EXPLORING THE ETIOLOGY OF POSTERIOR VAGINAL PROLAPSE WITH FINITE ELEMENT ANALYSIS

INVESTIGATING THE SYMMETRY OF GOVERNMENT ALLOCATION OF RESOURCES TOWARDS WOMEN'S HEALTH RESEARCH

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By
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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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Introduction

Pelvic organ prolapse (POP) is the herniation of pelvic organs into the vaginal wall, causing symptoms including the feeling of pressure or bulging within the vagina, urinary or fecal incontinence, and exposure of the vaginal wall below the vaginal introitus (Rogers & Fashokun, 2022). Though prevalence has not been thoroughly defined due to non-uniform classification, high asymptomatic rates, and large amounts of symptomatic women who do not seek medical attention, upon examination, approximately 41 percent of post menopausal women experience prolapse, and there is an approximated 11 to 19 percent lifetime risk of undergoing a prolapse or incontinence surgery for women (Rogers & Fashokun, 2022).

Posterior vaginal prolapse (PVP) occurs due to the descent of the rectum into the posterior vaginal wall, making up 18 percent of prolapse cases, but is repaired in 87 percent of prolapse surgeries (Luo, 2012; Rogers & Fashokun, 2022) (Figure 1). Although treatment with surgeries and pessaries (medical device inserted into vagina to mechanically support vaginal wall) is abundant, approximately 30% of surgeries to correct prolapse fail, and pessaries are not effective in relieving symptoms of 56% of those who experience PVP (Manzini, van der Vaart, van den Noort, Grob, & Withagen, 2022; Rogers & Fashokun, 2022).

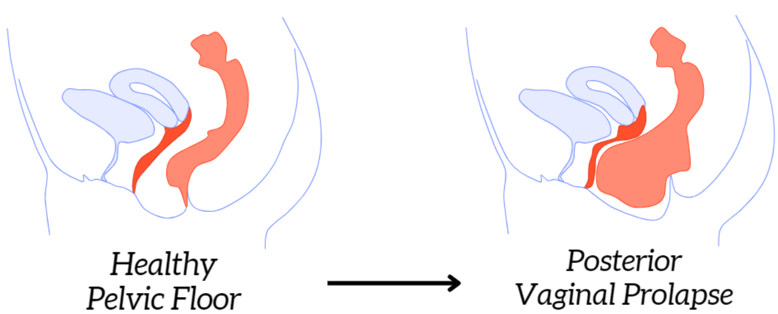

Figure 1. Schematic of changes in pelvic floor morphology during posterior vaginal prolapse.

Prolapse can cause negative effects on patients' health-related quality of life, particularly in regards to mental and sexual health, necessitating the development of effective treatment options (Lowder, Ghetti, Nikolajski, Oliphant, & Zyczynski, 2011; Robinson et al., 2022). However, knowledge in women’s health has historically neglected research pertaining to women outside of their reproductive years (Weisman, 1997). Due to prolapse predominantly afflicting postmenopausal women, many gaps exist in the general understanding of the fundamental biomechanics that drive prolapse pathologies. To begin to improve current treatment options, a better understanding of the underlying mechanics of PVP is necessary.

Finite element analysis provides the opportunity to non-invasively explore complex biomechanics through simulating interactions between anatomical players (Sharma & Paul Khurana, 2018). Computational biomechanical models have been recently introduced to the women’s health field to better understand pelvic floor dynamics, especially during pregnancy and pelvic floor disorders (Dias et al., 2017; Routzong, Moalli, Maiti, De Vita, & Abramowitch, 2019; Westervelt et al., 2017). Due to the low cost of resources to produce, computational models have the potential to be designed with vast variability in subject anatomy and pathological conditions, enabling an in-depth understanding of the effects of discrete changes of mechanical properties that is not attainable with human studies.

To contribute to closing gaps in women’s health research, and specifically to the understanding of the PVP pathology, a computational model of the female pelvic floor will be constructed to explore the mechanical changes of the pelvic floor that contribute to PVP.

Posterior Vaginal Prolapse Model Development

This capstone will build upon my previously constructed finite element (FE) model of the female pelvic floor. This model was developed through segmentation of cryosections from the National Library of Medicine's female Visible Human Project, an open-source three-dimensional representation of a healthy female cadaver (Figure 2a). These images were used to create components of the organs, muscles, mesentery, fat, bones, and ligaments of the pelvic floor. Each component underwent smoothing and boolean subtraction to create interfaces with adjacent components to ensure continuous force transmission throughout the pelvic floor (Figure 2b). The final geometries were meshed with adaptive tetrahedral meshing (Figure 2c) and assembled into a complete pelvic floor model of 28 tissue components (Figure 3).

