Understanding Pelvic Organ Prolapse:
A Comprehensive, Biofidelic Computational Model of the Pelvic Floor

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A Biofidelic Computational Model of the Female Pelvic Floor

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Abstract

Pelvic organ prolapse (POP) occurs when pelvic organs descend into the vagina, causing painful symptoms including a bulging sensation and disruption of daily activity. In the US, POP afflicts 50 percent of women over the age of 50; over 20 million women will be affected by 2030. Pessaries provide mechanical support to non-surgically treat POP, but are inefficient in treating rectocele, or prolapse of the posterior vaginal wall. Computational modeling of the pathology of rectocele may reveal new treatment possibilities. A three-dimensional model was created from healthy female MRI data to run finite element analysis (FEA) in FEBio. FEA simulations were first conducted by changing the force of the rectum onto the rectovaginal fascia, then measuring the displacement of the posterior wall of the vagina. The results showed increased displacement upon greater applied force, validating that FEA of the 3D model can be used to study rectocele. Then, the mechanical properties of the rectovaginal fascia and vagina were varied to model possible causes of rectocele. The data indicates that rectocele can be attributed to weakened mechanical properties in the vagina. Changing the rectovaginal fascia did not impact displacement of the posterior vaginal wall. This model can be applied to the study of pelvic organ prolapse etiology and eventually work towards the development of novel, personalized treatments for rectocele.

Keywords: Computational Modeling, Women's Health, Finite Element Analysis

Introduction

Pelvic organ prolapse (POP) is characterized by a descent of pelvic organs into the vagina. Aging, vaginal childbirth, and a history of connective tissue disorders are common risk factors[1,2]. There are many types of prolapse, which can lead to the descent of the posterior or anterior vaginal wall. The most common categories of POP (**Figure 1**[3]) relate to the three pelvic organs: cystocele

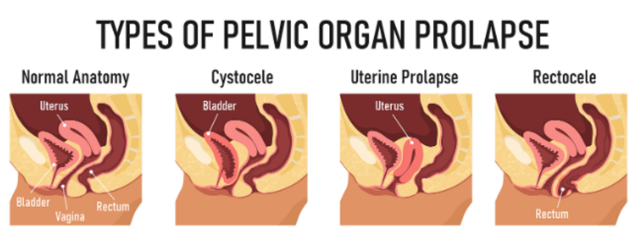

Figure 1: Three main types of pelvic organ prolapse

(prolapse of the bladder), uterine (prolapse of the uterus) and rectocele (prolapse of the rectum)[1]. Current understanding of the etiology of POP is limited, with many papers referencing vague and qualitative statements that lack evidence to support. There is little agreement on specific structures of the pelvic floor that cause prolapse[4]. Common theories include weakening of the levator ani complex, impaired ligament function, stretching of connective tissue, or changes in the collagen matrix as possible causes of prolapse[2].

Symptoms of POP tend to be very general, with patients describing "heaviness" or "lump" sensations[5]. In clinic, POP is diagnosed using the Pelvic Organ Prolapse Quantitative Exam (POP-Q). The POP-Q exam measures displacement of pelvic organs in centimeters at six points (Aa, Ba, C, D, Ap, Bp) as referenced from the hymen[5]. This allows physicians to objectively diagnose the stage of prolapse in patients. The POP-Q exam has improved ability to treat the vague symptoms that accompany POP[6], and has shown good reliability as a tool[5].

The three main treatments of POP are physical therapy, surgery to re-suture ligaments, and pessaries. Pessaries are a broad class of mechanical devices used to mechanically support the pelvic floor. Design of pessaries can be selected based on the type of prolapse, and they come in various sizes to best fit a patient. However, pessaries have a lot of barriers to use in practice. Home self-care of pessaries makes them difficult for long-term use[7]. Pessary use is difficult due to other conditions such as arthritis or decreased flexibility, as well as mental barriers to care of the pessary at home, time constraints around teaching care in clinic and performing care at home, and misfitting in clinics[8]. While the POP-Q gives a standard exam to diagnose the stage of prolapse, there is no equivalent for pessary fitting, meaning the process is very subjective[9]. Poor pessary fit is a major factor in the success of a pessary for the patient[10].

