Shifting and Shaping Perceptions: Towards the Characterization and Literacy of Female Pelvic Organ Support

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Pelvic Organ Prolapse (POP) is a pelvic floor condition characterized by the unnatural descent of pelvic organs into the vagina. It occurs as the result of compromised connective tissues and musculature following vaginal delivery and/or changes in tissue composition due to aging. Approximately 50% of women in the United States experience some degree of POP during their lifetime, with symptoms that include altered urination and defecation, physical discomfort, depression, and anxiety. Over the last decade, POP treatments have gained public notoriety due to surgical complications and recurrence of prolapse after surgical repair. Both outcomes stem, in part, from gaps in knowledge regarding the complex interactions of pelvic viscera, tissues, and musculature, and is exacerbated by the significant time span between events surrounding vaginal birth injuries and symptomatic prolapse.

Over the last century, fields such as cardiovascular medicine and orthopedics have made significant strides to improve the human condition through the application of biomechanics, diagnostic imaging techniques, and modeling. Such methods have been used to reliably differentiate normal and diseased anatomy with respect to orientation, location, and other geometric attributes. In contrast, urogynecology remains decades behind as a result of a failure to adopt new interdisciplinary methods, limiting our ability to effectively treat POP. Thus,

approximately 80% of women with symptomatic POP choose to suffer in silence. This is troubling, given that POP and related disorders will become increasingly prevalent due to the advancing age of the global population.

This dissertation explores the assessment and development of diagnostic tools that improve our ability to quantify the position of the vagina with respect to physiologic changes that may occur over the lifespan within the normal range. These tools provide valuable information regarding the physical changes that occur over time and the differences between populations while serving as a potential standard by which pelvic anatomy can be quantified. Furthermore, this work explores our knowledge, perceptions, and attitudes regarding female pelvic health to challenge misconceptions surrounding normal and abnormal physiological functions, foster attitudes of empathy and acceptance for disorders, and improve health literacy by illustrating the impact that it has on lives worldwide.

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Preface

As I reflect on the past several years, I choose to interpret my experiences through the lenses of humility, wisdom, passion, and hope. My mistakes, rejections, and setbacks taught me humility, appreciation, and wisdom. Opportunities then revitalized my hope, strengthened my faith, and cultivated my true passions. The pursuit of a PhD is, in essence, a scientific experiment through which a specimen is subjected to incredible pressures. The result of these pressures turns a specimen "into dust or a diamond". There were countless moments when I was certain the pressures and expectations of my process would render me to dust. I frequently asked myself, and others, "What is the point of all of this?" "Is this really worth the sacrifice?" "Why bother?" Responses to these questions differ for everyone, but I determined that my process was indeed worth it! While I found some pressures uncomfortable, I began to understand that each challenge was necessary for growth and perspective. Many researchers would agree that experiments that do not yield expected results are still important, because each reveal previously unknown data. In my case, each experience pushed me to dive deeper into my "why". It was then that I determined my "why" was about more than just myself. My reverence and drive to pursue the highest terminal degree was destined by my past, directed by my present, and the revelation of my future. I persevere for my ancestors who were punished for learning to read, asking questions, and seeking knowledge. I persevere for my great-great grandfather (Sydnor Jennings), who yearned for formal education, but surrendered the opportunity and worked his entire life to secure formal education for his children and the community. I persevere for the family members I knew, and the ones I did not, who transitioned to glory before reaching their full potential. I persevere for those who were never afforded the opportunity to participate in education beyond the fourth-grade level. I persevere for all of those who have considered quitting and feel defeated but need to know that others who have wanted to quit or felt defeated still made it through. I persevere for my friends, my colleagues, and my fellow doctoral students who lean on each other for support. I persevere for my friends who desired this path but were hindered by circumstance. I persevere for my mentees, tutees, and those who could benefit from research opportunities and a role model to look up to. I persevere for the future doctors and engineers who need a living, breathing example of what can be done, and what can be overcome. The title of Dr. Deanna Christine Easley Sinex does not solely belong to me, but also to the several groups and individuals that taught, supported, and impacted me in insurmountable ways. These groups and individuals made this moment possible. I therefore would like to publicly acknowledge my gratitude to those who have helped me face and climb the mountain, to show others that it can be moved!

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1.0 Introduction

Pelvic Floor Disorders (PFDs) are highly prevalent physical or functional abnormalities that impact the organs, connective tissues, and musculature within the pelvis [1], [2]. The physical and emotional impact of PFDs are experienced worldwide by men, women, young, and old [3]. However, one of the most bothersome PFDs is Pelvic Organ Prolapse (POP). POP is an anatomical condition characterized by the herniation of pelvic organs (i.e. bladder, rectum, uterus), into the vagina, and in the most severe cases can be visualized as a protrusion of the vagina beyond the introitus (i.e. opening of the vaginal canal) [4]–[6]. This disorder can occur when there is a failure of the active and passive soft tissue support to the vagina, which is commonly referred to as the central organ responsible for pelvic organ support. POP often occurs with other PFDs including urinary and/or fecal incontinence and pain (UI & FI) [7], [8]. The U.S. population is approximately 51% female, and reports on the prevalence of POP indicate that approximately half of these women will suffer from varying degrees of POP during their lifetime [9]. Furthermore, population statistics indicate that the U.S. population is aging and life expectancy is increasing; thus it is projected that by 2050, over 44 million women in the U.S. will be impacted by a pelvic floor disorder forecasting a substantial societal burden (i.e. POP, UI, FI) [10]–[12].

Common risk factors associated with the onset of POP are parity, age, obesity, menopause, and connective tissue disorders, although the etiology of POP remains unknown [13]–[15]. Physical symptoms of POP include dyspareunia, pain, a pulling sensation or heavy feeling in the pelvis, and a bulge that mimics the sensation of sitting on a ball. These symptoms may depreciate enjoyment and quality of life, and are often accompanied by emotional symptoms, including embarrassment, low self-esteem, poor body image, depression and anxiety [16]–[18]. These symptoms are compounded by barriers, including socioeconomic status, cultural beliefs/practices, and lack of knowledge/awareness, leaving most women isolated, under-diagnosed, and under-treated [1], [19]. In fact, 80-90% of affected women accept the circumstance of their PFD symptoms as a way of life rather than seeking support from their gynecologists/healthcare providers, family and friends [15]–[17], [20]–[23].

The earliest written records of gynecological practices date back to Ancient Egypt, where medicinal practices favored religious beliefs over anatomical correctness [24], [25]. Evidence suggests practitioners had knowledge of pelvic organs, including the vagina, uterus and bladder. However, practitioners were unable to correctly identify and treat the physical symptoms for POP [24]. Methods for correcting “the falling of the womb”, or a prolapsed uterus around 1835 B.C.E. included coating the body of the patient with petroleum, manure and honey [26]–[28]. Thousands of years later, similar cocktails and fumigation techniques were created for application with the intent of “stimulating the uterus to retreat”, and as a last resort, succession, which was a method that included hanging women by their feet and bouncing them until the prolapse reduced. Following this procedure, women were bed-bound for three days with their legs tied together, as, by this point, the brightest minds of the time were convinced that the uterus was a rebellious, wondering animal that required taming [26], [29], [30].

Some gynecological practices were adapted by the Hebrews into their biblical texts, which are interpreted as divine edicts, and often reinterpreted through political or historically patriarchal lenses. Biblical texts define several circumstances in which women are “unclean”, such as during menstruation. Other passages describe “not bleeding from defloration” on the wedding night and prolapse as an indicators of female infidelity, which was punishable by death [24], [31], [32]. Through a scientific lens, these beliefs can arguably be interpreted as ostracizing and demeaning towards women and their bodies. Although these beliefs, laws, and edicts were created to promote positive hygiene and health, practices such as these have permeated countless cultural and religious practices and influenced global attitudes and perceptions surrounding the medical interpretation, diagnosis, and treatments for natural processes and disorders in women for centuries [25], [33]–[36].

Public knowledge and acceptance surrounding normal and abnormal biological processes and sexuality are still deeply influenced by taboos, myths, and misconceptions [37], [38]. This has led to young girls in South Africa missing up to 2.5 months of school due to scarcity of appropriate/effective measures for containing menstrual flow [39]. In Nepal, women are overtly isolated by their communities during menstruation for fear of contamination from uncleanliness, or fruition of superstitions [40]. In extreme cases, Nepalese women are forced to build their own huts and retreat to the wilderness, which has led to numerous deaths from accidents such as smoke inhalation, carbon monoxide poisoning and animal attacks [40]. Although laws have been created to make the ostracizing of women due to menstruation illegal, many women and families still believe in the ritual, despite the risks. Women are also ostracized due to physical symptoms of POP, and some husbands restrict their wives from receiving corrective medical treatment due to the need to abstain from sex during post-surgical recovery [38], [41]. In fact, reports have indicated that some women feel so isolated and in fear of losing their husbands, that they attempt to perform the surgery to correct the prolapse themselves, which often leads to death [41].

Religion and faith-based communities are important pillars of society, which provide comfort, instruction, and serve to communicate morality [42]. While there are several benefits, the early intertwining of medical treatments and religious beliefs has created challenges that still impact conversations regarding female pelvic anatomy and disorders today [42]–[44]. For example, in India, menstruation is still considered a major taboo[45], [46]. Women who are menstruating do not attend temple and are told that their prayers will not be heard during that time due to “pollution” or uncleanliness [46]. In the United States, both men and women have expressed discomfort when discussing female health and sexuality [47]. In fact, most religious groups and institutions do not promote topics surrounding anatomy beyond the concepts of abstinence and purity [44], [48]. To control the “situation”, religious and community leaders may employ fear tactics to minimize conversation and discussion of reproductive body parts and organs, particularly with youth [42]. The practice of withholding information and commanding obedience through fear results in a feeling of shame around topics of sex and sexuality which, in turn, creates a breeding ground for misinformation [49]. If societies struggle to accept healthy biological processes, how do they even begin to effectively identify, study, understand and treat disorders such as POP?

While tradition can impact our views of female pelvic health, the modern media also has a significant impact through its portrayal of societal norms. The media often depicts women as perfectly proportioned, airbrushed beings; whose bodies can “bounce back” from each pregnancy with ease. In fact, postpartum challenges experienced by women are frequent but rarely discussed, and often dismissed as “a female problem”. This encourages disassociation from female anatomy and health concerns among both men and women [50]. Thankfully, the conversation and interest regarding some of these topics is changing due to the outreach of highly successful and respected celebrities such as Beyoncé Carter, Serena Williams, Gabrielle Union, Chrissy Teigen, and many others. Using their celebrity as a platform, these women have emphasized the social implications of these unrealistic beliefs and expectations, by sharing their realities and struggles surrounding conception, infertility, and postpartum recovery [51].

Dismissive views regarding women's health are not limited to religion, culture, or the media, but can be found in medical and STEM fields as well, which were, and still are, male dominated. However, our perception of the necessity of diversity in science has shifted over the past several decades, given the scientific evidence that proves purposeful exclusion of diverse populations from the STEM workforce has negatively impacted the advancement of solutions that address the varied needs of populations [52]–[54]. Examples of everyday solutions that could have been more inclusive are seatbelts, manufacturing and drug dosing, and even building temperatures. While seatbelts are an incredible invention that undoubtedly save lives, they are safer for men than women. In fact, women are 47% more likely to be injured in a car crash than men, as crash test dummies that were used to understand impact forces during crashes used test dummies that mimicked the weight, height, and shape of the average male [55]–[57]. Women are more susceptible to chest and spine injuries because women are generally shorter and postured differently from men while sitting in a car. Many common drugs that are available over the counter worldwide were primarily tested on white males, which does not account for the fact that men, women, and children may respond to drugs differently [58], [59]. Even with concepts that seem as innocent as setting the temperature of a building, the standards for calculating HVAC systems were based on 1960s measurements of a 154 pound male, which is often why women feel much cooler in office and standard environments [60]–[62].

