Tensile and Compressive Anisotropic and Time Dependent Material Properties of Human Cervical Tissue

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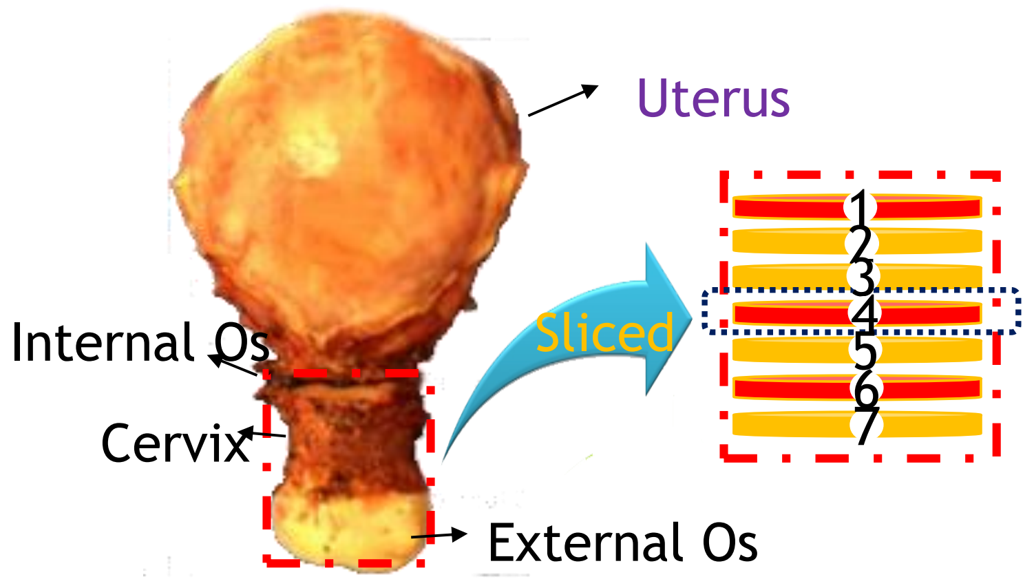
Introduction

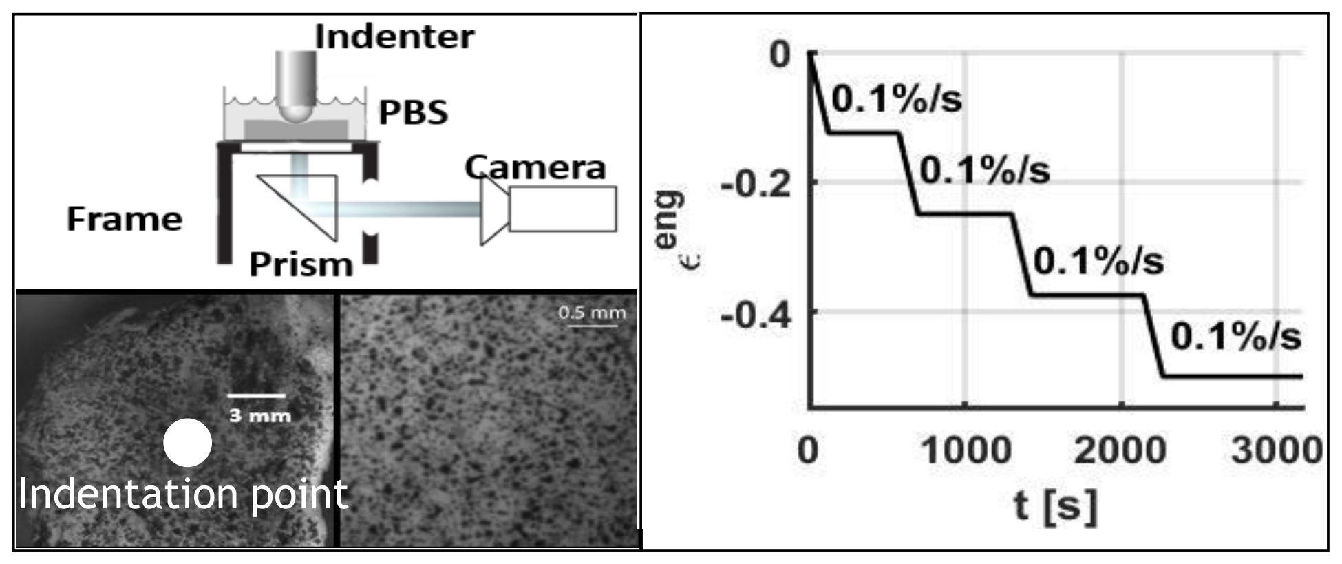
- The mechanical properties of the cervix are believed to be related to preterm birth.
- The cervix is a soft collagenous tissue exhibiting anisotropic, visco- and poro-elasticity, and tension-compression asymmetry.
- Human cervical tissue was tested using both indentation and uniaxial tensile tests to formulate a material constitutive model that can capture the nonlinear, time-dependent, anisotropic material response of the cervix.