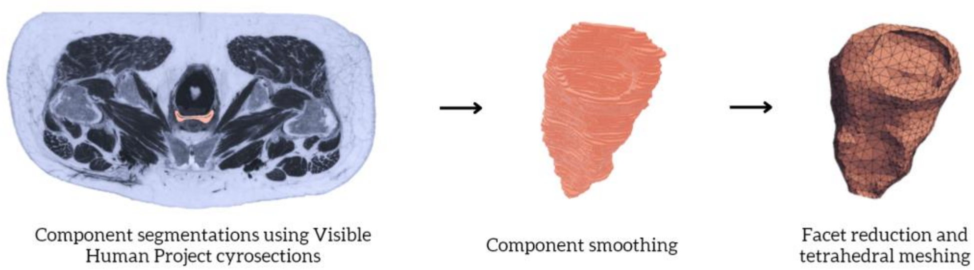

Figure 2. Representative pipeline of model development, using the vagina as example.

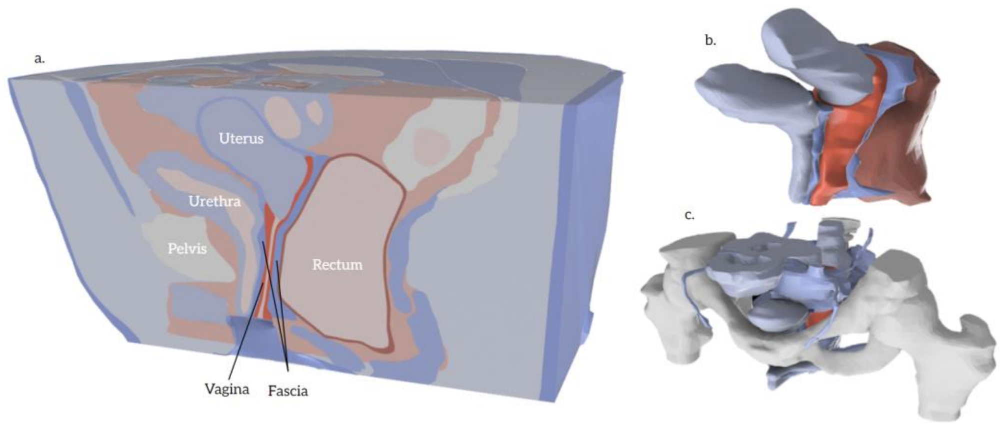

Figure 3: Renderings of a) a mid-sagittal cross section of the fully assembled pelvic floor model, b) the isolated pelvic organs (bladder/urethra, uterus, vagina, rectum) and connective tissue, and c) the isolated pelvic organs, bowel, reproductive ligaments, pelvis, and femurs.

Neo-Hookean material properties were applied to each component, informed by literature review of parameters used in existing pelvic floor models and healthy tissue tensile testing (DeLancey, 2016; Dias et al., 2017; Luo, Chen, Fenner, Ashton-Miller, & DeLancey, 2015). The model will simulate the execution of the Valsalva maneuver, a clinical technique to visualize prolapse dynamics by having the patient "bear down", increasing the patient's intra-abdominal pressure. To represent this in the model, a graded pressure of 100 cmH_2O will be applied to the anterior surface of the abdominal muscles and the top surface of the model (Dias et al., 2017).

The model will then be used to understand mechanical changes of the pelvic floor that contribute to PVP. Currently, it is theorized that prolapse may occur due to force reduction by the pelvic floor muscles (i.e., levator ani), defects in the reproductive ligaments, and/or material changes causing weakness of the vaginal wall or rectovaginal fascia, though the exact mechanisms contributing to PVP specifically are not well understood (DeLancey, 2016). Using the developed FE model, each of these pathologies will be tested by reducing the elastic modulus of the relevant bodies, representative of respective weaknesses.

To evaluate feasibility of hypothesized pathologies in contributing to PVP, the simulations will be visualized and, with the support of UVA Health radiologists, qualitatively compared to morphological changes seen in dynamic magnetic resonance imaging of healthy and PVP patients during Valsalva. This comparison will be used to determine which pathological state simulations exhibit morphological changes representative of PVP. Using the subset of simulations representative of PVP, vaginal wall kinematics will be measured using the Pelvic Organ Prolapse Quantification system (POP-Q) by digitizing and tracking points along the vaginal wall to quantify prolapse severity compared to standard clinical measurements (Persu, Chapple, Cauni, Gutue, & Geavlete, 2011). Displacements under varied pathological states will be used in a sensitivity analysis to decide which mechanical changes most influence PVP morphology.

Women's Health Research Does Not Adequately Address Women's Health Needs

It is evident that large research gaps exist in the understanding of PVP, perpetuating ineffective treatment options for prolapse and leaving millions of women with physical and emotional distress as a result of prolapse. However, this issue speaks to a much larger systemic health care crisis pertaining to the awareness and investment in women's health research. Due to the historically male-dominated nature of medicine, the understanding of fundamental women's health principles is severely lacking, making medicine less effective, and even harmful for women (Cleghorn, 2021). For instance, it was not until 1991 that the National Institutes of Health (NIH) required female participation in clinical trials. As a result, decades of research pertaining to risk factors of developing drugs were explored with no female representation (NIH, n.d.-b). Decades later, women continue to experience adverse drug reactions nearly twice as often as men (Zucker & Prendergast, 2020).