To fully comprehend the impact of the exclusion of diverse populations in science with respect to women's health and well-being, we must again visit the origins of these notions. Throughout our history, medical leaders, almost exclusively male, have used "science" to justify the inferiority of women [54], [63], [64]. Men were viewed as examples of perfection, while women were viewed as being weaker physically and emotionally, due to their "flawed anatomy".

For example, the vagina was believed to be an underdeveloped inverted penis, and women's bodies were viewed as leaky due to menstruation, and lactation [24], [30]. Menstruation was even viewed as a harmful expulsion of venom from the woman's body, capable of infecting all those around them [25]. Misconceptions such as these have significantly impeded scientific progress with respect to our clinical and scientific understanding of female anatomy and sequelae [65].

One area in which the study of female pelvic anatomy is significantly behind is in the application of bioengineering. Bioengineering describes the application of engineering concepts to the physiology of living species. Biomechanics is a branch within the field of bioengineering that aids in defining the mechanics of dynamic biological processes. Generally, the goal is to define normal function and identify root causes of abnormal function, thereby allowing clinicians to better treat, and even prevent, disease [66]. The application of biomechanics has led to a renaissance within several medical fields, including orthopedics, rheology, and cardiovascular medicine, resulting in solutions such as prosthetics, artificial limbs, extracorporeal circulation, rehabilitation techniques, and many others [66]. Given that the pelvic floor is the foundation of the human trunk, or body, one would expect that biomechanics has been undoubtedly applied to women's health. However, until recently, the application of biomechanics towards solving disorders of the pelvic floor was largely overlooked, in spite of the fact that women have unique and complex anatomies, that, unlike male anatomy and physiology, have the ability to grow and sustain life.

Over the last few decades, concepts of biomechanics have been applied to urogynecology to characterize the material and structural properties of the vagina, bladder, rectum, cervix, uterus, connective tissues and musculature of the female pelvis [10], [67]. Although our understanding of female anatomy has improved, there are still many important challenges left unexplored. Research remains underfunded relative to those issues resulting in male urogenital dysfunction [47]. The reality is that research is driven, in large part, by either public outcry or private interests. For example, the investment in ACL research alone, which is largely supported by the athletics industry, eclipses the entire investment in women's health [68]. Lacking private backing for this work, the advancement of this field hinges upon convincing the public that the long suffering of women deserves the same attention and public outcry as those issues impacting male anatomy.

This chapter offers a review of existing knowledge regarding the maturation, form, and function of female pelvic anatomy; the diagnosis and treatments for pelvic floor disorders (PFDs); and the challenges we currently face that impede progress, which served as motivation for this dissertation.

1.1 Maturation and Anatomical Development of Female Pelvic Anatomy: From Gestation to Adolescence

Human anatomical development is a remarkable process that initiates in utero and undergoes several morphological changes throughout the lifespan. In particular, the viscera, connective tissues, and musculature associated with female pelvic anatomy, undergo some of the most extraordinary changes of any tissue in the human body, many of which enable the continuation of the human species [69]. Analogous to how understanding the historical implications of our attitudes and beliefs regarding women contributes to the current climate, it is important to define and understand scientific factors that impact the development and functional capabilities of female pelvic health. Life events, hormones, genetics, and environmental factors can impact the development and functional capabilities that enable women to become pregnant, successfully develop and deliver their children, recover from the physical impact of childbirth, and transition through menopause into later life can all affect the ability to maintain pelvic health, quality of life, and longevity.

The differentiation between male and female begins after seven weeks gestation. Notably, the anlage of the female reproductive tract is the Mullerian duct system, which dictates structural and functional characteristics of what eventually differentiate into genitalia [70]. Malformations during this period are generally a function of Mullerian duct anomalies, which are the result of early developmental failure. Thus, Mullerian anomalies impact the structure and function of pelvic organs, which have been linked to agenesis or duplication of the uterus or vagina, anomalies that are often unnoticed until puberty [71]. The uterus and ovaries begin forming at approximately 63 days of gestation, and the genital track begins forming at approximately 80 days from gestation, forming the vagina and cervix following cellular proliferation by 20 weeks [72]. Between 20 and 22 weeks, the vagina and urethra separate into two distinct structures, the clitoris is formed, and ovarian follicular growth begins, concurrent with the development of external genitalia. Following birth, the female child’s body and viscera grow in size, however, no major changes occur to the female reproductive system until the onset of puberty. Puberty, or adolescence, is the transition period between childhood (prepubescence), and adulthood, and is driven by morphological and physiological changes, which typically occur between the ages of 13 and 19 [73]–[75]. A rise in levels of estrogen trigger the development of secondary sex characteristics, which include growth of the uterus, and menarche, widening of hips, and redistribution of fat [76]–[78]. These natural processes occur in preparation for reproduction and care of offspring [79].

1.2 Adult Female Pelvic Anatomy

Maturation into adulthood is marked by the onset of the menstrual cycle along with a peak in height, muscle, bone, and organ growth; and specifically in women, a fully developed pelvic floor that supports viscera through a complex highly interdependent network of muscles, connective tissues, and ligaments [75], [80]. However, the precise anatomy, physiology and function of this network is complex, and not completely understood.

We do know that approximately 4 million years ago, humans evolved into bipedal mammals, which required significant structural changes to pelvic anatomy [81], [82]. The pelvic floor in bipedal mammals serves as the primary load bearing structure for abdominal and pelvic viscera, unlike in quadrupeds, which rely on their abdominal wall for visceral support [81]. Thus, a discussion that defines the function and location of anatomical components establishes topical literacy, which serves as the foundation for the introduction and application of methods that enhance our understanding of the complex interactions of organs, musculature, and connective tissues, and our ability to improve our ability to quantitatively define female pelvic anatomy.

1.2.1 Bony Pelvis

The process of human evolution necessitated morphological alterations in pelvic bone structure and load bearing. Thus, the bony pelvis increased in physical size, and is shorter in the superior-inferior plane. In general, the orientation shifted from more coronal to more sagittal, which alters the position and location of viscera and musculature to support bipedal movement [81]. Typically, the bony pelvis is described as having four main parts: two hipbones, the sacrum and coccyx, which are collectively described as the pelvic ring [83]. With the onset of puberty and development, these four parts of the bony pelvis become more fused, which provide distinguishing anatomical differences in bony structure based on developmental stages (i.e., puberty and adults). Even through developmental changes, the bones of the pelvis are the least movable anatomical components in the body, which makes them ideal landmarks for comparative measurements between and within patients.

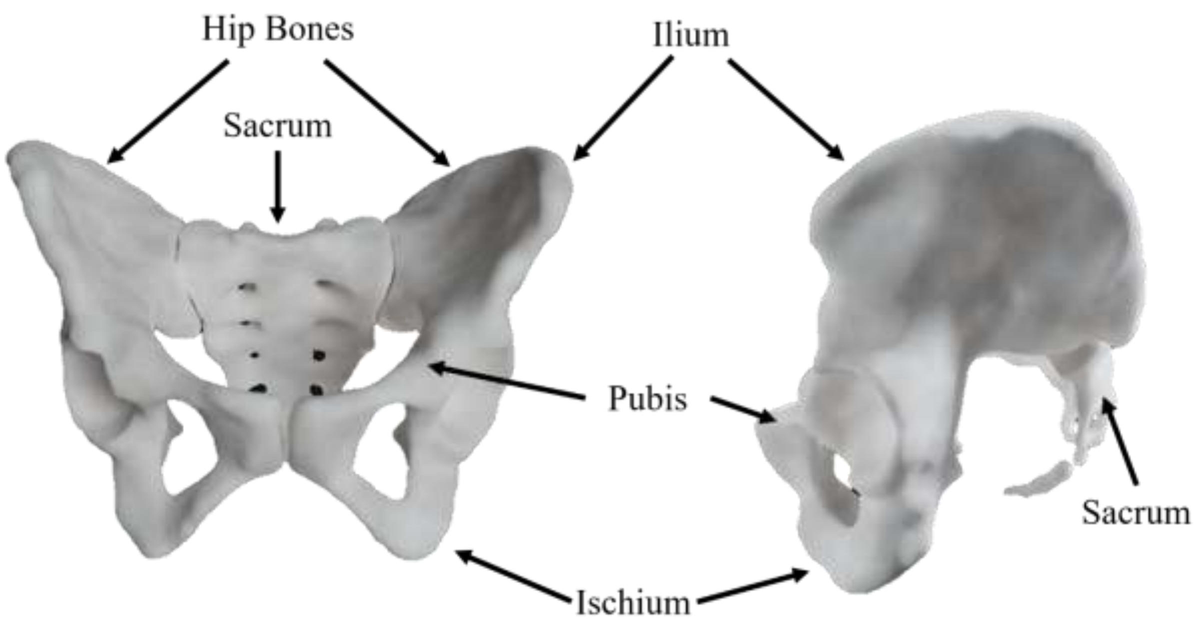


Figure 1 Frontal and side view of bony pelvis

The hipbones are symmetric, mirror images of each other, and can be further described as the ilium, ischium, and pubis, illustrated in Figure 1. The ilium of each hipbone articulates with the sacrum, which separates the hipbones posteriorly. The crest of each ilium is identifiable through placing hands-on hips. The human ilium has broad faces, which serve as insertions for muscles that support upright posture and abdominal viscera [81]. The pubis of each hipbone articulates at the pubic symphysis, which is a cartilaginous joint that connects the anterior portion of the hipbones, maintaining rigidity and allowing for little to no movement, and forming the pubic arch [84]. The pubic symphysis is oriented at approximately 45 degrees when standing, which enables it to provide support to pelvic viscera [81], [85]. Portions of this joint are wider in females, possibly to allow for some mobility, during events such as delivery [84], [86]. The ischium rests between the ilium and pubis, which together, create the hip bone, and is responsible for supporting weight while seated. Inferior to the fifth lumbar vertebra lies the sacrum, which contains five fused, and broad shield-shaped vertebrae. These vertebrae are frequently described as the “keystone of the pelvic ring”, as its position within the pelvis enables bipedal movement through the transfer and dissipation of forces between the ground and body [81], [84], [87]. The coccyx, or tailbone, articulates inferiorly with the sacrum forming the coccygeal joint, and is comprised of three to five vertebrae, which may separate early in life, and fuse with aging.

The morphology of the human pelvis exists in stark difference from other mammalian species, and has been associated with the “obstetrical dilemma”, which suggests that while human anatomy was optimized for bipedal motion through a narrower pelvis, this adaptation was not optimal for vaginal delivery [81]. Thus, in the 1930s, the female pelvis was classified into 4 distinct shapes, illustrated in Figure 2, based on the ratio between the anterior-posterior and transverse diameters as a means to assess the likelihood of successful vaginal birth [88], [89].

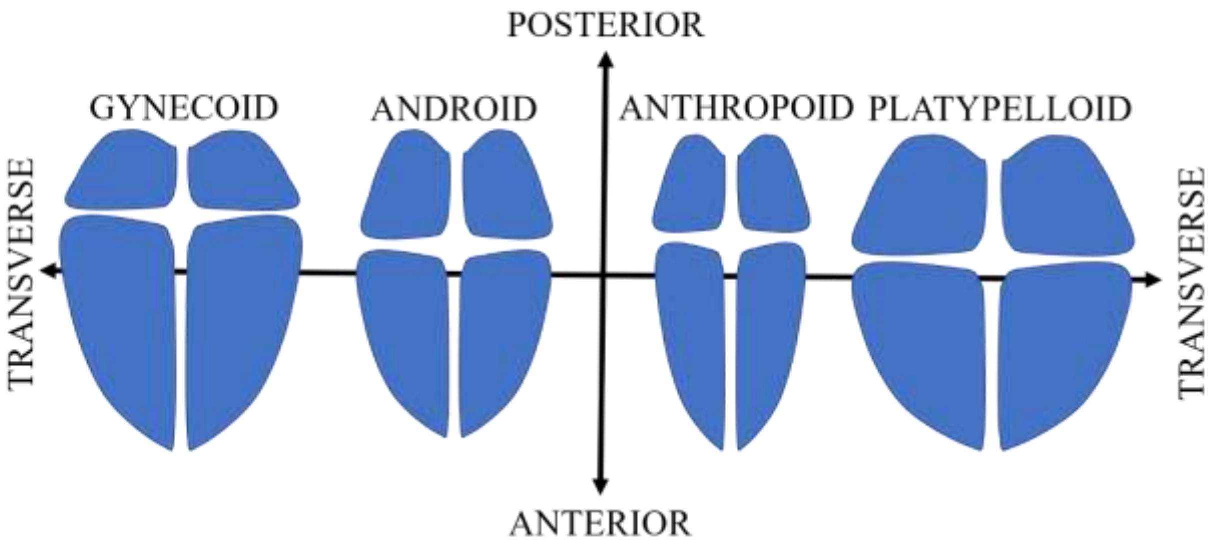


Figure 2 Illustration of female pelvic classifications, determined by the ratios between the anterior-posterior diameter and the transverse diameters.