POP in each patient is further defined by the anatomy of the pelvic floor, which is fairly well understood. Epithelial cells make up the outer layer of the uterus, called the perimetrium[11]. The perineal body – which connects to the pubic bone via the pubovaginalis and puborectalis muscles – to the perineum of the uterus and supported with transverse perineal muscles, plays an important role in continence[12]. This region is often injured during episiotomies and childbirth, and is an important consideration in POP because it functions to support pelvic floor musculature. Key muscular components of female pelvic floor support include the levator ani complex - composed of the iliococcygeus and pubococcygeus muscles -, and the puborectalis muscle, which interface the pelvic bone and the vagina[13]. These structures provide mechanical support of the pelvic organs.

Computational models are widely used in the field of engineering to model, test and understand hypotheses. These tools are extremely useful in biomedical science to apply mechanical forces and model disease states. Finite element models can be used to understand the pathophysiology of pelvic floor disorders[14]. The most common method to create these 3D models of human anatomy is to use magnetic resonance image (MRI) data to trace each structure in the sagittal, axial and coronal planes[15–17]. Previous finite element studies have only included the three pelvic organs: bladder, vagina, and rectum, leaving out the rest of the pelvic floor. These models have strengths in understanding large scale deformations, but lack fine supporting structures such as ligaments, muscle and fascia. These components are necessary to reduce inaccurate motion of the pelvic organs[18]. A model that includes all aspects of pelvic floor musculature would provide a more accurate understanding of female pelvic floor biomechanics.

The broad goal of this Capstone project is to design a novel, comprehensive 3D computational model of the pelvic floor. Finite element analysis (FEA) of the model can test the theories of rectocele etiology by varying the force from the rectum onto the vagina in the anterior direction, weakened mechanical properties of rectovaginal fascia, and weakened mechanical properties of the vagina. Weakened mechanical properties were modeled by decreasing the stiffness of the tissue by 100 fold and comparing displacement of the posterior vaginal wall to control conditions.

Results

An extensive literature review was conducted to find an open-source, MRI database. Sources such as the Visible Human Project[19] were considered, but the data was not in .DICOM or .NRRD format required for segmentation in 3D Slicer with high quality resolution. The National Cancer Imaging Archive is an extensive, open-source database for medical imaging. The database contains image sets from a range of imaging modalities, including over 500 scans of the female pelvis. A majority of these scans were unusable due to poor quality or

