material behavior after the transient force relaxation response died away. In this present study, we used a randomly distributed collagen fiber network as opposed to a preferentially aligned collagen fiber network as presented in [22]. Cervical material properties used in this study (Table 3) represent collagen fiber parameters fit to the nonpregnant and term pregnant human uniaxial tension-compression data reported in Refs. [24,25], and [22], with the ground substance material properties kept constant. Considering we do not know material properties for the cervix at 25 weeks, we chose to approximate interim cervical fiber stiffness at constant increments between the known values. Uterine material properties represent a material model fit to passive, nonpregnant, and term pregnant human uniaxial tension data reported in Ref. [26]. Fibers in both the uterus and cervix are randomly distributed. They rotate and stretch in the direction of principle stress. Previous work compared the difference between preferential and randomly distributed fiber directionality in an initial finite element model of pregnancy and found a negligible difference between the two scenarios [16]. As we continue to characterize the directionality and dispersion of the collagen fiber architecture for both the uterus and the cervix [27,28], we will examine the effects of tissue architecture on tissue loading.

The outer abdomen was treated as a soft nearly incompressible neo-Hookean material with a modulus of 5 kPa. An incompressible Ogden material model based on equibaxial tensile loading of human amnion [29] was employed for the fetal membrane layer material properties (Table 4), where the particular form of the Ogden strain energy density, as defined in Ref. [30], was given by

$$\Psi^{\FM} = \sum_{i=1}^3 \frac{1}{m_i} \left( \lambda_i^{m_i} + \lambda_2^{m_i} + \lambda_3^{m_i} - 3 \right)$$

Table 3 Uterine and cervical tissue variables taken from material fits to experimental data. These values are implemented in a continuous fiber distribution material model used in TRELIS 2.4.1.

<table>
<thead>
<tr>
<th>Tissue description</th>
<th>$E^{\GS}$ (kPa)</th>
<th>$\nu^{\GS}$</th>
<th>$\beta$</th>
<th>$\xi$ (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterus—remodeled</td>
<td>2</td>
<td>0.3</td>
<td>2.71</td>
<td>190</td>
</tr>
<tr>
<td>Uterus—not remodeled</td>
<td>2</td>
<td>0.3</td>
<td>3</td>
<td>199</td>
</tr>
<tr>
<td>Cervix—remodeled</td>
<td>2</td>
<td>0.3</td>
<td>3.12</td>
<td>1.71</td>
</tr>
<tr>
<td>Cervix—interim 1</td>
<td>2</td>
<td>0.3</td>
<td>3.12</td>
<td>7.89</td>
</tr>
<tr>
<td>Cervix—interim 2</td>
<td>2</td>
<td>0.3</td>
<td>3.12</td>
<td>36.3</td>
</tr>
<tr>
<td>Cervix—interim 3</td>
<td>2</td>
<td>0.3</td>
<td>3.12</td>
<td>167</td>
</tr>
<tr>
<td>Cervix—not remodeled</td>
<td>2</td>
<td>0.3</td>
<td>3.12</td>
<td>769</td>
</tr>
</tbody>
</table>

Table 4 Fetal membrane (FM) material properties described by an Ogden material model in Eq. (5).

<table>
<thead>
<tr>
<th>Tissue description</th>
<th>$c_1$ (MPa)</th>
<th>$c_2$ (MPa)</th>
<th>$c_3$ (MPa)</th>
<th>$m_1$</th>
<th>$m_2$</th>
<th>$m_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM</td>
<td>0.859</td>
<td>0.004</td>
<td>0.756</td>
<td>27.21</td>
<td>27.21</td>
<td>-16.64</td>
</tr>
</tbody>
</table>
2.5 Boundary Conditions and Loading. Boundary conditions were applied as described in Fig. 4. The abdomen was fixed in the x, y, and z directions on its outside surface. The fetal membranes were prescribed a no-slip, tied contact along its outer surface (cyan in Fig. 4) to the inner surface of the uterus (purple) and to the inner surface of the upper cervix region (green). A frictionless sliding contact condition was assigned between the outer surface of the fetal membranes (cyan) and the internal os region (yellow). Anatomically, in normal pregnancy, the outer layer of the fetal membranes is adhered fully to the uterine wall and the upper cervix throughout gestation, and detaches at the onset of labor.