Experiment

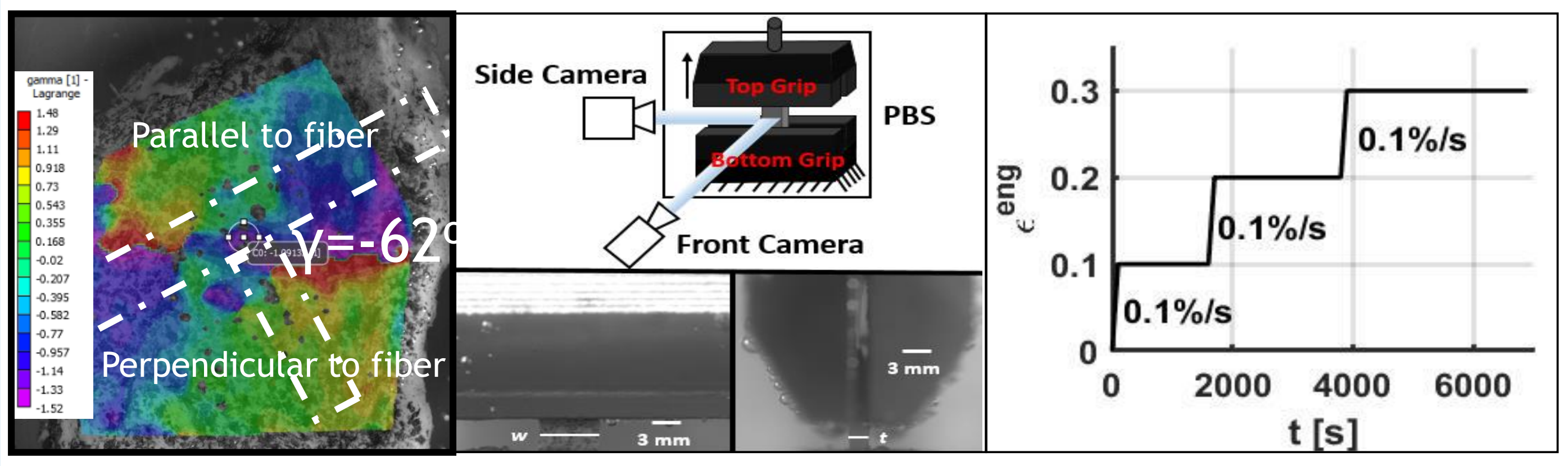
- 4 nonpregnant (NP) and 2 pregnant (PG) human cervices were collected with an IRB-approved protocol.



- Slices were cut from each cervix along the axial direction and stored in -80ºC until the time of mechanical testing.
- Each sample was microtomed, speckled using India ink, and equilibrated in phosphate-buffered saline (PBS) at 4ºC for 24 hours before indentation experiments.
- The cervical slice was immersed in PBS solution on glass.A displacement-controlled, 4-stage ramp-hold indentation test was conducted at each sample using a 2.5mm stainless steel sphere, with a slow rate.
- A camera was placed in front of the setup and captured the deformation of the bottom surface using a right-angle prism. The deformation was tracked and calculated using a digital correlation imaging (DIC) system.