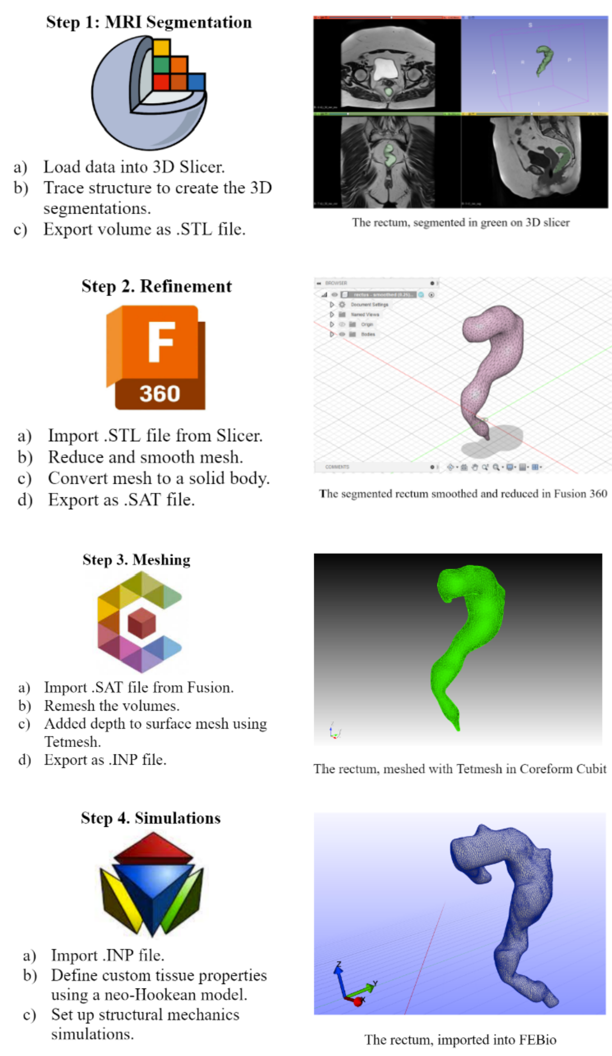

Figure 2: Workflow for building a 3D model from MRI data to finite element simulations in FEBio.

presence of cancer. Promising scans identified were vetted by radiologists at the UVA Health Center. The Subject ID C3N-01879 dataset was identified to best suit the needs of segmentation due to clarity of the image. The scan shows signs of endometrial cancer, so segmentation ended at the cervix and the uterus was omitted from the final model.

The data was taken through the workflow depicted in Figure 2. Each structure was segmented individually and assembled in Fusion 360 to create a comprehensive, 3D model of the female pelvic floor.

The complete 3D model can be seen in Figure 3, constructed in Fusion 360. The model includes the rectum, vagina, bladder, rectovaginal fascia, pubocervical fascia, ischiococcygeus muscles, iliococcygeus muscles, abdominal muscles, and gluteal muscles, as well as the femurs, illiums, sacrums, and pubic bones. A smaller version of the model

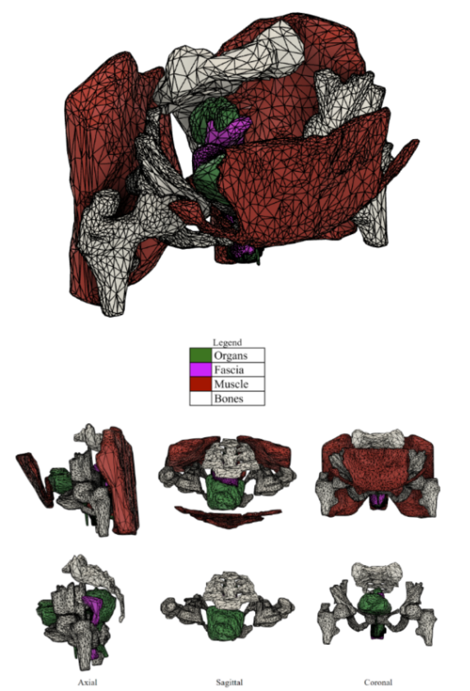

Figure 3: Complete, assembled model in Fusion 360.

was included in FEBio, consisting of the rectum, rectovaginal fascia, vagina, and bladder.

To simulate rectocele, forces of 1 N, 5 N, and 11 N were applied in the anterior direction. This force was applied to the anterior wall of the rectum towards the posterior wall of the rectovaginal fascia. For each simulation, the displacement of the posterior wall of the vagina relative to the initial position was measured.

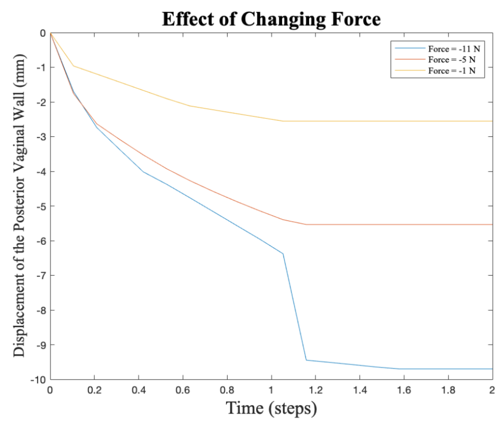

Figure 4: Displacement of posterior vaginal wall upon changing the force of the rectum in the anterior direction (towards rectovaginal fascia). Simulations show an increase in displacement of the vaginal wall upon increased force.

