Using Computational Mechanics to Improve Preterm Birth Risk Assessment

Jayla McCoy[1], Camilo A. Duarte-Cordon, Ph.D.[2], Abigail Laughlin, Ph.D. Candidate,[2] Kristin Myers, Ph.D.[2]
[1]Department of Mechanical Engineering, University of Kentucky, Lexington, KY
[2]Department of Mechanical Engineering, Columbia University, New York, NY

Introduction: Preterm birth (PTB), defined as birth before 37 weeks of pregnancy, is the leading cause of childhood morbidity and mortality [1], affecting 1 in every 10 infants in the U.S. [2]. Shockingly, the global PTB rate has decreased by just 0.14% from 2010 to 2020 [2], highlighting very few advancements in the past decade. Up to 70-80% of all PTB cases occur unexplained or spontaneously (sPTB) [3], often resulting from premature rupture of membranes, premature uterine contractions, and premature cervical softening pathways that activate the remodeling of the cervix. Currently, there is no reliable method to predict sPTB. For routine check-ups, transvaginal ultrasound measurement of cervical length (TVCL) is the preferred method for sPTB risk stratification but has limited sensitivity [4]. A possible new and promising method is the Pregnolia aspiration device system [5], which can assess the stiffness of the cervix through a proxy parameter known as the aspirated cervical stiffness (aCS) index. Since changes in cervical stiffness correlate to different stages of cervical remodeling during pregnancy [6], this device has the potential to help better understand and quantify cervical remodeling to predict sPTB. By combining the aCS index with patient specific measurements obtained from ultrasound through in-silico computational mechanics tools such as finite element (FE) modeling, we can obtain further insights to the deformation and stress fields in the cervix and aim to further improve this method for sPTB prediction.

Methods: To understand how cervical stiffness plays a role in sPTB, we built simplified FE models of the cervix and the Pregnolia aspiration device, as shown in Fig. 1A. Using ultrasounds from three patients at high risk for sPTB (CL < 25 mm) and three patients at low risk for sPTB (CL > 25 mm), measurements were obtained to build 3D Solidworks geometries for each patient. Models were then meshed in Hypermesh and imported to FEBio Studio 2.7, where relevant boundary conditions were applied (Fig. 1A). Sliding-elastic contact was applied at the specimen and probe interface. A pressure was applied on the top face of the cervical specimen, simulating the vacuum pressure the device applies until the tissue is displaced 4 mm (Figure 1B). Inspired by the collagenous microstructure of cervical tissue, a material model consisting of a continuous fiber distribution embedded in a neo-Hookean material is used in the FE model. Inverse Finite Element Analysis (iFEA) is used to determine the stiffness of the fibers from the simulations, generating a computed cervical stiffness (cCS) index for each patient.

Results: From the iFEA results, we observed that throughout patients, cCS ranges from 1 to 67 kPa. The patient with the lowest cCS index corresponds to the patient who delivered extremely preterm (24 weeks). This patient also had the lowest cervical length. A larger sample size is needed to assess the correlation between fiber stiffness and gestational outcome. We also studied the effect of the precompression usually applied by the physician during examination. As the level of precompression increases, the cCS index obtained from iFEA also increases exponentially, suggesting that physicians must be careful not to press significantly on the cervix during testing. Finally, we studied the effect of viscoelasticity on the cervix. The relaxation of cervical tissue when taking consecutive measurements with the probe may affect the aCS index obtained from the Pregnolia aspiration device. In FE models, the displacement of cervical tissue is affected by the viscoelastic relaxation time, thus reinforcing the importance of letting the tissue relax to equilibrium before taking measurements.

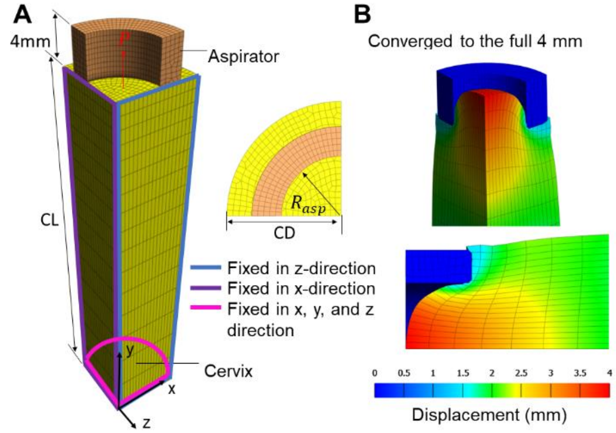

Figure 1(A) Representative geometry and boundary conditions of one of six patients (B) Deformation field

Conclusions: This study shows that FE models can be reliable tools to enhance the potential of the Pregnolia system for sPTB risk assessment. Fiber stiffness could correlate to sPTB risk level and has the potential to be used for routine check-ups as a complementary quantity to TVCL. Furthermore, precompression and viscoelasticity of the cervix during examination affect the calculation of cCS index. Future testing in more patients is needed to determine if cCS index can be used to predict sPTB.

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