Historically, these shapes: Gynecoid, Anthropoid, Android, and Platypelloid, were inappropriately used towards the agenda of racial stratifications, however, several studies have demonstrated that pelvic shape is a poor predictor of race, as the most common shape is Gynecoid, and is present among all races and ethnic groups [88]. Current research efforts seek to measure and define how pelvic morphology could contribute to maternal birth injuries and common pelvic sequela, as the shape of the bony pelvis provides the structure and origin/insertion points for pelvic floor musculature and connective tissues [90].

1.2.2 Musculature

Pelvic musculature is critical for several functions, including leg movement, maintaining bipedal stature, supporting pelvic viscera, maintaining continence, and resisting intrabdominal forces such as coughing, and childbirth [91]. Analogous to other muscles groups within the body, the pelvic region contains both skeletal and smooth muscle [92], [93]. By definition, these muscles provide active support, which means they can generate force through contracting and relaxing voluntarily or involuntarily, respectively [80], [94]. While it is common to refer to these muscles collectively as "pelvic muscles" or "pelvic floor muscles", the complexity of the interactions between these muscles and other components of the pelvis warrants a more detailed discussion of specific muscle locations and functions.

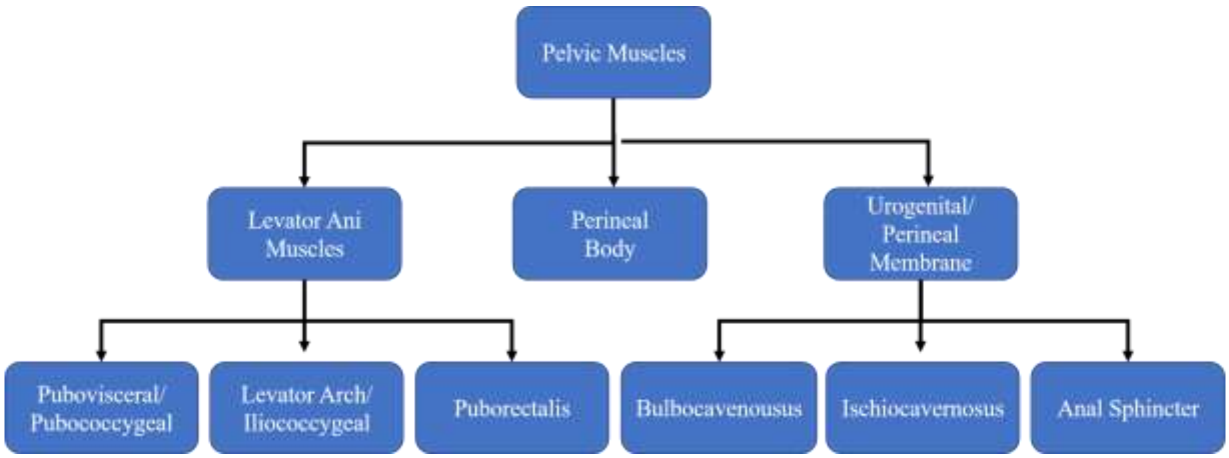


Figure 3 Subdivisions of Pelvic Musculature

Figure 3 illustrates the three distinct subsets of pelvic muscles are the pelvic diaphragm and the urogenital diaphragm. The pelvic diaphragm consists of the levator ani muscles, which are the amalgamation of several muscles that originate at the pubis (i.e. pubovisceral/pubococcygeal muscles, puborectalis muscle), and the levator arch (i.e. Iliococcygeal muscle) [95], [96]. The urogenital diaphragm, also referred to as the perineal membrane, contains superficial and deep muscles (i.e., Bulbocavernosus, Ischiocavernosus, and Anal Sphincter) that are penetrated by pelvic viscera (i.e., rectum, vagina, and urethra), shown in Figure 4. These striated muscles are critical for maintaining continence of excretory viscera, and providing structural support to the distal vagina [92].

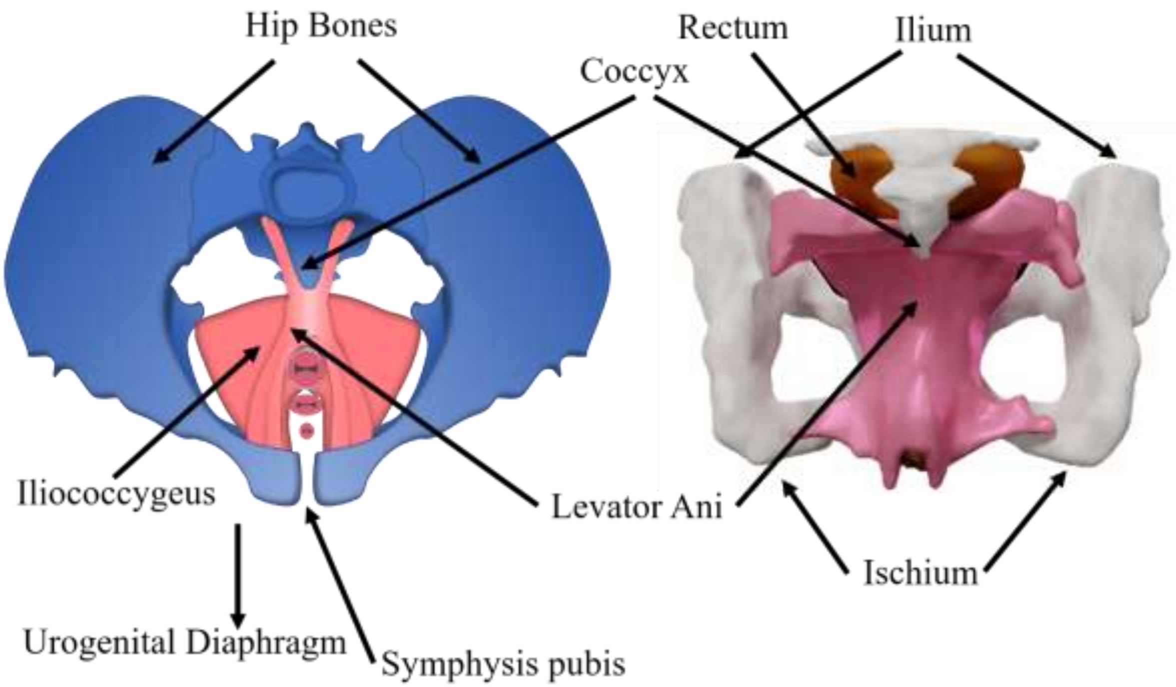


Figure 4 Axial view of urogenital muscles (left). Coronal and posterior view of Levator Ani muscles (right).

Given the mechanical importance of pelvic musculature, damage to one or more muscle groups can have significant consequences. Gestation and delivery are events that have the greatest potential to incur muscular injury due to the prolonged increased load on the pelvic floor, and significant stretch and strain, and potential laceration of muscles during delivery. The specific challenges associated with pregnancy and delivery will be discussed further in Section 1.2.5.

1.2.3 Female Pelvic Viscera

The pelvic cavity contains anterior and posterior compartments, which are separated by the vagina. The vagina is one of the most mechanically adaptable organs in the human body. It is the primary organ for female sexual function and provides passive mechanical support for the other pelvic organs (i.e., bladder, rectum, urethra, and uterus). This unique organ is fibromuscular, and expands exponentially to accommodate the event of childbirth, and remarkably returns to its original size [69], [94]. Furthermore, the shape, and width of the vagina changes significantly as it traverses the pelvis. Colloquial descriptors for vaginal shape include "H" and "W" shapes, which resemble open and collapsed positions [97]. Furthermore, several studies have hypothesized, and shown, that due to the non-uniform nature and complexity of vaginal shape and function, it is not possible to effectively characterize the vagina based on individual demographic characteristics [97]–[99].

Interestingly, the width of the introitus is significantly smaller than the apex, where the cervix is located. The cervix serves as an anchor for Level I support (Section 1.2.4), and facilitates transfer of content between the uterus and vagina connects the vagina to the uterus i.e. (menses, semen, fetus) [94]. The uterus, a usually pear-shaped (7.6cm long x 4.5 cm wide x 3.0cm thick) organ, and serves as the incubator for the development of a fetus from conception [10], [100], [101]. Thus, it is mechanically adapted to grow and stretch significantly during the nine-month gestation process, and contract during delivery. The uterus can also be anteverted, straight, or retroverted, and the position tends to vary, although most appear to be anteverted [102].

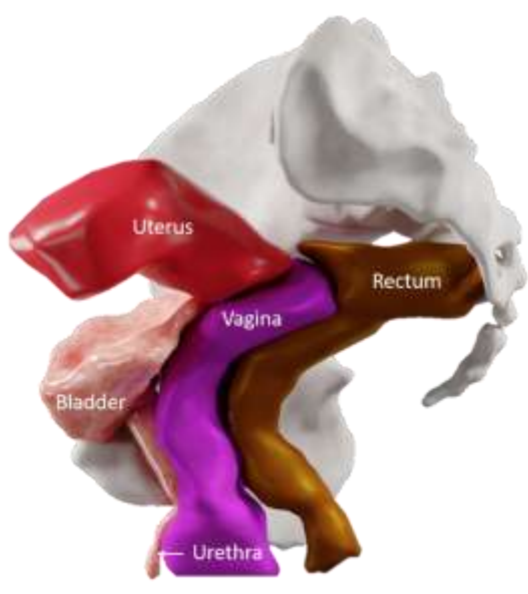


Figure 5 Sagittal depiction of female pelvic organs.

Generally, the pelvic organs can be described in terms of anterior and posterior compartments, which are separated by the vagina. The anterior compartment houses the bladder, and the rectum is located in the posterior compartment. The rectum and bladder are similar in that they both are organs whose primary function is to store and eliminate bodily excrement. Both organs are regulated by smooth muscle contractions that enable them to expand when more waste needs to be stored and return back to their original state following elimination. When the smooth muscles of these organs contract, they enable the elimination of fecal matter and urine, through the anus and urethra, respectively, and both organs return to their empty state. Directly inferior and connected to the bladder, the urethra serves as a passage way for urine to exit the body [94]. The bladder, urethra, rectum, and vagina are all supported by musculature described in Section 1.2.2. Their connective tissues and ligaments are described in Section 1.2.4. This network of support enables the approximate configuration illustrated in Figure 5, where pelvic viscera naturally fit together. While the support structures maintain this configuration and enable expansion and reduction of organ size, alterations in this complex support thereby alters the location and possibly orientation of pelvic viscera in such a way that can impact their function. Therefore, organ location and orientation could serve as a proxy for visualizing changes in muscle and connective tissue support.

1.2.4 Connective Tissues and Ligaments

A healthy, well-supported vagina offers complimentary support for pelvic viscera (i.e., bladder urethra, rectum and uterus). The vagina, in turn, is supported by the complex interactions between the levator ani muscles and connective tissue and ligament attachments between the vagina, other pelvic viscera, and the pelvic sidewalls [5], [103]. In humans, the connective tissues and ligaments of the pelvis provide the necessary forces to counteract gravity and intra-abdominal pressures, and prevent the pelvic viscera from falling out of the body [104]. Mechanically, these specialized tissues are passive, as they do not actively generate force and must be engaged through interaction to experience a force. Pelvic connective tissues and ligaments are comprised of collagen, adipose tissue, nerves, blood vessels, and lymphatics, and commonly categorized into three distinct levels of support - (I, II, and III), illustrated in Figure 6 [105].