The first experimental simulation varied force. A force of either 1 N, 5 N, or 11 N was applied to the anterior wall of the rectum on the posterior wall of the rectovaginal fascia. The lower end values of this range were based on literature[19]. The results of the simulations are summarized in Figure 4. The displacement of the posterior wall of the vagina changed upon different applied forces of the rectum. This shows that applying force of the rectum onto the rectovaginal fascia, and consequently the posterior wall

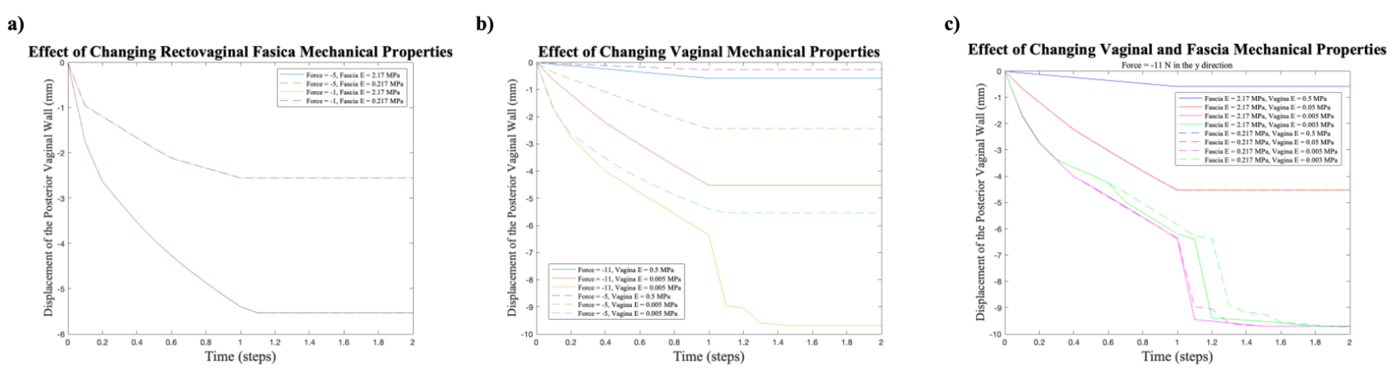

Figure 5: Results of simulations. The Young's modulus of each structure was changed by 100 fold at two different forces. a) When the Young's modulus of the rectovaginal fascia was changed, no difference in displacement was observed. b) When the Young's modulus of the vagina was changed, a large difference in displacement was observed. c) When the Young's modulus of the vagina and rectovaginal fascia were changed at the same time at varying forces, the only change that impacted displacement was the changing of vaginal properties.

of the vagina, can be used to model rectocele. Statistical analysis of this simulation can be seen in Figure 6a. These simulations were also used as the control groups for the subsequent simulations, because the mechanical properties of the rectovaginal fascia and vagina were under normal conditions.

Reports often describe pelvic organ prolapse as a weakening of the pelvic floor. Some discuss disruptions in the rectovaginal fascia that cause rectocele. Others discuss weakening of the vagina itself as a cause. In the second simulation, the vaginal properties were of normal conditions, while the mechanical properties of the rectovaginal fascia were altered. A smaller Young's modulus was used to model a loss in strength of tissue. Young's modulus of the rectovaginal fascia was simulated at 0.217 MPa and 2.17 MPa, a 100-fold difference, and both conditions were tested at 1 N, 5 N, and 11 N force values. Results of this simulation can be seen in Figure 5a. The values for displacement of the posterior vaginal wall were almost identical, regardless of the Young's modulus value of the fascia (Figure 6b).