A pressure was applied to the internal surface of the fetal membranes to represent the intrauterine pressure (IUP). IUP magnitude was informed by previous studies that measured the amniotic sac pressure via catheter puncture of the fetal membranes, was reported after subtracting the gravitational pressure head from the reading [30]. IUP at 25 weeks (0.817 kPa) was calculated with the following equation from the Fisk et al. study:

\[
\ln(y + 1) = 0.12 + 0.23x - 0.010x^2 + 0.00015x^3
\]

where \(y\) is the amniotic pressure in millimeter of mercury and \(x\) is the gestation in weeks [30]. To compare stretch patterns between models, we ramped the pressure to the value of 40 weeks (2.33 kPa) and to the value of a labor contraction (8.67 kPa) [31].

2.6 Finite Element Analysis and Evaluation. Finite element (FE) analyses were performed in FEBIO 2.4.2. Stress and stretch data were plotted as a function of IUP in POSTVIEW (POSTVIEW 1.19.1), FEBIO’s postprocessor for visualization and analysis. These data were then imported into MATLAB (MATLAB R2014A) for further postanalysis. To describe the deformation of the cervix, the extent of cervical first principal stretch was evaluated as a percentage of the cervical internal os volume (Fig. 2) above a 1.05 stretch threshold. The right stretch in this context is the symmetric tensor \(U\) in the polar decomposition of the deformation gradient \(F = RU\).

2.7 Sensitivity to Cervical Structural Parameters. After the evaluation of the baseline model, cervical structural parameters were scaled individually in order to assess each variable’s impact on cervical internal os stretch. The range of values were based on literature values and represented clinical significance [32,33]. These parameters were as follows: anterior uterocervical angle (AUCA), cervical length (CL), posterior cervical offset (PCO), and cervical stiffness (Table 5). Stretch magnitude and distribution were compared at a contraction-level IUP of 8.67 kPa to illuminate patterns.

AUCA in this analysis was defined as the angle between the cervical inner canal and the anterior LUS (Fig. 1(e)). AUCA was varied in 10 deg increments from 90 deg in the baseline model to the most extreme value of 110 deg with respect to the anterior LUS. CL was varied in 5 mm increments from 25 mm (a clinical short cervix) to 40 mm. CL in this analysis was defined as the distance from the longest uterine diameter to the cervical internal os (Fig. 1(e)). PCO was varied in 5 mm increments from 0 mm to the baseline value of 25 mm. PCO in this analysis was defined as the distance from the longest uterine diameter to the cervical internal os (Fig. 1(a)). Cervical stiffness was varied by decreasing fiber stiffness \(\xi\) from the NP value of \(\xi = 769\) kPa in even increments to reach the PG value of \(\xi = 1.71\) kPa. All other parameters in the material model were kept constant.

3 Results

3.1 Baseline Model. The baseline pregnancy model at 25 weeks of gestation shows minimal deformation under amniotic sac cavity pressure estimated for that week (Eq. (6), IUP = 0.817 kPa). At this level of pressure, the maximum level of tensile stretch for the cervix, uterus, and fetal membranes reached 1.04, 1.05, and 1.06, respectively, and the maximum level of compressive stretch for the cervix is 0.86. Minimal tissue stretch at this stage of pregnancy is supported by previous X-ray and histologic studies, where evidence shows that the uterus undergoes dramatic growth with limited stretching in the first half of pregnancy to accommodate the fetus and amniotic fluid [34]. Analysis was done for both remodeled (PG) and not remodeled (NP) uterine and cervical tissue properties for baseline IUP at 25 weeks (Figs. 5(a) and 5(d)), baseline IUP at 40 weeks (Figs. 5(b) and 5(e)), and contraction-magnitude IUP (Figs. 5(c) and 5(f)).

To illuminate the pattern of tissue stretch, the model is investigated under a contraction-level intrauterine pressure of 8.67 kPa. There is a jump in tissue stretch distribution at the boundary of the uterus and cervix because of material property definition. Overall, the highest amounts of stretch are located near this uterocervical boundary for the uterus and at the internal os of the cervix. Because of the ellipsoidal shape of the uterus and the placement of the cervix in relation to the uterine axis, tissue stretch patterns follow anatomic quadrants. Zones of high stretch are apparent in the anterior–posterior sections of the uterus and the left–right sections of the cervix (Fig. 5(f)). For the uterus, the maximum stretch is directed along the meridian in the anterior and posterior quadrants and along the circumference in the left–right quadrants. Throughout the uterine thickness, the stretch is at a maximum on its outer surface and decreases toward the inner surface. These stretch concentration patterns may vary for differing uterine shapes and sizes.