Level I, commonly referred to as apical support, is arguably the most important level of support, and is comprised of the cardinal and uterosacral ligament (CUSL) complex. Notably, the physical presentation and structural properties of these pelvic ligaments starkly contrast ligaments in other parts of the body, such as the Anterior Cruciate Ligament (ACL) in the knee. Thus, applying graft replacement techniques that work well with knee ligaments may not lead to desired results [106], [107]. One leading theory suggests that optimal CUSL complex support results in the anchoring of the vagina towards the sacrum, and failure of this support system results in inferior movement of the vaginal apex and laxity of the anterior (cystocele) and/or posterior (rectocele) vaginal walls. For this reason, the apex (Level I) support is often referred to as the “keystone of pelvic organ support” [108].

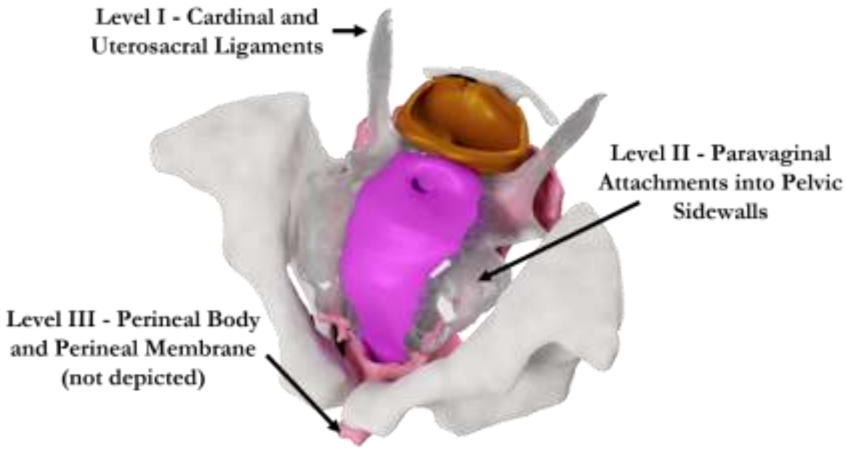


Figure 6 Subdivision of supportive connective tissue and ligament passive support.

Level II provides lateral support to the vagina through dense paravaginal (endopelvic fascial) attachments that connect to the muscles of the pelvic sidewalls [92]. These attachments are critical in not only maintaining the position and shape of the vagina, but aids, in maintaining the position of the bladder and rectum. Thus, changes in Level II support may also contribute to functional challenges that impact visceral function [109].

Level III is the most distal level of support and is positioned immediately above the hymenal ring. Here, the vagina fuses with the pubovisceral portion of the levator muscles, and the perineal body, serving as the final level of pelvic floor integrity, and the level that incurs the most direct trauma during labor.

1.2.5 Impact of Gestation and Delivery on Female Pelvic Anatomy

The development and delivery of infants is a remarkable process in mammals, especially humans. Following conception, the female body initiates a 9-month process of adaptation to accommodate the growth of the fetus. This adaptation is mediated through hormonal fluctuations that results in significant structural and mechanical tissue changes. During the third trimester, the uterus expands to house the growing fetus, which restricts the bladder pelvic and other pelvic viscera due to lack of space. Other changes that occur include changes in joint laxity (as a result of hormonal changes), and an anterior shift of center of gravity and pelvic tilt, which contributes to increased curvature of lumbar vertebrae. All of these changes alter the mechanical load on pelvic musculature and connective tissue supports [80], [110]. In fact, it is not uncommon for pregnant women to report urinary incontinence, as well as urgency during pregnancy as a likely result of increased intra-abdominal pressure and decreased bladder capacity these mechanical shifts. In fact, recent data suggests that women with urinary incontinence in pregnancy are much more likely to have incontinence one year postpartum [7], [8].

Vaginal delivery necessitates significant vaginal canal expansion longitudinally and circumferentially to aid passage of the fetus [92]. In fact, the vagina expands 4-8 times its average size [70], [111]. The distal vagina is integrated central to the perineal membrane, which, along with Level III tissues, and maintains distal support for the vagina and other viscera. During childbirth, the perineal body and levator ani muscles distend to aid the passage of the fetal head, and ideally, return to their pre-pregnancy positions post-partum. However, many women experience vaginal birth injuries (VBIs), especially during births that have lengthy second stages of labor, or conversely, a precipitous second stage of labor. This is believed to be due to the strain to muscles and connective tissues and can lead to common injuries include tearing (i.e., perineal tears) and stretching (i.e., levator avulsions). If injuries are severe or heal improperly, the sustained alterations to pelvic mechanics can contribute to impeded visceral function [112].

1.2.6 Impact of Aging on Female Pelvic Anatomy

Aging is a dynamic and natural process experienced by all biological organisms, albeit at markedly varying rates. Hallmarks of aging include the progression and decline of physiological integrity and reproductive fitness, as well as declined or impaired cellular function, which are ultimately driven by changes in hormone production and collagen ratios within the extracellular matrix (ECM) of tissues [113], [114]. While menarche marks the completion of reproductive development in women, menopause marks the senescence of their reproductive capabilities through reductions in progesterone and estrogen levels [115]–[117]. Thus, menopause is commonly linked with aging, due to the average onset of menopause occurring between ages 45-55, and per the National Institute of Aging, the average age for the onset of menopause in the United States is 51 [116], [118].

Elastin is a protein that provides elasticity and recoil characteristics that help maintain the structural integrity of the vagina [119]. Evidence suggests that aging is associated with a decrease in elastin density, which thereby increases the stiffness of vaginal tissues. Furthermore, the gradual reduction of hormone production is concomitant with changes in the ratios of collagen content, which also provide mechanical integrity to the extracellular matrix of tissues flexibility [119], [120]. There are several types of collagen in the body. Pelvic tissues primarily exhibit Collagen I, which provides structure and tensile strength, and Collagen III, which provides flexibility to the tissues[119], [121], [122]. Thus, the ratio of Collagen I/(III+V) directly influences the mechanical integrity of tissues. Vaginal stiffness increases with age, as a result of collagen deposition (fibrosis), glycation end products, and degradation of Collagen I. Age-associated changes combined with long-term effects of direct trauma (i.e. VBIs), and/or repetition of activities that create sudden or prolonged increases in intra-abdominal pressures (i.e. coughing, lifting, straining, multiple births, etc.), can contribute to a decrease in the mechanical integrity of the supportive tissues of the pelvis, which can impair visceral functions [103], [123], [124].

Improvements in scientific knowledge, technologies, and health awareness have increased overall life expectancy, which has also contributed to an unprecedented shift in demographics characterized by significant growth in the elderly population [117]. Naturally, this population growth would warrant greater attention towards improving quality of life for the elderly, and enhancing our understanding of challenges that plague this population in order to improve quality of life for future generations [125].

1.3 Pelvic Floor Disorders (PFDs)

The functions and relative locations of pelvic viscera, musculature, and connective tissues are summarized in Section 1.2. Markedly, the vagina is positioned centrally within the pelvis, and is supported by a complex network of muscles and connective tissue attachments that insert into the pelvic sidewall [5], [103]. Damage to this complex network can result in the development of pelvic floor disorders (PFDs) [126]. PFDs can be categorized as anatomical defects, such as Pelvic Organ Prolapse (POP), or functional conditions, such as Urinary Continence (UI) or Fecal Incontinence (FI). In this context, anatomical defects are characterized as physical or structural abnormalities concerning the body, while functional defects are defined as deviations from optimal function within the body. PFDs are often concomitant, which further obscures the etiologies of these conditions [127]. In 2008, the Pelvic Floor Disorders Network (PFDN) reported that approximately 25% of women 20 and older experience symptoms of at least one PFD during their lifetime [1], [128]. Of these women, the lifetime risk for reconstructive surgery is 12.6%, and the risk for repeat surgery due to failure or complications is approximately 40% for native tissue repairs [2], [11], [128]–[130]. The risk for recurrence increases to 60% by 7 years [129], [130]. More alarmingly, the prevalence of PFDs is steadily increasing due to an aging population, coupled with economical inflation of treatment costs; which are expected to double over subsequent decades [12], [19], [131], [132]. Thus, PFDs are, and will continue to be, a global public healthcare concern [19].

1.3.1 Pelvic Organ Prolapse (POP)

Pelvic Organ Prolapse (POP) is an anatomical defect characterized by the failure of the active and passive soft tissue support of the vagina. These defects cause the pelvic organs (i.e. bladder, rectum, uterus), to descend into the vaginal cavity, causing an outward protrusion or bulge [5], [6], [133], [134]. Approximately 50% of American women who are 50 and older are affected by POP, with lifetime prevalence estimates between 30% and 50% [12], [135]. By the year 2050, it is estimated that the incidence of POP will increase by 46% [12], [37]. Physical symptoms of POP include urinary and fecal incontinence, the sensation of a bulge in the vagina, pressure in the pelvis, sexual dysfunction, and obstructed urination/defecation. Regardless of the age at which prolapse develops, the physical symptoms quickly translate to emotional symptoms for many women, including social isolation, anxiety, and depression, which impairs quality of life for women and their families [16], [17], [20], [136].

Table 1 Prevalence of Prolapse among Parous Women, data from Swift et. al [137]

Prevalence of Prolapse Amongst Parous Women	
Stage 1	30%
Stage 2	55%
Stage 3	3%
Stage 4	1%

POP is commonly described using the POP-Q, a clinical method described in section 1.3.3. There are 5 categories or stages associated with POP, with 0 representing no measurable vaginal descent, and stage 4 representing complete vaginal eversion, illustrated in Figure 7. The development of a clinical method for characterizing prolapse has resulted in several studies, such as the study summary in Table 1, which summarizes the prevalence of prolapse in parous women from the Pelvic Health Network (PHN) study. The table suggests that milder forms of POP are very common (i.e., stages 1 and 2), and more severe cases tend to be rarer (i.e., stages 3 and 4). However, questions such as what factors specifically contribute to clinically significant POP, and effective methods to predict if mild POP will progress to severe POP, or vice versa, still remain unclear [138].

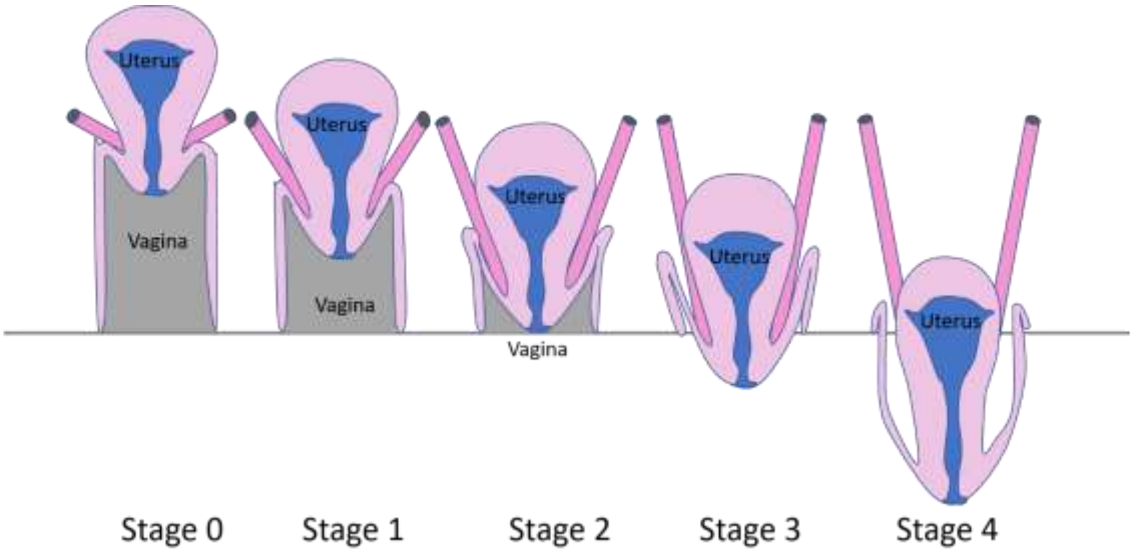


Figure 7 Schematic illustrating the stages of prolapse; uterine prolapse pictured here.