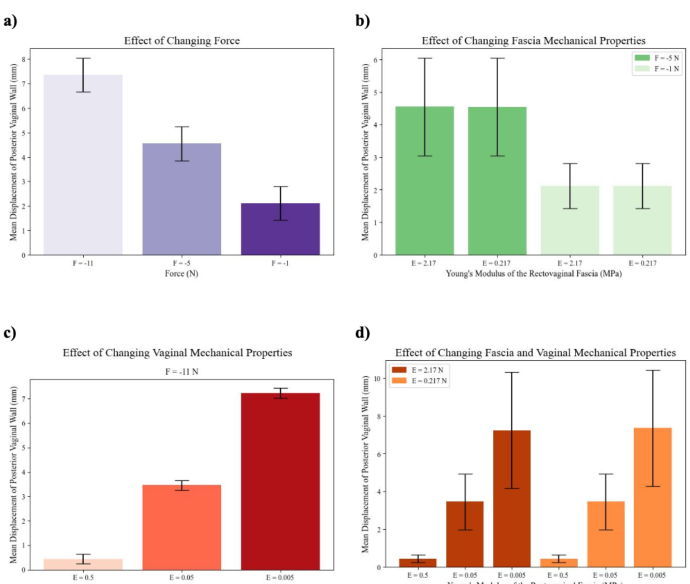

Figure 6: Time-averaged displacement of the posterior vaginal wall, with error bars representing standard deviation.

In the third simulation, the properties of the rectovaginal fascia were of normal conditions, while the vaginal mechanical properties were altered. Young's Modulus of the vagina was simulated at 0.005 MPa, 0.05 MPa, and 0.5 MPa (100-fold differences), tested at a force of 11 N. The results of these simulations are summarized in Figure 5b. To determine significance, the time averaged mean displacement of the posterior vaginal wall was compared. A statistically significant difference was found in the displacement of the posterior vaginal wall (Figure 6c).

In the fourth simulation, the mechanical properties of both the vagina and rectovaginal fascia were altered. The results of these simulations are summarized in Figure 5c. The statistical analysis (Figure 6d) indicated that there was no significant difference in solely modifying vaginal properties compared to modifying both vaginal and rectovaginal fascia properties.

Discussion

The data indicate that rectocele may be attributable to weakening of the vagina, but not the rectovaginal fascia. Literature suggests that the tearing or deterioration of the rectovaginal fascia could be connected to rectal prolapse, but there is no quantitative data to support the claim[20]. To test this theory, simulations of the 3D model explored varying the mechanical properties of the rectovaginal fascia. Young's modulus is correlated with flexibility of tissue, so it was used to vary the mechanical properties. The data show that disruptions of the rectovaginal fascia are likely not linked to the etiology of rectocele.

Although less frequent, literature also cites weakening of the vagina as the cause of rectal prolapse, but again, there is no quantitative evidence to support this claim[21]. To test this theory, the Young's modulus of the vagina was changed by a hundred fold. These simulations showed a significant difference in the displacement of the posterior vaginal wall when altering the mechanical properties of the vagina. From this analysis, rectal prolapse is more likely connected to weakening of the mechanical properties of the vagina than to weakening of the rectovaginal fascia.

To analyze the effect of both the rectovaginal fascia and the vaginal tissue being compromised, the last simulation combined a weakened rectovaginal fascia and a weakened vagina. In the third simulation, the weakening of the vagina resulted in a significant difference in the displacement of its posterior wall. However, in comparison, this final combination simulation, the displacement of the vaginal posterior wall was not changed. This indicated that regardless of changes in the mechanical properties of the rectovaginal fascia, the only significant differences in displacement of the posterior wall of the vagina are connected to the weakening of the vagina itself. This further supports that rectal prolapse is due to weakened vaginal properties, but not weakened rectovaginal fascia properties.