For the upper part of the cervix, its outer edges are dictated by the direction of the uterine wall tension, where the anterior–posterior cervix is pulled in a radial direction, and the left–right quadrants are pulled in circumferential tension. The stretch pattern of the inner core of the cervix does not show quadrant patterns. Instead, the first principal stretch is directed circumferentially in all anatomic shapes and sizes.
quadrants (Fig. 6(a)). For compressive stretch, the distribution is off-centered and the maximum magnitude is located in the posterior section (Fig. 6(c)). Second principal stretch is largest in the left and right quadrants of the uterus (Fig. 6(b)), and maximum shear strain occurs at the posterior uterus and uterocervical interface (Fig. 6(d)). These stretch patterns are most likely dominated by the geometric features of the uterus and fetal membranes adhesion at both the inner uterine surface and the inner surface of the upper cervix region. The stretch plotted here is for a uniform intrauterine pressure and does not include the fluid pressure head due to gravity. Gravitational forces will most likely shift this distribution toward the anterior direction.

3.2 Cervical Structural Parameters. Both the geometric and material properties of the cervix influence the distribution and magnitude of tissue stretch. Results indicate that geometric variations in anterior uterocervical angle (AUCA), cervical length (CL), and posterior cervical offset (PCO) are all more influential in a softer cervix (Table 6). The geometric parameter PCO has the largest effect on the loading at the internal os for both the soft pregnant (PG) cervix and the stiff nonpregnant (NP) cervix. Aligning the cervical canal with the uterine longitudinal axis reduces the amount of tissue stretch at the internal os. For the PG cervix, when PCO = 0 mm, the volume fraction of cervical tissue above the 1.05 stretch threshold reduces by 50% compared to the most extreme case investigated, which is the baseline value of PCO = 25 mm. Even for the NP cervix, aligning the cervical canal with the uterine axis reduces the tissue stretch volume fraction by 16%. For the NP cervix, CL and AUCA have a negligible influence on the outcome tissue stretch measurement. For the PG cervix, lengthening the cervix from 25 mm to 40 mm results in a 22% reduction in the volume fraction of the cervical internal os above the 1.05 stretch threshold, while varying cervical angle still has

Table 5  Model geometries, with ranges for each varied parameter. Note: AUCA—anterior uterocervical angle, CL—cervical length, and PCO—posterior cervical offset.

<table>
<thead>
<tr>
<th>Model</th>
<th>Cervical angle (deg)</th>
<th>Cervical length (mm)</th>
<th>Cervical offset (mm)</th>
<th>Cervical fiber stiffness $\xi$ (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>90</td>
<td>30</td>
<td>25</td>
<td>1.71 and 867</td>
</tr>
<tr>
<td>AUCA</td>
<td>90 → 110</td>
<td>30</td>
<td>25</td>
<td>1.71 and 867</td>
</tr>
<tr>
<td>CL</td>
<td>90</td>
<td>25 → 40</td>
<td>25</td>
<td>1.71 and 867</td>
</tr>
<tr>
<td>PCO</td>
<td>90</td>
<td>30</td>
<td>0 → 25</td>
<td>1.71 and 867</td>
</tr>
<tr>
<td>Cervical stiffness</td>
<td>90</td>
<td>30</td>
<td>25</td>
<td>1.71 → 867</td>
</tr>
</tbody>
</table>

Table 6  Summary of results for volume fraction of cervical internal os above a 1.05 stretch threshold. Note: AUCA—anterior uterocervical angle, CL—cervical length, and PCO—posterior cervical offset. The geometric parameter PCO had the largest influence on the amount of tissue stretch at the cervical internal os, for both a soft PG cervix and a stiffer NP cervix. The most drastic reduction in cervical tissue stretch, identified in boldface, occurs for a soft cervix that is aligned with the uterine longitudinal axis compared to a 25 mm PCO.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>AUCA (deg)</th>
<th>CL (mm)</th>
<th>PCO (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NP cervix (stiff) volume fraction above 1.05 stretch</td>
<td>25.3</td>
<td>25.3</td>
<td>26.1</td>
<td>26.2</td>
</tr>
<tr>
<td>PG cervix (soft) volume fraction above 1.05 stretch</td>
<td>92.6</td>
<td>92.6</td>
<td>94.2</td>
<td>94.8</td>
</tr>
</tbody>
</table>
little effect on the volume fraction. There are no scenarios in which an NP cervix had the same amount of loading as the PG cervix.