Current theory suggests one of the critical components of vaginal support is the CUSL complex, described in Section 1.2.4, which provides support to the vaginal apex. When properly functioning, the CUSL complex pulls the vagina up and back toward the sacrum at an angle of approximately 45^o relative to the levator ani muscles. Failure of this complex results in loss of the vaginal angle and movement of the vaginal apex toward the introitus, which in turn causes laxity of the anterior (cystocele) and/or posterior (rectocele) vaginal walls [105]. In fact, descent of the anterior vaginal wall is cited in approximately 83-87% of POP cases [105]. In addition to these common forms of prolapse, enterocele (prolapse of the intestines), uterine prolapse (prolapse of the uterus), and vaginal prolapse (prolapse of the vagina) can occur as well [139]. Although POP has impacted women at least as long as the earliest written records, the etiology is poorly defined due to an incomplete understanding of how identified risk factors impact the complex interactions of pelvic organs, musculature, connective tissues, and events over the lifespan of women [11], [127], [140].

1.3.2 Risk Factors for POP

The precise etiology of POP is poorly defined due to events linking vaginal birth to prolapse later in life remain elusive. Epidemiological studies suggest that significant risk factors for POP include, parity, age, obesity, maternal birth injuries, diabetes, connective tissue disorders, neurological diseases, and menopause [10]. Here, we will focus on parity/maternal birth injuries, age/menopause, and obesity/prolonged increase in intrabdominal pressures.

Section 1.2.5 explores the impact of pregnancy and delivery on pelvic viscera and support structures. Parity is defined as the number of successful births, and vaginal parity is recognized as the leading risk factor for the development of POP, as approximately 50% of vaginally parous women develop prolapse [137], [141]–[143]. However, estimates of prolapse prevalence vary due to multiple definitions for defining characteristics of prolapse. Figure 8, which was adapted from Mant et. al (1997), illustrates a positive correlation between the number of births and the relative risk for developing prolapse. Given the myriad chemical, mechanical and structural changes needed to prepare the body for a nine-month gestation and subsequently birth, the correlation between vaginal parity and symptomatic prolapse is not surprising. Another study conducted by Ashton-Miller & DeLancey in 2009 based on Mant et. al (1997), found that women who have given birth once are 4 times more likely and women with two births are 8.4 times more likely to develop POP warranting admission to the hospital compared to nulliparous women. Notably, most vaginally parous women develop some degree of prolapse, as described by the PHN (Table 1) [137], [138]. However, even with 0 births, there is still an 1.8% risk of developing prolapse later in life [142]. This suggests that other factors contribute to the onset of prolapse, requiring a more complex and robust understanding of female pelvic anatomy over the lifespan.

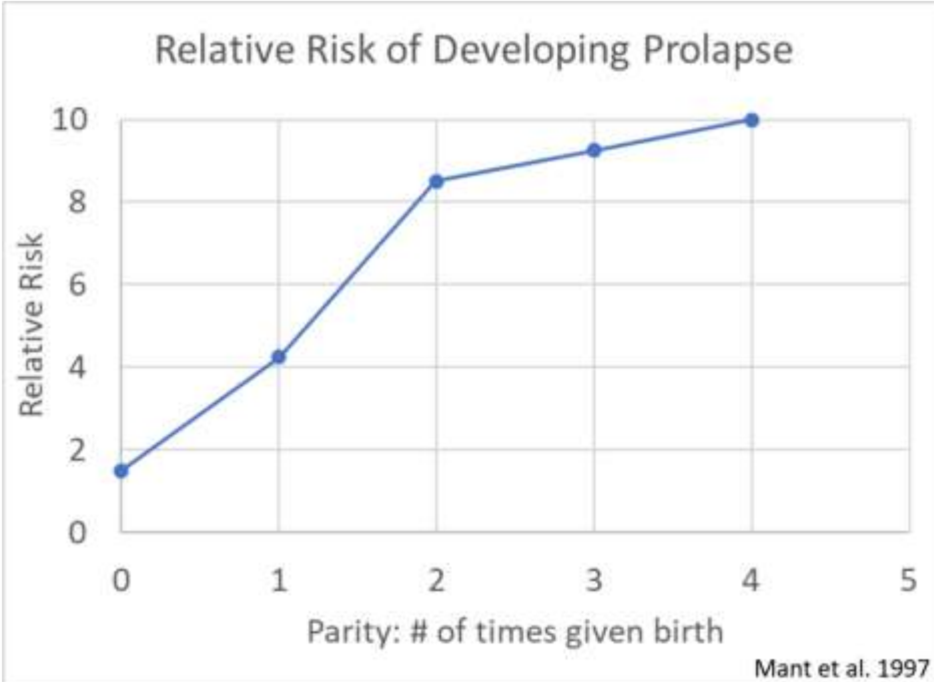


Figure 8 Relationship between parity and the relative risk for the development of prolapse

Obesity is defined as excessive body fat that negatively impacts health through causing strain on body systems, leading to an increased likelihood of developing serious health conditions and life-threatening illnesses, such as cardiovascular disease [144]. Furthermore, obesity increases inflammation and inflammatory mediators, glycation end products, as well as other nonmechanical events that contribute to poor health. Obesity is a growing epidemic, with rates of child and adolescent obesity doubling over a single generation [145], [146]. Several studies have examined the potential impact of weight gain on the eventual development of prolapse. Given the lens of biomechanics, we can view the musculature of the pelvic floor, which are responsible for providing support to pelvic organs, and resisting intra-abdominal pressure from events such as coughing, would be placed under great strain from excessive fat; or fat that does not play a functional role in maintain healthy equilibrium within the body.

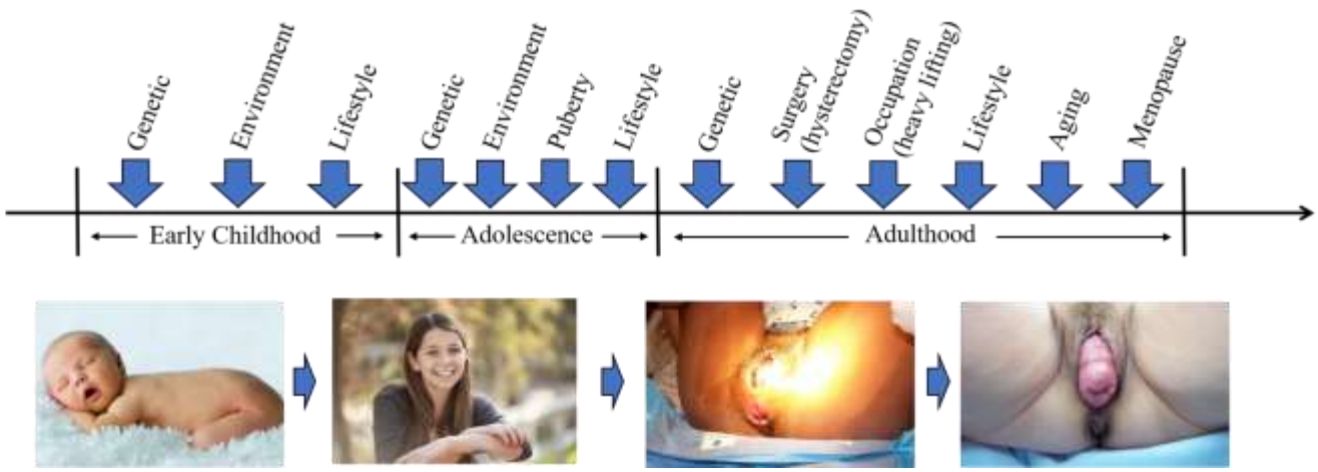


Figure 9 Visual depection of natural history timeline of life events that have been linked to symptomatic POP

Occupations that require heavy lifting also induce significant intraabdominal pressures. Once the physiological threshold is reached, pressures greater than this limit can cause injury to the connective tissues and musculature supporting pelvic organs. This is quite common in areas such as Nepal, where women are valued based on their work productivity, which can require full workdays of carrying, lifting, and moving heavy items over long distances [38].

Aging is identified as a secondary risk factor in the development of POP, as a result of changes in mechanical integrity of the support structures described in section 1.2.6. For example, well supported women experience changes such as a decrease in vaginal length and width coupled with stiffer vaginal tissues as a result of aging. For many, these adaptations yield the bothersome physical symptoms associated with PFDs. However, the challenge remains in pinpointing precise mechanisms that contribute to the gradual development of symptoms that reduce quality of life. Despite our best efforts, female pelvic anatomy remains one of the most complex biological systems to unravel. From birth, genetics and environment play a critical role in the ability for the body to adapt and recover from events such as those described in Figure 9. Furthermore, the primary risk factor, parity, and VBIs often occur 20-40 years prior to the appearance of physical symptoms, although increased likelihood for symptomatic POP does not guarantee symptomatic POP, nor does low likelihood prevent symptomatic POP [67], [147], [148].

1.3.3 Clinical characterization of prolapse: POP-Q Exam

Clinical methods for diagnosing and assessing PFDs include physical examinations and diagnostic imaging. The following section will explore these methods and the limitations that impede our ability to fully characterize the nature of POP [149].

Pelvic organ support is most commonly assessed through standardized POP Questionnaire (POP-Q) physical examinations. It was primarily developed to provide clinicians with a method to describe the appearance of a patients prolapse. Descent of pelvic organs is quantified through measuring distances in the anterior, posterior and apical vaginal compartments relative to the hymen, which is thin tissue around the vaginal introitus [150], [151]. These exams are performed in a physician’s office and are measured at maximum Valsalva except for total vaginal length (TVL).

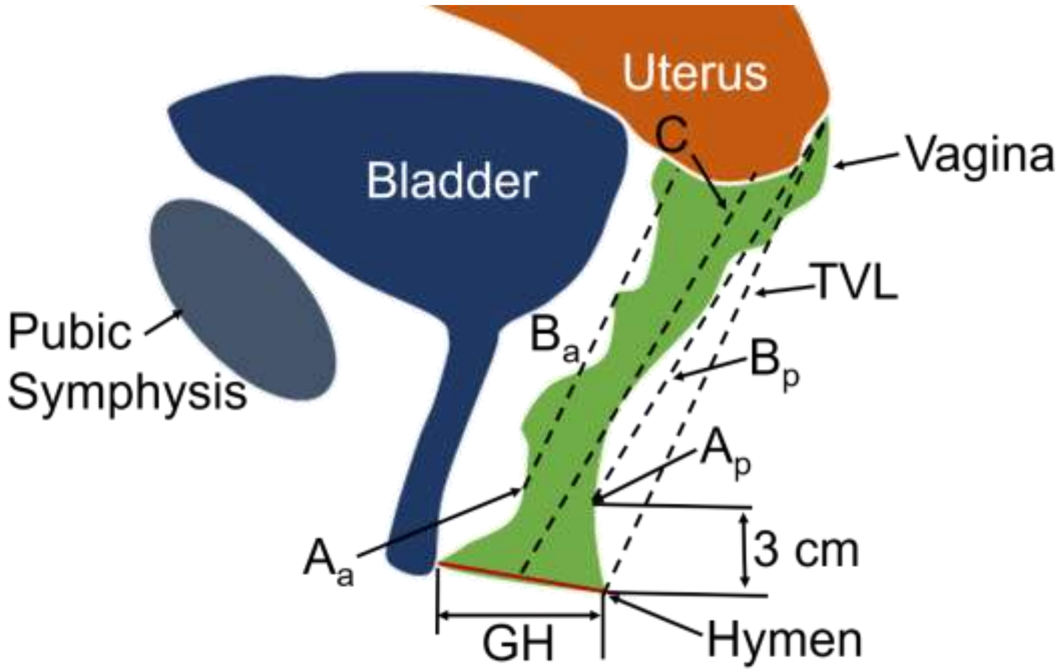


Figure 10 Visual depiction of POP-Q measurements.