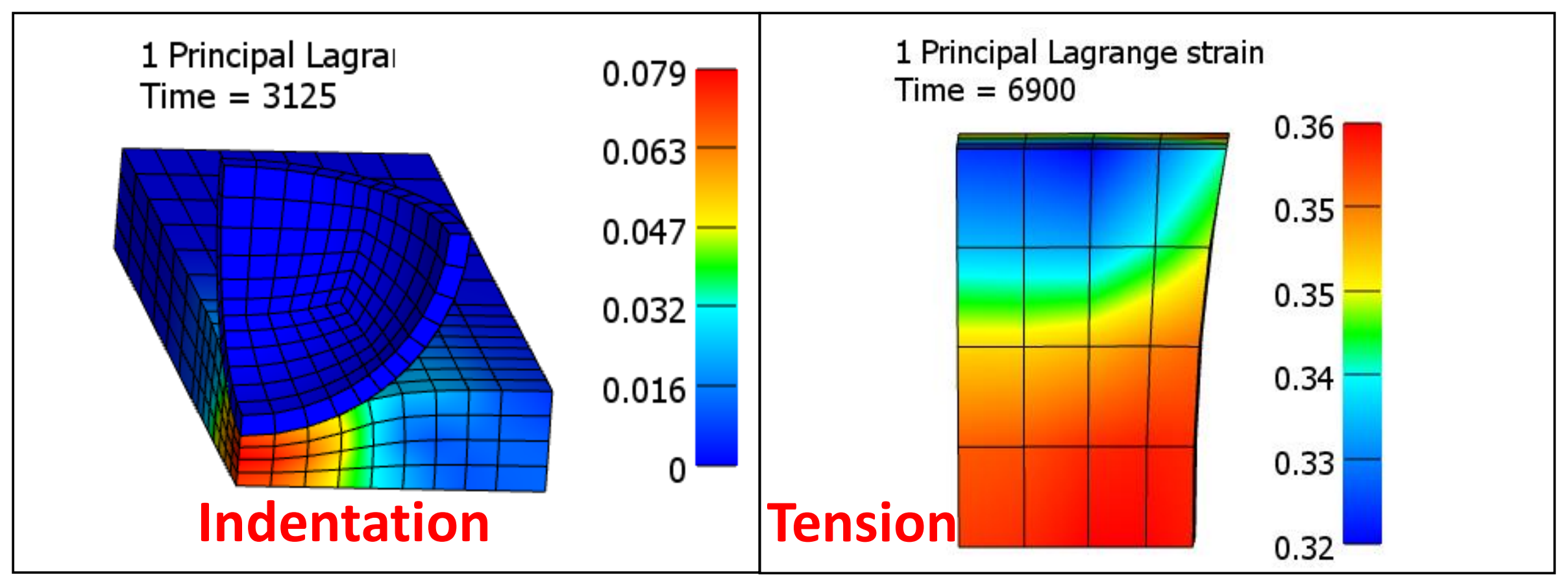
- After the indentation tests, two strips were cut from each slice along the directions perpendicular and parallel to the fiber principal direction. The fiber direction was found by the principal strain angle (γ), determined via digital image correlation (DIC, Vic-Snap v6, Correlated Solutions Inc., Irmo, SC)



- Each sample was gripped tightly on both ends and put in the PBS solution. Two cameras were placed perpendicular to each other to capture the front- and side-view deformation during the test.
- A displacement-controlled, 3-stage ramp-hold uniaxial tensile test was conducted with a ramp rate = 0.1thickness/s.
- After indentation, two tensile strips were cut from each slice perpendicular and parallel to the principal fiber direction. The change of width (w) and thickness (t) was discerned by a custom U-Net based deep learning code.

Modeling

- The FEA models were created in FEBio (V2.9.1, url: febio.org) to simulate the indentation and uniaxial tensile experiments. To save the computational resource, the model was simplified by applying the symmetric boundaries.
- The cervix was modeled as a reactive viscoelastic material (Eq. 1-3), where the elastic part (Eq. 4-6) of the material is a fiber composite with a von Mises fiber network (details in [1]). The material parameters of the elastic part were E, υ, ξ, b, and α, which were the Young's modulus, the Poisson's ratio, the fiber stiffness, the distribution coefficient, the fiber polynomial index, and the fiber exponential coefficient, respectively.



- The viscous part (Eq. 7-9) was modeled as the similar form of the elastic part to reflect the anisotropy, with 5 parameters E_v, υ_v, ξ_v, b_v, and α_v. The "power distortional" form of relaxation function (Eq. 3) was adopted in this model. In this study, only 4 parameters (E_v, υ_v, τ_0, τ_1) of the viscous and relaxation parts were used for IFEA.