A limitation of the simulations was the extent of the exploration of varying mechanical properties. Tensile strengths were not varied. Although the simulations indicate that variations in the mechanical properties of the vagina are linked to rectocele, it is only supported by changes to the Young's modulus of the vagina. Further studies using this model should investigate methods to alter the tensile strength of materials to fully analyze the mechanical properties of the rectovaginal fascia and vagina. A second limitation of the study was the omission of a majority of the components of the 3D model from the FEBio simulations and FEA. The 3D model included the pelvic organs and the surrounding supportive muscles and bone structure. The FEBio simulations were limited to the rectum, rectovaginal fascia, vagina, and bladder. These structures were selected for FEA because they are directly involved with pelvic organ prolapse. The supporting musculature and bones were omitted for two reasons. First, the operating capacity of FEBio was limited. Increasing the number of volumes in the simulation drastically increased the time required to run the simulations. It also caused frequent errors in running the simulations, due to the large number of abnormal interactions that occur between the volumes. Second, the supporting musculature and bones could be modeled as "rigid constraints" in FEBio. The top and bottom of each volume – rectum, rectovaginal fascia, vagina, and bladder – were constrained in all directions. This equates to preventing any rotation or displacement of the top and bottom of each volume, which simulates the effect of the supporting musculature and bones.

Future Work

The research project was limited by the use of one MRI dataset. This is due to the limited open-source data available for studying the female pelvis. Future studies can repeat the methodology developed in this project to repeat simulations on different patients. Obtaining institutional review board approval to acquire a more recent, healthy patient MRI scan is essential to continuing work on this project. An accurate and clear dataset will allow segmentation of the uterus, uterosacral ligament, and cardinal ligament, which are also important in structural integrity of the female pelvic floor[22]. Inclusion of these components will increase the accuracy of the model. Repeating model building and simulations with more data sets would confirm that this method is reproducible and bolster the conclusions.

Further simulations using the model are important. Next steps would be to include the pubocervical fascia, ischiococcygeus muscles, iliococcygeus muscles, abdominal muscles, gluteal muscles, and bone structures, in FEBio simulations. Exploring software that can handle this kind of large model, or looking into high performance computing methods, could be a route to success. Weakened properties of the musculature and tissue found in the pelvic floor can be further understood through changing tensile strength. Future studies should include analysis of tensile strength in addition to tissue elasticity.

Results of this project have implications for the design of novel pessaries to treat rectocele. Preliminary findings of association of prolapse with weakened vaginal properties provides the initial evidence needed to begin to develop a pessary that better supports the posterior vaginal wall. Understanding of the role of tensile strength in prolapse can identify areas of weakness in the pelvic floor and serve as potential targets for pessary design. Long term, the method can be used in the development of personalized medicine for treatment of pelvic organ prolapse. Using patient-specific MRI data to populate the model and identify exact locations and causes of prolapse will provide opportunity to provide improved treatment options and better outcomes.

<u>Materials and Methods</u>

An overview of the modeling process is given in Figure 2.

MRI Segmentation in 3D Slicer

MRI data was obtained from the Cancer Imaging Archive (Subject ID: C3N-01879), an open source database containing de-identified medical images available for download. 3D Slicer was used to trace the pelvic structures in three planes: axial, sagittal, and coronal. Each structure (organs, fascia, muscle, and bone) was manually traced in all three planes using the “Paint” tool in the Segmentation Editor mode, with varying brush diameter from 1-4%. The segmented volumes were exported as .STL files.

Refinement in Fusion 360

Pixelation of MRIs in 3D Slicer led to jagged and sharp edges. Volumes from 3D Slicer were imported into Fusion 360 as meshes to refine these artifacts from segmentation. In the mesh editing environment, the smooth tool was used to smooth rough/creased regions in the mesh. Meshes were first smoothed with a 0.25 degree of smoothness, then increased or decreased as necessary. Next, the reduce tool was used to decrease the complexity of the mesh by reducing the number of faces. Meshes were first reduced to include 25% of the original number of faces in the reduced mesh, then adjusted as necessary. If regions of the mesh were still overly complex or jagged, direct edit mode was used. Groups of faces were manually selected, then edited using the erase and fill tool, which fills the selected region with the least amount of faces possible.

Building the Computational Model in Fusion 360

After refinement, the comprehensive, biofidelic computational model was constructed by compiling each of the individual bodies into one file. As seen in Figure 3, each structure was colored according to type: green for organs, purple for fascia, red for muscle, and white for bone. Meshes were converted to bodies and were exported as .SAT files for remeshing in Cubit.