Figure 10 is a sagittal representation to illustrate the measurements necessary for a POP-Q exam [151]. The genital hiatus (GH) is an external measurement that spans the external urethral meatus to the posterior hymen midline. The perineal body (PB) is also an external measurement, spanning the posterior margin of the GH to the middle of the anus. Total Vaginal Length (TVL) is an internal measurement that measures the total length of the vagina. The next 6 points are internal measurements, with respect to the hymen. C represents “the most distal edge of the cervix”, while D represents the position of the posterior fornix. Aa and Ba represent the position of the anterior and posterior vagina 3cm proximal to the hymen ranging from -3cm (perfect support) to +3cm. While negative values represent position above the hymen, positive values represent points beyond the hymen. Ba and Bp represent the measurement of the most distal point of the remaining anterior and posterior vaginal walls beyond Aa and Ap respectively. B ranges from –3cm to TVL. Based on the measurements obtained from the POP-Q exam, prolapse can be categorized into 5 stages ranging from Stage 0 (no loss of support) to Stage 4 (complete vaginal version) [151]. Table 2 demonstrates the characterization of POP-Q measurements into stages.

Table 2 POP-Q Staging Criteria, described in Bump et. al.

POP-Q Staging Criteria	
Stage 0	Aa, Ap, Ba, Bp = -3 cm and C or D ≤ -(TVL - 2) cm
Stage 1	Stage 0 criteria not met and leading edge < -1 cm
Stage 2	Leading edge ≥ -1 cm but ≤ +1 cm
Stage 3	Leading edge > 1 cm but < (TVL - 2) cm
Stage 4	Leading edge ≥ (TVL - 2) cm

REFERENCE: Bump RC, Mattiasson A, Bo K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfuction. Am J Obstet Gynecol. 1996; 175:13.

While POP-Q measurements provide a fairly quick, clinically relevant, and quantitative description of the severity of POP, the system has several limitations. Given that the POP-Q exam is a physical exam, it can only provide information based on an external view, and little information regarding underlying structures. This limitation contributes to the lack of sensitivity in detecting subtle anatomical changes (i.e. early stages of prolapse), which can contribute to underestimations of prolapse severity or complexity [138], [152], [153]. In fact, Karp et. al. determined that "eyeball" estimations of POP-Q values provide comparable results to the full POP-Q exam [154]. Furthermore, studies indicate that POP-Q measurements can vary significantly depending on patient position, patient activity during the day, and clinical examination techniques, ultimately limiting relevant comparisons between patients [150], [155]. Nonetheless, this exam has been utilized by several researchers to elucidate the natural history of pelvic organ support through periods of gestation and menopause [138], [156].

1.3.4 Treatments for POP

A range of treatments exists for POP, and the use of treatments is determined by the severity of the prolapse, age of the patient, and doctor preference. Conservative methods for treating POP include lifestyle/behavioral modifications, pelvic muscle physical therapy training, and pessary use [1].

Lifestyle/behavioral modifications would be adequate for patients who suffer from mild prolapse (i.e., Levels 0 and 1), or patients with concerning habits that have been identified as potential contributors to the onset of POP. Given that obesity has been cited as a risk factor for POP, weight loss is a behavioral modification that could help prevent the onset of POP or cease the progression of POP. Sustained increases in intra-abdominal pressures could be induced by several habits, which include but are not limited to persistent coughing, heavy lifting, frequent constipation, and many others. Addressing the causes of coughing and constipation would decrease instances of high intra-abdominal pressures, thereby reducing unnecessary stress to the pelvic floor. Significant evidence suggests that heavy lifting and prolonged manual labor, is a major contributor to the onset of POP, thus, reducing physical loads could reduce the risk of developing prolapse [38].

Pelvic floor muscle training (PFMT), is a conservative method developed to target and strengthen pelvic muscles, and reduce the progression of mild PFDs, though the specific impact on POP remains unclear [157], [158]. Pessaries are medical devices that can be inserted into the vagina to provide temporary mechanical support to prolapsed viscera [159]. There are several types of pessaries, such as the ring pessary (Figure 11), and selection is dependent upon the progression of physical symptoms.

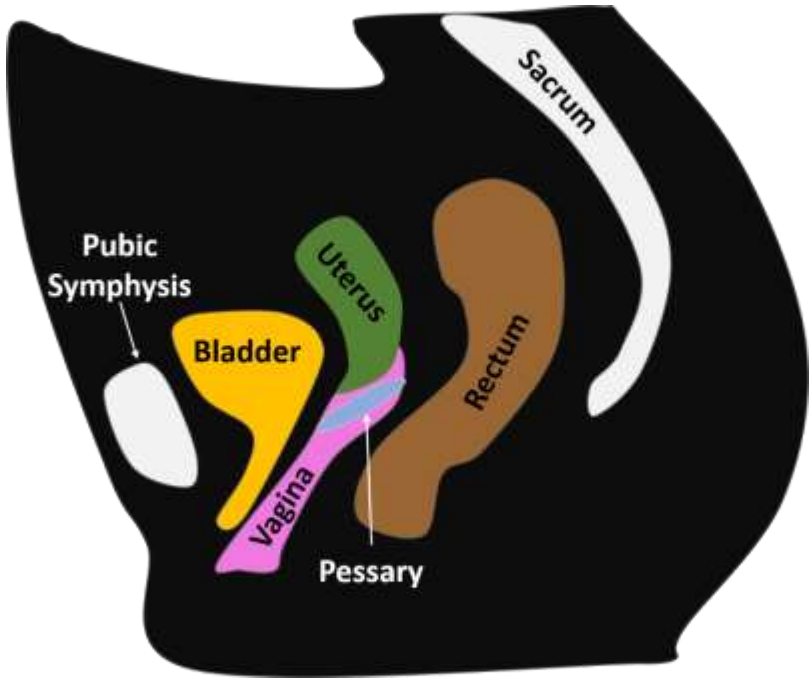


Figure 11 Example of placement of a pessary.

Soranus of Ephesus is credited with developing the first surgical treatment (i.e. a hysterectomy for uterine prolapse) in 120 AD [12]. Today, the goal of surgical treatment is to restore anatomy, or repair anatomy to its original/proper state. Given that POP is characterized as damage or compromised support to the musculature and connective tissues that support the vagina, these surgical procedures aim to add supports for the vagina, with the intent of restoring healthy function through the elimination of physical symptoms.

Surgical interventions can use a patient's own tissues to reconstruct support, the so-called native tissue repair. Common apical support (Level I) native tissue repairs include suspension of the vaginal apex to the uterosacral or sacrospinous ligaments [160]. If a bulge persists following an apical support procedure, surgeons plicate the adjacent fibromuscular tissue to reduce the bladder (cystocele repair) or the rectum (rectocele repair). Approximately 300,000 such native tissue repairs are performed in the United States each year to repair POP, which, according to the PFDN, 40% will fail within 2 years, and 13% of patients will undergo repeat or additional surgeries within five years [15], [161]. This is likely due to our incomplete understanding of the pathologies that led to compromised support in the first place, thereby compromising our ability to perform surgeries that are truly anatomical. Given the relatively high failure rates associated with native tissue repair, synthetic meshes are commonly used to restore anatomy by supporting the vagina and pelvic organs. Approximately 1/3 of the aforementioned surgeries utilized synthetic meshes. Meshes are made of polypropylene, and can vary in overall shape and size, as well as pore density and orientation [162]–[164]. The 1976 medical device amendment act, which allowed medical devices to be repurposed for similar use without premarket testing, enabled vaginal meshes to be adapted from abdominal hernia meshes [165]–[167]. In fact, the meshes used to repair both abdominal hernias and prolapse are the same.

Two of the most common surgeries that utilize meshes are abdominal sacrocopolpexy and vaginal colpopexy procedures. The abdominal sacrocolpopexy procedure is the gold standard procedure [168]. For this procedure, which is performed through a minimally invasive abdominal approach, following a hysterectomy, a strap of mesh between the bladder and the vagina, and a second strap between the rectum and the vagina (shown in Figure 12). The two straps are then attached to the longitudinal ligament of the spine at the level of the sacrum through a common stem. Thus, the vagina is lifted back into its position in the pelvis and attached to the sacrum via a mesh bridge. While this procedure yields anatomical success rates of 80-95%, its complexity and potential for significant morbidity makes it challenging to perform. Transvaginal colpopexy was developed as a safer easier approach in which mesh is attached to the vagina and then the pelvic side wall and/or the sacrospinous ligament via a vaginal incision. Although easier to perform, this surgical method only has a success rate of 70-85%, and a higher risk of complications. Reported complications include pain, mesh shrinkage/contraction, exposure, encapsulation, erosion, and infection. Given the severity of these complications the FDA issued public health notifications in 2008, and 2011 to warn patients of the risks associated with mesh repair [169]–[171]. The meshes were upgraded from Class III to Class II devices in 2018 requiring industry to perform premarket clinical trials proving efficacy over native tissue repairs and comparable safety outcomes. When industry failed to do this by a congressionally mandated time point, the FDA mandated that manufacturers of transvaginal meshes stop selling and distributing their products immediately. As a result, there are now fewer surgical options for surgeons and their patients.

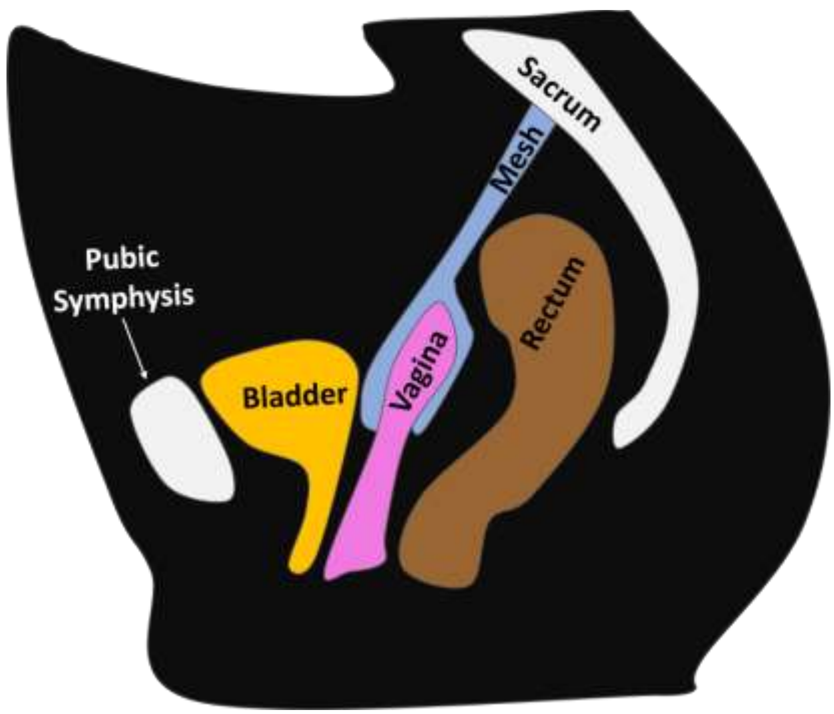


Figure 12 Example of mesh placement for abdominal sacrocolpopexy.

Although the both abdominal and urogenital prolapses occur due to compromised or weakened support, and even appear to have similar “bulges”, the mechanisms that contribute to these disorders are vastly different; indicating an urgent need for studies and solutions that are specific to pelvic organs.