3.2.1 Sensitivity to Anterior Uterocervical Angle. As anterior uterocervical angle (AUCA) increases and the external os of the cervix is tilted toward the posterior, cervical stretch of the internal os region increases and the distribution of stretch moves posteriorly (Fig. 7). In the not remodeled cervix material model, the 110 deg AUCA experiences a 3.2% increase in the volume fraction of cervical tissue above the 1.05 stretch threshold from the 90 deg AUCA. In the remodeled cervix material model, the 110 deg AUCA experiences a 2.4% increase in the volume fraction from the 90 deg AUCA. In both models, cervical tissue stretch is minimized when the cervix is aligned with the longitudinal uterine axis (AUCA = 90 deg).

3.2.2 Sensitivity to Cervical Length. Cervical length (CL) has an influence on cervical loading patterns only when the cervix has remodeled material properties (Fig. 8). When the cervix has not remodeled and is as stiff as the nonpregnant state, increasing the cervical length does not alter the loading pattern at the internal os. For a cervix that has remodeled and is as soft as the term tissue, as cervical length is decreased the stretch at the internal os increases. The 25 mm CL experiences a 28.6% increase in the volume fraction of tissue over 1.05 stretch from the 40 mm CL.

3.2.3 Sensitivity to Posterior Cervical Offset. As posterior cervical offset (PCO) increases, cervical stretch of the internal os region increases (Fig. 9). In the not remodeled cervix material model, the 25 mm PCO experiences a 19.3% increase in the volume fraction of tissue over 1.05 stretch from the 0 mm offset, with intermediary values corresponding to this increasing trend. As can be seen with the CL parameters, the softer cervix is more sensitive to changes in geometric variables.

3.2.4 Sensitivity to Cervical Stiffness. As the cervix is made softer by decreasing the value of the collagen fiber stiffness parameters $\xi$, cervical stretch of the internal os region increases (Fig. 10). Keeping all other material parameters the same, the collagen fiber stiffness associated with a remodeled cervix experiences a 266% increase in cervical stretch from collagen fiber stiffness value associated with the not remodeled cervix.

4 Discussion
This work develops a method to generate a patient-specific finite element model of the uterus, cervix, fetal membrane, and surrounding anatomy derived from maternal ultrasound scans. For a baseline investigation, we model a pregnant patient at 25 weeks of gestation and convert ultrasound measurements into a parametric computer model. With this computer model, and basing engineering assumptions on previously published data, we assess tissue stretch at various levels of intravaginal pressure (IUP). Results indicate that the distribution and magnitude of stretch of the cervix are affected by uterine wall mechanics, where direction and magnitude of cervical stretch are pulled toward uterine wall tension. Our results show a stretch concentration at internal os of the cervix, matching findings from previous finite element models [16,35,36].
mass grows from 70 g to 1100 g and its volume capacity goes stretches to accommodate the enlarging amniotic sac. Uterine 25 week gestation time-point considering the uterus grows and ment and upper cervix. Minimal tissue loading is expected at the whereas in this study, they are tied to both the lower uterine seg- different fetal membranes adhesion scenarios. In the previous study, the fetal membranes were only tied to the lower uterine segment, whereas in this study, they are tied to both the lower uterine segment and upper cervix. Minimal tissue loading is expected at the 25 week gestation time-point considering the uterus grows and stretches to accommodate the enlarging amniotic sac. Uterine mass grows from 70 g to 1100 g and its volume capacity goes from 10 mL to 5 L. Early histologic, X-ray, and amniotic cavity pressure catheter studies offer the most complete view of pregnant uterine anatomy. We learn from these data that in the first 12 weeks of pregnancy, hormonal signals initiate a considerable uterine growth process under negligible mechanical loading. From 12 to 16 weeks, the lower section of the uterine corpus unfolds into the lower uterine segment to allow for expansion of the amniotic sac without stretching the uterine wall. X-ray data of pregnant anatomy confirm that the uterine wall thickness stays constant until 16 weeks and then begins to thin and elongate along its diameters as the fetus begins its rapid growth between 16 and 24 weeks. During this time, the uterus both grows and stretches. After 24 weeks, X-ray and ultrasonic evidence supports that the uterus stops growing and continues to stretch and thin considerably until term.