$$\Psi_r(\mathbf{F}) = \Psi_r^e(\mathbf{F}) + \textstyle\sum_u w^u\, \Psi_0^b(\mathbf{F}^u) \tag{1}$$

$$w^u(X,t) = \begin{cases} 0 & t < u \\ 1 - g(t-u) & u \le t < v \\ g(t-v) - g(t-u) & v \le t \end{cases} \tag{2}$$

$$g(\mathbf{F}^u(v); t-v) = \left[1 + \left(\frac{t-v}{\tau_0 + \tau_1\left(K_2^u(v)\right)^2}\right)^2\right]^{-1} \tag{3}$$

$$\psi_r^e(\mathbf{F}^S, \boldsymbol{n}, b) = \psi_r^{eGS}(\mathbf{F}^S) + \psi_r^{eCOL}(\mathbf{F}^S, \boldsymbol{n}, b) \tag{4}$$

$$\psi_r^{eGS}(\mathbf{F}^S) = \frac{\mu}{2}\,(I_1 - 3) - \mu \ln J + \frac{\lambda}{2}(\ln J)^2 \tag{5}$$

$$\psi_r^{eCOL}(\mathbf{F}^S, \boldsymbol{n}, b) = \int_0^{2\pi}\int_0^{\pi} \frac{\xi}{2\alpha}\left[e^{\alpha(I_n-1)^2} - 1\right]\frac{e^{b(2\boldsymbol{n}^2-1)}}{2\pi I_0(b)} \sin\phi\, d\phi\, d\theta \tag{6}$$

$$\psi_r^v(\mathbf{F}^u, \boldsymbol{n}, b) = \psi_r^{vGS}(\mathbf{F}^u) + \psi_r^{vCOL}(\mathbf{F}^u, \boldsymbol{n}, b) \tag{7}$$

$$\psi_r^{vGS}(\mathbf{F}^u) = \frac{\mu^u}{2}\,(I_1^u - 3) - \mu^u \ln J + \frac{\lambda^u}{2}(\ln J)^2 \tag{8}$$

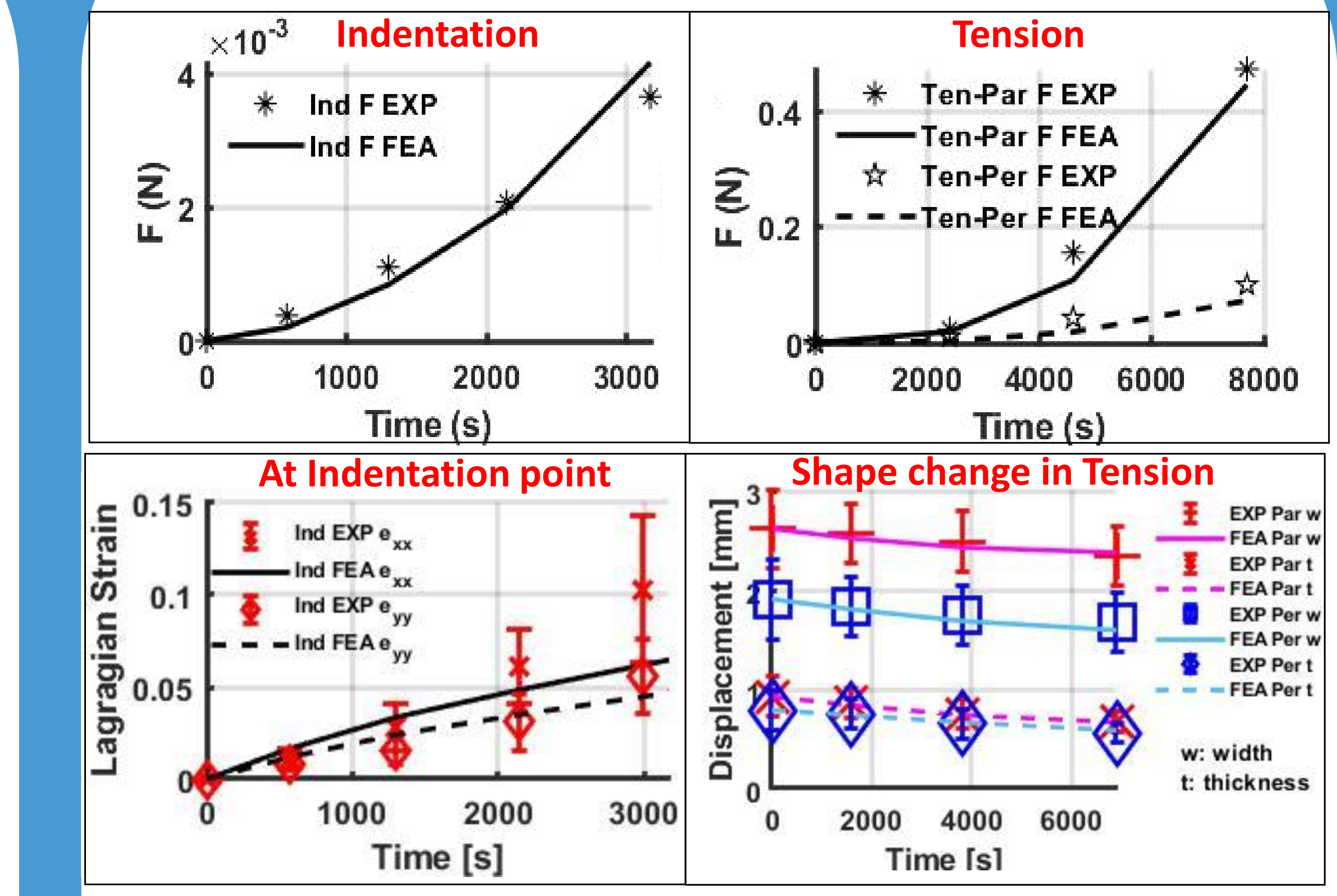
$$\psi_r^{vCOL}(\mathbf{F}^u, \boldsymbol{n}, b) = \int_0^{2\pi}\int_0^{\pi} \frac{\xi}{2\alpha}\left[e^{\alpha(I_n-1)^2} - 1\right]\frac{e^{b(2\boldsymbol{n}^2-1)}}{2\pi I_0(b)} \sin\phi\, d\phi\, d\theta \tag{9}$$