1.3.5 Application of Diagnostic Imaging Towards the Characterization of POP

Since the 1980s, the advancement of technology and electronics shifted our capabilities for understanding POP and related disorders through the advancement and application of non-invasive imaging techniques. Non-invasive imaging of patients with POP is increasing in popularity and sophistication for both the diagnosis and assessment of surgical procedures, as well as the relationship between function and anatomy. Computed Tomography (CT), ultrasound, and Magnetic Resonance Imaging (MRI) are the most common diagnostic imaging tools used to visualize pelvic anatomy. While CT is effective in capturing the bony pelvis, it can be challenging to parse out the boundaries of soft tissue structures such as the vagina; thereby limiting its effectiveness for visualizing the pelvic floor in its entirety. Figure 13 provides a pictorial comparison of each imaging technique. Figure 13c, which depicts a CT image, specifically illustrates the clear boundaries of bones, but minimal visualization of soft tissue borders. Furthermore, CT images are captured through X-ray beams, which exposes patients to moderate or high doses of radiation; of which prolonged exposure can contribute to other health challenges.

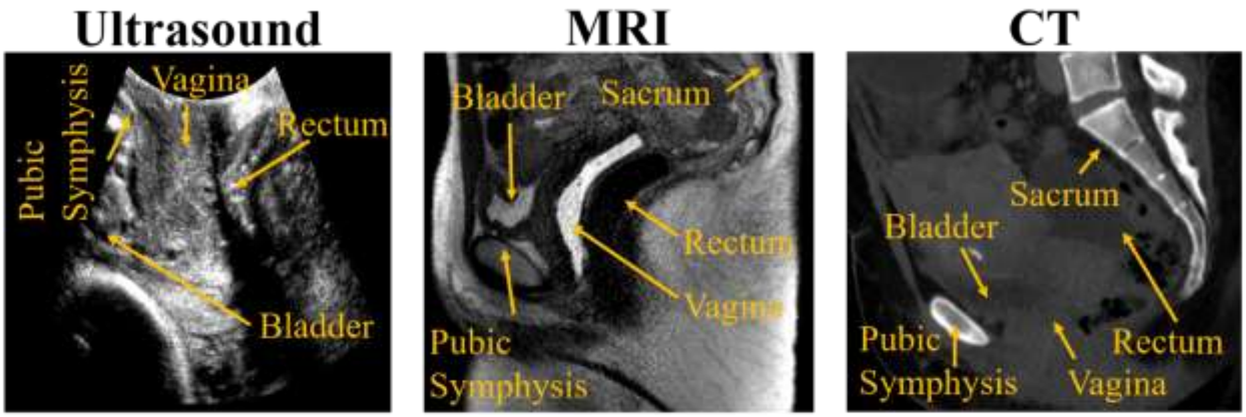


Figure 13 Ultrasound [left] versus MRI [center] versus CT [right] visualization of pelvic soft tissues

3D ultrasonography is another imaging modality that addresses many of the aforementioned challenges associated with CT, with the additional advantage of visualization of structures in real time. It is most commonly used to visualize the progression of pregnancy, however, scientific publications involving the use of 3D ultrasonography for evaluation of pelvic floor disorders has undergone exponential growth in recent years [172]. The increasing availability of ultrasound equipment in the clinical setting, and the recent development of 3D and 4D ultrasound technologies have stimulated interest in using this modality to image pelvic anatomy and understand pelvic floor dysfunction [173], [174]. 3D endovaginal ultrasound (EVUS) is widely accepted by international societies because of its ability to precisely visualize detailed anatomy of pelvic floor structures in the anterior and posterior compartments, as well as levator ani muscle subdivisions [172], [175]. Figure 13 (left) illustrates visualization of pelvic organs through ultrasound imaging. Additionally, excellent inter-and intra-rater reliability was demonstrated for identifying normal and abnormal pelvic structures with this modality [176], [177]. Transperineal Ultrasound (TPUS) is a leading method for assessment of pelvic floor injury [178]. Applications of this technology enable clinicians to visualize the structure and analyze changes in function with complex pelvic floor anatomy [174], [178]. For example, the ability to visualize the anterior and posterior compartments of prolapse, as well as provide visualization of mesh dislodgment or muscle avulsion enables clinicians to develop a more accurate assessment of damage to the pelvic floor [153], [179]–[181].

One of the primary concerns regarding the endovaginal ultrasound approach versus a translabial or TPUS approach is the distorting effect that the vaginal probe could have on the targeted tissues of the pelvic floor [174], [182]. In particular, the insertion of a vaginal probe can cause anatomical distortions that may interfere with clinical diagnoses. While geometric changes in the vagina are indeed likely because insertion of a straight probe will cause the vagina to tend to assume the probe's shape, it remains unclear what, if any, impact this imaging modality has on the other pelvic organs that can be easily visualized with this approach (urethra, rectum, levator ani muscles).

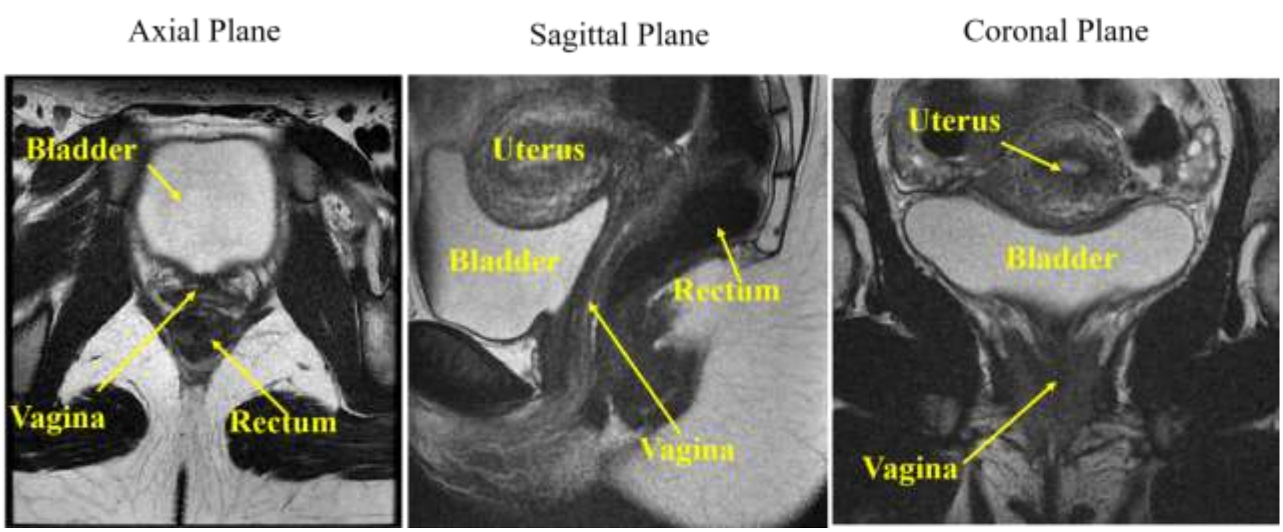


Figure 14 Visualization of axial, sagittal, and coronal body planes of female pelvic MRI.

MRI is a diagnostic imaging technique that utilizes magnets to produce detailed images of soft tissues and bones, while affording the ability to quantify the progression of pathologies [168], [183]–[185]. MRI has served as the gold standard of pelvic imaging, as it provides clinicians with a large field of view and relatively good tissue contrast, allowing for the complexity of the pelvic floor to be visualized as an integrated system [186]–[188]. Furthermore, the capability of generating image volumes in each anatomical direction (i.e. axial, sagittal, coronal) enables researchers and clinicians to develop detailed and anatomically accurate 3D computer models [189], [190]. These models can then be utilized in finite element analysis or statistical shape modeling methods; both of which combine existing knowledge of pelvic floor tissue mechanics and morphology to define, control, simulate, and predict *in vivo* scenarios for the purpose of improving individualized patient care. [191]. Unlike ultrasound technology, which captures images in real time, MRI technology requires significant space, powerful magnets, and computer technology; all of which are costly to implement and maintain. Furthermore, this method of diagnostic imaging requires patients to remain still for extended periods of time in order to capture enough information to generate images with the level of detail necessary to diagnose conditions. Generally, the type of sequence and level of image detail required dictate the amount of time necessary; with greater detailed images requiring significantly more time, which in turn, requires more money.

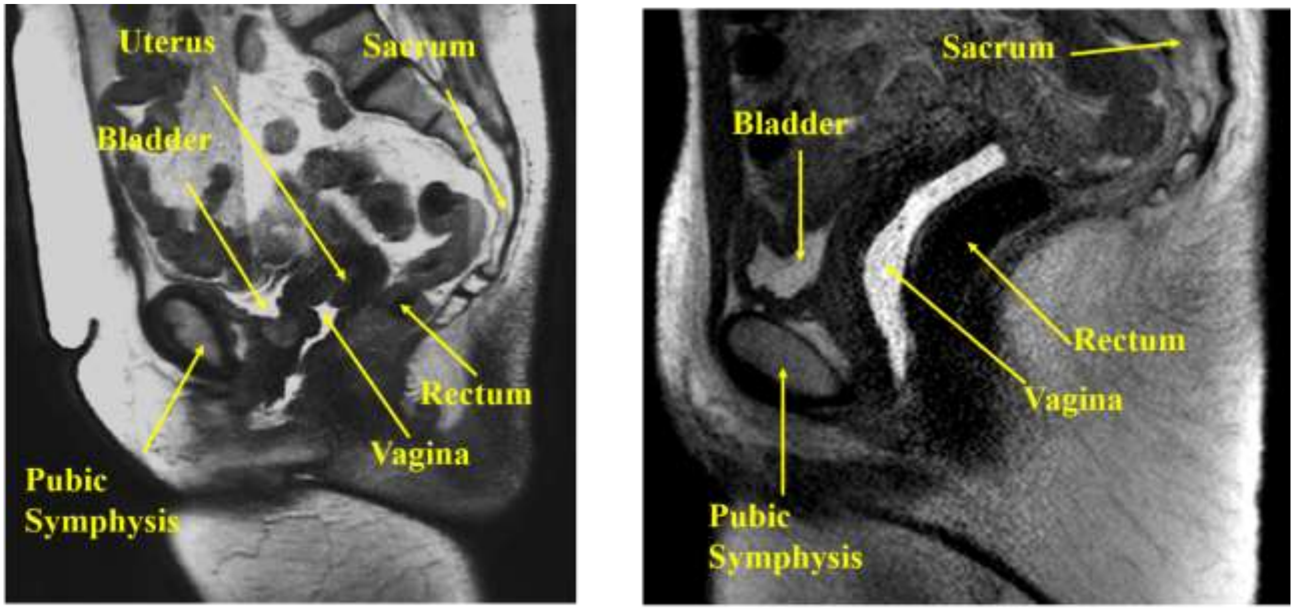


Figure 15 Demonstration of anatomical differences visualized between patients with and without prolapse on sagittal MRI.

While defects in connective tissue support can be challenging to visualize directly via imaging, changes in the anatomical position of pelvic organs could aid clinicians in identifying defects and elucidating the onset of prolapse [192]. In fact, studies have demonstrated that a single 2D mid-sagittal MRI can be used to quantify differences in the anatomical positioning between healthy and prolapsed vaginas [178], [193], [194]. Figure 15 demonstrates the stark visual differences between the relative location and shape of a healthy vagina and a prolapsed vagina during a Valsalva maneuver. In an effort to quantify these differences, research teams from the University of Michigan and the University of South Florida, among others, developed and applied 2D quantification systems to identify correlations between PFDs and injuries to pelvic musculature, which are further detailed in Chapter 3 [183], [195]. Results from these efforts coupled with POP-Q correlation studies, and biomechanics suggest correlations exist between apical support and POP [196]. However, to date, the inherent limitations that accompany 2D measurement systems, in addition to a lack of consensus among researchers and clinicians regarding the use and application of these systems hinder the ability to recognize, evaluate, and assess apical support [197].

1.4 Ethical and Practical Limitations Associated with Conducting Urogynecology Research

The application of biomechanics towards improving our understanding of POP is challenged by the complexity of developing feasible studies necessary to advance our knowledge. One of these barriers is the ethical issues surrounding the procurement and study of pelvic tissues. The ideal way to study the complex interaction of pelvic anatomy, *in vivo* experiments and testing, would provide a wealth of information regarding the mechanical interactions taking place under various conditions. However, such studies would be unethical, given the unknown risks to the patient, and the large number of patients that would need to consent and participate to obtain statistically significant and generalizable results.