We also demonstrate the flexibility of this model by investigating the effects of cervical angle, length, offset, and material properties on the stretch generated at the internal os due to contraction-magnitude IUP. The sensitivity study of cervical structural parameters indicates that the effect of geometric parameters is magnified for a soft cervix, and that cervical tissue stretching was most sensitive to posterior cervical offset (PCO) and is least sensitive to anterior uterocervical angle (AUCA). Cervical tissue stretch is most sensitive on cervical tissue stretch, we evaluated model outcome variables at a contraction-level IUP. Cervical tissue stretch is most sensitive to posterior cervical offset (PCO, Fig. 9) and is least sensitive to anterior uterocervical angle (AUCA, Fig. 7). Cervical tissue stretch is only sensitive to cervical length (CL, Fig. 8) if the cervix has already remodeled and is soft.

### 4.1 Clinical Considerations

These results of this initial sensitivity study help explain the conflicting results seen in the clinical literature. The mechanical role of the cervix is recognized clinically, where both risk assessment and management of spontaneous preterm birth (sPTB) rely heavily on the serial ultrasound assessment of cervical length. The positive predictive value of a sonographic short cervix is low as many women with a short cervix go on to deliver near term. Our results show that assessing cervical length alone will not indicate the likelihood of the cervix to continue to deform. Instead, both cervical length...
Cervical angle has recently been the topic of clinical studies focusing on diagnosis and prevention of preterm birth. Two retrospective cohort studies investigating cervical angle as an indicator of sPTB showed conflicting results. One study found that an extreme posterior angle is associated with preterm birth [32] and the other did not [59]. The efficacy of clinical interventions that are thought to restore the mechanical function of the cervix to prevent preterm birth also remains unclear. The cervical pessary, a silicone ring-shaped diaphragm meant to angle the cervix away from the mechanical load [17], is currently the subject of multiple large-scale randomized clinical trials in the U.S. and in Europe. Results have been conflicting. A Spanish clinical trial of pessary use showed a benefit to pessary use in singleton [18] and twin [19] pregnancies at risk for sPTB. However, this success has not been replicated in the largest clinical trials to date for twin [20] and singleton [21] pregnancies. It was concluded that the use of the pessary did not result in the reduction of sPTB nor adverse neonatal outcomes. Our simulation results suggest that cervical angle has a minimal effect on cervical tissue stretch.

In contrast, our results show the novel notion that posterior cervical offset (PCO) could be measured sonographically to contribute to risk assessment of preterm birth. Yet, this contradicts the Bishop score method used traditionally in clinic to predict readiness for birth. A posterior cervix results in a low Bishop score, which correlates to a low chance of labor induction. A midline cervix has a moderate Bishop score, and an anterior cervix has a high Bishop score. Most often in pregnancy, the cervix lies posterior throughout gestation and moves anteriorly nearing labor. Since our baseline model is symmetric, the increased stretch in a large posterior cervical offset may also be observed in the case of a large anterior cervical offset instead. Future iterations of this model will investigate an anterior cervical offset, in addition to each scenario for a retroverted uterus (uterus tilted posteriorly). We believe that the posterior and anterior cervical offset parameters will yield similar results, and having the cervical canal axis aligned with the longitudinal uterine axis is ideal to minimize cervical stretch at the internal os.

It should be noted that hydrostatic pressure on the internal os is neglected in this model. The only scenario in this sensitivity study that would be affected by including hydrostatic pressure would be the posterior cervical offset, since changing this parameter moves the internal os to a different height within the uterus. However, moving the cervix posteriorly by a maximum of 25 mm would change the hydrostatic pressure by no more than 0.2 kPa, which can be considered negligible in comparison to the 8.67 kPa intrauterine pressure applied in the analysis.