- A custom genetic algorithm based inverse finite element analysis routine was conducted to fit the experimental force responses by Eq. (10).

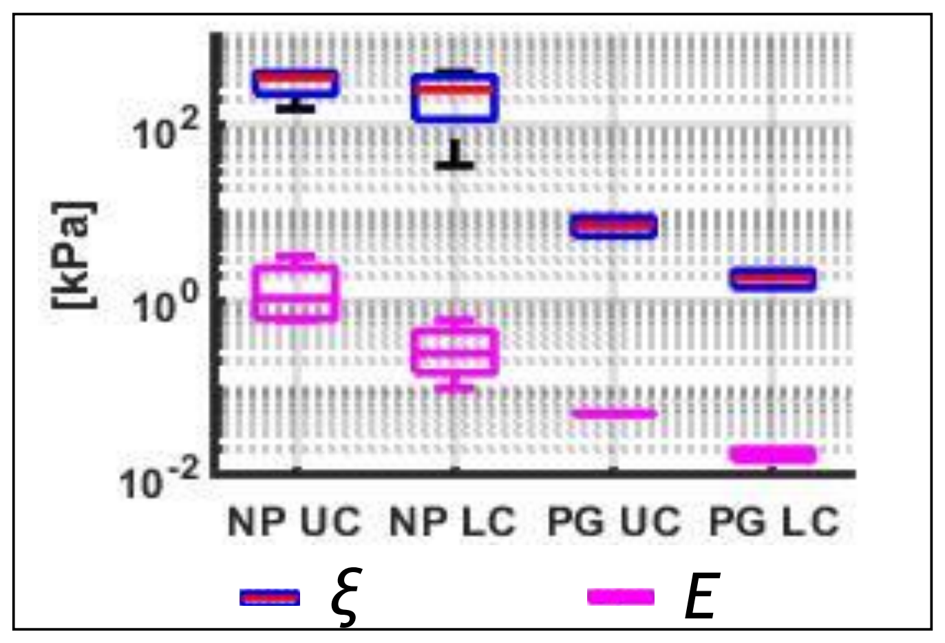
$$\chi = \frac{1}{n+2m}\left(\sum_i^n \frac{\left|F_i^{Ind_{EXP}} - F_i^{Ind_{FEA}}\right|}{F_i^{Ind_{EXP}}} + \sum_i^m \frac{\left|F_i^{Par_{EXP}} - F_i^{Par_{FEA}}\right|}{F_i^{Par_{EXP}}} + \sum_i^m \frac{\left|F_i^{Per_{EXP}} - F_i^{Per_{FEA}}\right|}{F_i^{Per_{EXP}}}\right) \tag{10}$$