Remeshing in Coreform Cubit

The mesh on the surface of the bodies from Fusion 360 is composed of 2D triangles, which is inadequate for the thickness requirements of running simulations in FEBio. To give the mesh a volume, structures are remeshed in Coreform Cubit with the TetMesh tool. The TetMesh tool meshes volumes with an unstructured tetrahedral mesh. To export the meshes on the educational license, the mesh must have less than 50,000 elements. If this limit was surpassed, the number of elements generated was reduced by minimizing over-constrained tets, over-constrained edges, silver tets, and interior points. The finalized meshes were exported as .INP files.

FEBio - Defining Surfaces

Finalized meshes of the rectum, the rectovaginal fascia, the vagina, and the bladder were imported into FEBio. The bodies were first combined to create one object, which made each structure its own part. Each part was defined as a neo-hookean material with mechanical properties according to Table 1**.** Next, the specific regions were defined: top of the rectum, bottom of the rectum, front of the rectum, back of the rectovaginal fascia, front of the rectovaginal fascia, back of the vagina, bottom of the vagina, front of the vagina, back of the bladder, and top of the bladder. To define the regions, an empty rigid body material was created, then a rigid boundary condition (BC), which was then assigned to a group of faces on the desired organ or fascia. After defining, regions were constrained according to direction. Rigid constraints can be applied in 6 different directions: x-displacement, y-displacement, z-displacement, x-rotation, y-rotation, and z-rotation. Rigid constraints in all directions were created for the: top of the rectum, bottom of the rectum, bottom of the vagina, and top of the bladder. Rigid constraints in all directions, except for y-displacement (anterior/posterior anatomical direction) were applied to the: front of the rectum, back of the rectovaginal fascia, front of the rectovaginal fascia, back of the vagina, front of the vagina, and the back of the bladder. Next, the sticky contacts between regions were defined: the front of the rectum and the back of the rectovaginal fascia, the front of the rectovaginal fascia and the back of the vagina, and the front of the vagina and the back of the bladder. Finally, an analysis step was added to quantify simulations.

Organ	Young’s Modulus (MPa)	Poisson’s Ratio
Vagina	0.005[23]	0.46[24]
Rectum	0.1[23]	0.495[25]
Rectovaginal Fascia	2.17[26]	0.37[26]
Bladder	0.005[27]	0.46[27]

Table 1: Mechanical properties used in finite element simulations of the 3D model.

FEBio - Force Simulations

Force simulations were run by adding a rigid constraint with force as a load. Force was applied to the anterior wall of the rectum in the -y direction (in the anterior direction) onto the posterior wall of the rectovaginal fascia. 1 N, 5 N, or 11 N were simulated. Displacement of the back of the vagina was collected over time.

FEBio - Varied Mechanical Properties Simulations

Simulations varying the mechanical properties of the rectovaginal fascia and the vagina were run by modifying the Young’s Modulus of the original neo-hookean material defined for each structure. They were each run with an applied force of 1N, 5N and 11 N. First, the Young’s Modulus of the rectovaginal fascia was varied as 0.217 MPa and 2.17 MPa. Then, the Young’s Modulus of the vagina was varied as 0.005 MPa, 0.05 MPa, and 0.5 MPa. Lastly, these modifications to the Young’s Moduli of the rectovaginal fascia and the vagina were combined in a final simulation. Displacement of the back of the vagina was collected over time.

End Matter

Author Contributions and Notes

LJH assembled the team and proposed the project focus. MSY, MCR and LJH conducted literature reviews on pelvic organ prolapse. MSY sent MRIs to clinicians to be checked. MCR created the protocol to mesh bodies in Cubit. MSY, MCR and LJH segmented structures in 3D Slicer and ran simulations in FEBio. For the paper, LJH performed statistical analysis, MCR created visuals, and MSY created tables. LJH, MSY and MCR wrote the text included in the paper. WHG provided advising throughout the project.

The authors declare no conflict of interest.

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