### 4.2 Comparison to MRI-Based Model

To facilitate the creation of a more clinically applicable simulation and to reduce computational needs, we pursued the analytical method as shown here to create a pregant anatomy. To understand how these simplifications affect cervical tissue stretch patterns, we compared a parameterized model with a model generated from our previously published MRI-segmentation methods [16]. Briefly, dimensions of the uterus and cervix were measured from MRI data of the normal subject presented in Ref. [16], and these measurements were implemented in our parameterized procedure detailed here. Since this modeling method includes simplifications, the parameterized model does not contain bumps, divots, and variations in thickness that the segmented geometry includes. In Fig. 11, we compare tissue stretch patterns between the MRI-segmented and analytical geometries. Here, we use the same material models, mesh density, membrane thickness, contact definitions, and boundary conditions between the two models.

Overall, after application of intrauterine pressure of 0.817 kPa, the parameterized model predicts similar locations for strain concentration patterns as the MRI-segmented model does. Figures 11(a1)–11(d2) demonstrate that the largest differences occur at the site of a geometric feature in the MRI-based model at the location of the posterior internal os. At this location, the top of the cervix protrudes slightly into the volume of the uterus. This geometric irregularity cannot be captured in the current set of geometric measurements we have defined. Clinically, any measurements need to be well defined, repeatable, and easily teachable to ensure correct procedures are followed. Characterization of these kinds of geometric features is doubly challenging as the internal pelvic anatomy is not static and can change substantially even during the same ultrasound session (for example, with contractions or from the bladder filling or being emptied).

Because both models use exactly the same material models and membrane contact definitions, this disagreement must arise from differences between the geometries. In particular, the MRI model geometry is inherently less geometrically stiff in the mode of internal pressurization because it has hills and valleys on the surface, making it equivalent to a rope with slack being pulled under tension. On the other hand, the geometric primitive-based ellipsoidal geometry in the parameterized model has less play under increasing internal pressurization, because its basic geometry is more stable.

These effects will be important to characterize in future iterations of the model, and a mechanism to capture this behavior will be developed. The mechanism may take the form of better replicating the in vivo geometry or of modifying the constitutive model to reflect these findings.
reduce the low-strain stiffness to an amount equivalent to the geometric slack we see in the MRI models. Despite the differences between the results of each method, the parameterized model is an important tool in bridging the gap between future numerical clinical tools and the current clinical state of the art due to its unlimited flexibility and much reduced patient measurement to simulation timeline.

4.3 Limitations. As we work toward a more accurate finite element model of pregnancy, we use simplified simulations to explore the effect of model parameters on outcome variables. Simplifying assumptions in this model include the difference between actual anatomic geometry and the simplified geometry, the assumption of material property homogeneity, the lack of dynamic analysis and tissue growth, and the fact that measurements were taken in vivo in a loaded configuration. Additionally, for a more accurate model, we would need to directly measure intraterine and abdominal cavity pressures and in vivo fetal membranes, uterus, and cervix material properties. We would also need to measure the properties of abdominal boundary condition, such as the placenta, to accurately represent the displacement of the top half of the uterus and fetal membrane. While we work toward obtaining these data from minimally invasive methods, we relied on literature values of the intraterine pressure (IUP) [30,31] and mechanical measurements of ex vivo tissue samples.

5 Conclusion

We present here a method for incorporating simplified anatomic geometries, fetal membrane contact conditions, IUP interaction, and cervical material properties into a mechanical simulation of pregnancy. In this study, we calculate the first principal right stretch under contraction-magnitude IUP levels in sonographically estimated FE models of pregnancy. Various cervical structural parameters are varied over a physiological range to analyze sensitivity of each dimension on cervical stretch. Our results show that AUCA, PCO, and cervical stiffness are the most significant factors affecting the mechanical stretch state within the cervix, particularly near the internal os. Our simulation result supports the need for additional maternal anatomy parameters and the evaluation of cervical material properties to better predict the occurrence of preterm birth. In future studies, we will conduct sensitivity studies on uterine, fetal membranes, and boundary condition geometries and material properties as well. Our goal is that our model will serve as a preliminary platform for development of sPTB diagnostic tools and procedures. In addition, it serves as a first step in modeling the uterine and cervical growth and remodeling in pregnancy.

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Nomenclature

AUCA = anterior uterocervical angle
CL = cervical length
IUP = intraterine pressure
PCO = posterior cervical offset

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