Result

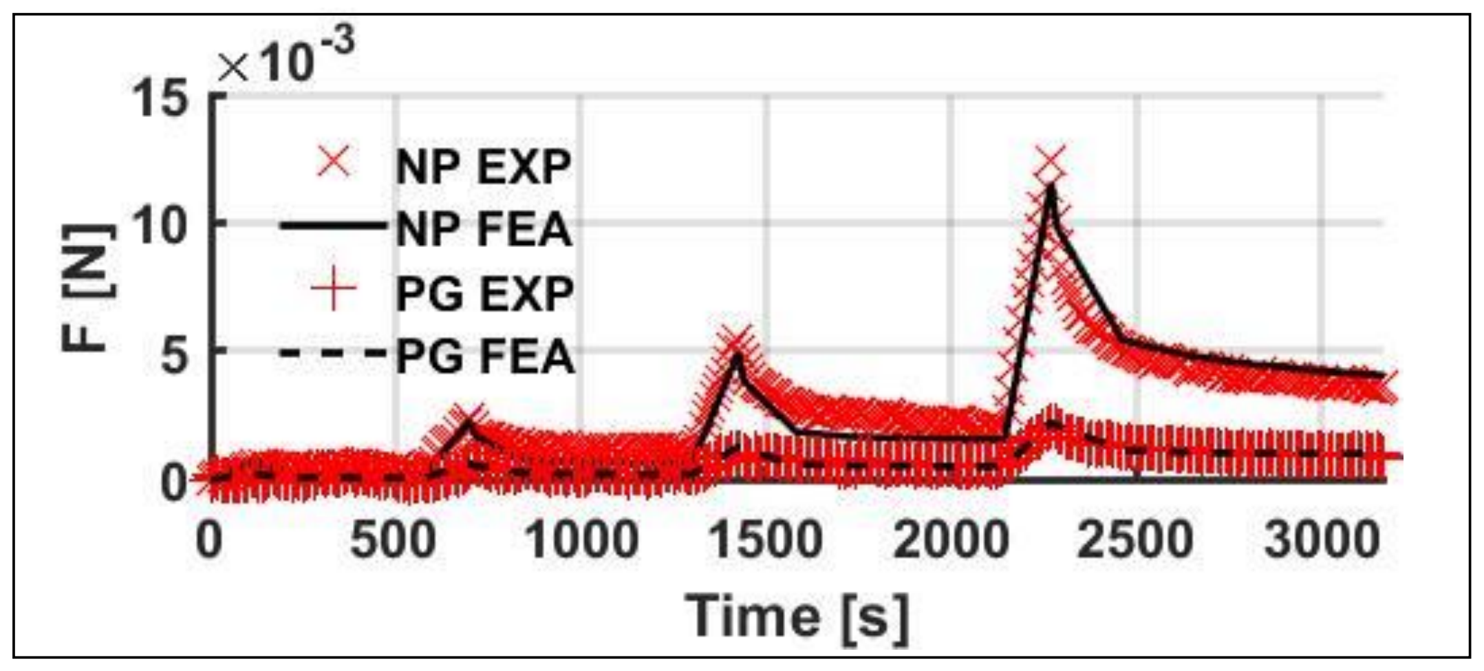
- The equilibrium material model represents a good approximation of the real tensile and compressive (indentation) experiments.
- The strain under the indenter spot is predicted lower (30~50% off) using this model. But the shape deformation of the uniaxial test was predicted well



- The elastic parameters E=1.2±1.0kPa, ξ=210±116kPa for nonpregnant samples, are found significantly different (p<0.05, one way ANOVA) from pregnant samples (E=0.05±0.02kPa, ξ=4.5±3.5kPa), illustrating the cervix remodeled to be softer during pregnancy. (E=0.05±0.02kPa, ξ=4.5±3.5kPa), illustrating the cervix remodeled to be softer during pregnancy. Other elastic parameters are v=0.43±0.2, b=1.2±0.8, a=1.5±0.7.



- The viscous parameters are E_v=5.5±3.5kPa, ξ_v=50±35kPa, τ_0=51±21s, τ_1=10±9s for nonpregnant samples and E_v=1.1±0.5kPa, ξ_v=8.9±6.3kPa, τ_0=56±11s, τ_1=13±3s for pregnant samples.
- The nonlinear viscoelastic model could approximately describe the indentation experiment well for both non-pregnant and pregnant samples.



Conclusion

- Both the equilibrium compressive and tensile mechanical behavior of the cervical tissue could be captured well by a proposed fibrous composite model.
- The nonlinear viscoelastic model could approximately describe the indentation experiment well

Reference

[1] Shi, L et al, 2019, J. BioMech. Eng. 141.9.

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