Efforts to expand women's health research have been largely driven through changes in the perception of the field and government led projects to prioritize reallocation of resources towards relevant research. In the mid-1990's the women's health definition was shifted from focusing on mental and reproductive health to including all conditions that disproportionately affect women, like autoimmune diseases and osteoporosis (Carnes, Morrissey, & Geller, 2008). Furthermore, through the NIH's implementation of the Office of Research on Women's Health (NIH-ORWH), more funding has been allocated to support women's health research with the intent to identify and understand sex-based differences in health and disease (NIH, n.d.-c). However, nearly thirty years since these changes, there still exists a general unawareness and underfunding of women's health research, especially for conditions that affect women outside of their reproductive years (Bustreo, Knaul, Bhadelia, Beard, & Araujo de Carvalho, 2012). For example, biological and environmental factors that influence the onset, symptoms, and comorbidities of menopause are still largely unknown, despite the condition affecting all women for up to forty percent of their lives. Even with these gaps, in 2019, only 28 NIH grant proposal titles included "menopause", whereas more than 300 included "pregnancy" (Aninye, Laitner, & Chinnappan, 2021).

The historical and continued neglect of women's health research that appropriately addresses women's health needs leaves a massive space for research to be conducted that engineers have the power to contribute to. However, for this power to be used effectively, it must be contextualized with relevant stakeholders. Sally Wyatt's paper on *technological determinism* highlights a multifaceted definition of symmetry in socio-technical systems (Wyatt, 2008). Wyatt discusses symmetry through balancing the perspective of the system from a “distance” to address problems based on research, while also considering the experiences of the relevant users (Wyatt, 2008). This framework can be used to inform the direction at which scientific funding and research should be prioritized when pertaining to women’s health to effectively address the needs of the population. By coupling quantitative records of disease burdens on women with the initiatives directed to advance women’s health exploration, efforts can be made to understand areas that are over and under acknowledged by government-funded research. This work can ultimately direct the reallocation of resources to appropriately address women’s health needs based upon the most abundant health burdens.

Research Question and Methods

This evolution of women’s health research prompts me to ask the question, have the initiatives and policies established through the NIH-ORWH appropriately addressed women’s health needs? This investigation will be conducted through the lens of Wyatt’s definition of technological determinism to understand the degree of symmetry of scientific advancements in women’s health and the experiences and needs of the populations who are affected by these advancements.

This research will be conducted through a review of the NIH-ORWH Biennial Report of the Advisory Committee on Research on Women’s Health from 1993 to 2020 (NIH, n.d.-a). These reports each outline the initiatives, policy changes, and future plans of the organization during the reported fiscal years. Upon thematic coding of these reports, I will identify what areas of development the NIH-ORWH most greatly prioritizes through analysis of the listed areas of research focus and publications, and what programs are developed to advance progress. Themes will delineate the subcategories of women's health that are most cited based on affected age groups (i.e., adolescence, reproductive age, menopausal) and condition type (i.e., reproductive health, autoimmune disease, respiratory disease) to observe trends in prioritized research areas.

I will parallel these observations with the documented allocation of NIH-ORWH funding towards women's health research in specific disease areas from the biennial reports. This data will be compared to the World Health Organization's quantifications of disease burdens (i.e., death and disability associated life years) to observe discrepancies between the NIH-OWRH initiatives/budget towards specific conditions and the condition's relative burden on women (World Health Organization, 2023). For example, in 2019-2020, 9.6% of NIH-ORWH funding was allocated towards projects related to maternal conditions which make up 2.9% of deaths in women aged 25 to 30, while only 3.4% of NIH-ORWH funding went towards lung disease that makes up 35.7% of deaths in women aged 60 to 65 (NIH, n.d.-a; World Health Organization, 2023). By understanding these sociotechnical relationships, awareness can be brought towards the changes necessary to adequately research the greatest health burdens experienced by women.

Conclusion

Due to the limited funding allocated towards women's health pathologies like prolapse, it is important to design low cost research methods to continue to advance the knowledge in the field. This project aims to begin to close gaps in women's health research by developing a computational model of the female pelvic floor to explore PVP pathologies to ultimately improve treatment options for PVP patients and reduce both the physical and mental burden of prolapse. This model can also be adapted to analyze a vast array of women's health conditions, including incontinence, pregnancy, or age-related morphological changes to the pelvic floor.

Furthermore, the socio-technical analysis of women's health government initiated research and funding will provide insight upon the priorities of these agencies. By identifying the trends in allocations of resources for research, awareness can be brought to begin to push efforts towards under-researched areas of women's health.

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