Thus, *ex vivo* testing is common in this field, albeit several limitations exist here also. Due to the natural variation within populations, the procurement of enough human tissues from cadavers for passive mechanical testing, as well as enough independent samples for analysis prove to be a major challenge. Furthermore, cadaveric tissues do not match the properties of live tissues entirely, given that cause of death can impact the quality of tissues. Lack of blood perfusion leads to hypoxemia and degradation which further alters biochemistry and structure of muscle and connective tissues, thereby altering mechanics. Additionally, rectal distention due to release of gases through chemical processes distorts the position of soft tissue and pelvic viscera [198]. Therefore, animal models are often used as a proxy for studying the mechanics of viscera, connective tissues, and musculature [5], [10].

To date, animal models used in urogyecological studies include: non-human primates, rats, swine, ewes, and rabbits [5], [148], [165], [199]. Although there are several structural, anatomical, and functional differences between the pelvic anatomy humans and these animals, these models provide researchers with the ability to perform controlled experiments, including simulation of gestation, birth and delivery, simulation of prolapse conditions, and implantation of synthetic products for pelvic anatomy correction. Furthermore, these controlled experiments enable researchers to explore specific life events, while also collecting enough tissue samples for statistical significance. Although animal studies address some of the challenges associated with human studies, there are practical challenges that must be considered. Implementation of animal studies require significant funding to cover costs associated with procuring housing, feeding, experimentation. No animal to date has pelvic floor anatomy identical to that of women. Naturally occurring prolapse is much less common in animals, thus requiring researchers to simulate injury. In addition to ethical concerns and that animals are a limited resource, there can be an emotional toll associated with euthanizing animals at the completion of research. The challenges presented above are common to bioengineering research, especially when funds are limited.

Given the state of the US economy, funding for research is more competitive than ever. Review committees are tasked with selecting projects that are beyond reproach, based on the strength of the proposed project, required funds, feasibility of completion, and the perceived impact of the solution, etc. However, the greatest flaw in this process remains its implicit bias. Everyone develops implicit biases, which, at its core, is a cognitive process that helps us make decisions based on patterns and generalizations, including stereotypes. Many believe that without these biases, our minds would experience cognitive overload as it is impossible to evaluate every piece of information that we encounter with time and great detail. Therefore, without increasing awareness and understanding of one's implicit biases, stereotypes that are ingrained in our psyche can impact the lens through which decisions are made. The history of scientific study is riddled with biases and stereotypes surrounding women's mental and physical conditions, and despite efforts to increase the matriculation of women in STEM, there remains a noticeable lack of representation in decision-making forums allowing biases to be unchecked, and widening the gap between our current knowledge and our ability to understand women's health challenges.

Generally, these biases are evident surrounding quality of life issues. A review of FY2014 NIH R01 funding revealed a 5 to 1 ratio for ACL study awards when compared to awarded funds for POP research [68]. Furthermore, a review of surgical procedures for ACL injuries and POP disorders performed in the US revealed that 150,000 ACL surgeries are performed annually on men and women, while POP procedures were performed on 200,000 women alone that same year [68], [135]. If there are more POP procedures performed annually, one may question why more funds are allocated for ACL research. In 2017, Americans spent $100 billion on sports, a common avenue through which ACL injuries occur. Thus, resources are naturally dedicated to developing solutions that generate money and are driven by public interest.

Research surrounding sexual dysfunction is an example that highlights the long-term implications of these biases. Sexual dysfunction includes pelvic health and impacts both men and women. Although studies have shown sexual dysfunction is more prevalent in women (43%) than men (31%), several drug options have been developed and approved to address male sexual dysfunction, while none currently exist for women, although it is important to note that there are some still being tested for use. The complex and tortuous history of attitudes, beliefs and treatments of female pelvic health have created a significant gap in the health literacy of populations, which, when unchecked, perpetuate the devaluation of the severity of female maladies.

1.5 Motivations and Specific Aims

Sections 1.1-1.3 summarize our current knowledge regarding female pelvic anatomy and common sequalae. The female pelvis and reproductive system are arguably among the most complex and critical biomechanical systems in the body, due not only to the wide range of physiological functions required, but its necessity for maintaining our species. Damage to one or more components of this complex can lead to the gradual progression POP and/or other PFDs, underscoring the multifactorial etiology. Despite decades of advancement, section 1.4 highlights several ethical and practical challenges that, to date, have limited our ability to characterize the pathology of PFDs. This is a critical juncture within the field of urogynecological research, as progress forward requires the continued development of more robust measurements and methodologies for precise characterization of the evident changes that occur over the lifespan of women.

Section 1.0 illustrates the progression of medical misconceptions regarding healthy female pelvic anatomy, as well as origins and treatments of maladies. These misconceptions originated from perceptions that, not only stunted scientific progress within urogynecology, but manifested into a larger gap in public knowledge regarding normalcy of female pelvic health that persists today. This gap in knowledge contributes to mismanagement of female pelvic health, by robbing patients of the ability to effectively articulate their health concerns to physicians. Furthermore, communication barriers between patients and physicians can expose the general public to treatments and products that are advertised to sell, rather than providing pelvic health solutions based in scientific support. This evident state of confusion among the general population is a byproduct of confusion within the scientific community regarding normal female pelvic anatomy. In fact, there is no definition that exists by which clinicians and researchers can clearly define the spectrum of normal. This presents an ultimate gap in knowledge, which challenges our ability to effectively manage and treat PFDs. Our emphasis towards helping women who present with symptomatic PFDs is limited because we have yet to improve our ability to characterize changes over the lifespan, such that we can determine what normal means during all stages of life.

Natural history, with respect to this study, is the quantification of observations of uninterrupted female pelvic development (i.e., longitudinal observation) over the lifespan. This would enable researchers to quantify anatomical changes associated with puberty and healthy adult pelvic anatomy, which could aid in characterization of links between the most prevalent risk factors (i.e. parity and age) and symptomatic POP [3], [140]. To date, longitudinal studies that address POP have been primarily epidemiological in nature. However, these studies are unable to account for position and orientation changes over time, thereby limiting the ability to precisely characterize anatomical changes that could improve patient quality of life [137], [149]. The burgeoning demand for improved quantitative measurement systems is a result of several factors. Advances in medicine and an abundance of resources have contributed to an increase in life expectancy that is unprecedented, which makes quality of life concerns in the aging population even more critical. The long-term impact of vaginal atrophy, sexual dysfunction, and other hallmarks of childbearing, vaginal birth injury, aging, and other life events described in sections 1.2.5 and 1.2.6 can develop into unprecedented challenges.

While surgical treatments for POP and PFDs aim to restore function and the anatomical location of pelvic organs, our limited knowledge of anatomy that contributes to a successful surgery, pelvic biomechanics and *in vivo* loading conditions contribute to an alarming number of surgical failures and/or the reoccurrence of symptoms. This outcome indicates that we have yet to adequately define normal ranges for the position and orientation of pelvic organs, or the precise functional role of connective tissues and musculature. MRIs of pelvic anatomy provide non-invasive visualization of pelvic anatomy, which can offer insight regarding the severity of injury and or/displacement of organs. However, to achieve improved surgical outcomes, and minimize complications and reoccurrences, efforts must be targeted at developing measurement systems that are robust enough to more precisely define the range of normal pelvic anatomy and quantify incremental changes in anatomy over the lifespan.

Ultimately, the long-term goal in the field is to unravel the etiology surrounding the progression of symptomatic POP, such that women who are at risk for POP can be identified earlier and prevent progression of symptoms altogether. However, to accomplish this goal, the more critical and necessary question that must be addressed is can we utilize available technology and resources towards improving our understanding of geometric variations within health populations? Furthermore, how can we begin to address the stigma and misconceptions surrounding female pelvic health within the general population? Thus, the immediate goal of the enclosed body of work is to advance our definitions and conversations of normal female pelvic anatomy through completion of the following aims:

Specific Aim 1): To define and assess changes in Level III support with respect to age and parity.

1A) To establish an MRI database derived from local patient populations.

1B) To evaluate the location of the Hymenal Ring position with respect to age and parity.

Rationale: Given that age and parity are cited as two of the greatest risk factors, it is important to evaluate landmarks within these populations. Furthermore, Level III support is commonly compromised as a result of maternal birth injuries and has also been cited as changing significantly as a result of age and parity. While the POP-Q exam provides quantitative information to aid in the characterization and progression of symptomatic PFDs, the inherent limitations of physical examinations, as described in Sections 1.1.3 and in Chapter 2, warrant investigation of additional measurements to enhance our understanding of Level III support.

Specific Aim 2): To establish a 3D pelvic coordinate system that allows for quantification of vaginal angle and spatial position within the pelvis and assess the inter-and intra- observer repeatability of the developed 3D coordinate system.

Rationale: Evidence suggests that changes in apical support such as vaginal descent are characteristic of symptomatic prolapse. Current methods for assessing changes in vaginal position rely on 2D MRI sagittal images. However, 2D measurement techniques are inherently limited when applied to complex 3D organs such as the vagina. Given our developing understanding and acceptance of the human body as a biomechanical system, it is critical to develop methods that define the position and orientation of the vagina with respect to a patient's individual anatomy. Ultimately, 3D characterization of the position and orientation of the vagina will enhance our current perceptions of normal female pelvic anatomy.

Specific Aim 3): To investigate the ability for high school students to comprehend and retain information pertaining to female pelvic anatomy when exposed to educational interventions.

3A) To develop an assessment tool to gage baseline knowledge, comprehension, retention and attitudes following the implementation of active learning techniques to educate high school students about female pelvic health.

3B) To assess the perceived impact each active learning intervention had on the comprehension, retention, and attitudes towards female pelvic health.

Rationale**:** Aims 1 and 2 emphasize the importance of characterizing normal female anatomy from a research and clinical perspective. However, in order for this research to have a meaningful impact, the underlying stigma and misinformation surrounding vaginal health must be addressed. Historically, issues regarding vaginal health, such as prolapse, incontinence and dyspareunia, have been normalized to such an extent that many women hide such issues rather than seek treatment. In order to shift this predisposition to hide vaginal distress, we must first normalize the conversation about such issues. Section 1.0 and Chapter 4 highlight several existing barriers surrounding public knowledge and perceptions regarding female pelvic health. Thus, it is important to explore mechanisms through which these barriers can be dismantled, thereby creating a pathway for women to seek and receive treatment.

The aims of this work support the fundamental belief that our ability to improve treatments and surgical outcomes for patients experiencing PFDs is inherently tied to a shift in focus is from reactionary techniques and assessments (i.e., symptomatic women), to identifying preventative biomarkers (i.e., asymptomatic women). Thus, it is of critical importance to understand how age and parity, the two greatest risk factors associated with symptomatic PFDs, correlate to changes in the location of pelvic viscera. Successful completion of these aims will improve our ability to define normal pelvic anatomy, such that we can improve our education and dissemination of understanding female pelvic anatomy among the general population. Long term, steps towards enhancing female pelvic health and literacy, through characterization of normal pelvic anatomical features could enhance our capacity for preventative treatments and improved reactionary treatments to support women globally.

2.0 The Evolution, Development and Applications of Patient Databases Towards the Characterization of Vaginal Position

2.1 Overview

Chapter 1 reviews current knowledge regarding female pelvic anatomy and the progression of pelvic disorders, while Section 1.3.5 summarizes how diagnostic imaging has been utilized as a mechanism to enhance our conceptualization of internal structures that could not otherwise be assessed without invasive surgery [200]. MRI has been particularly useful, as its large field of view enables simultaneous multi-compartmental visualization of musculature and viscera within the female pelvis [187]. In fact, pelvic MRIs are often coupled with physical exams to assist clinicians and surgeons in developing treatment plans that are more specific to patient needs. Static T2-weighted pelvic MRIs show enhanced soft tissue contrast, which enables clinicians and researchers to visualize visceral borders and anatomical landmarks, while also providing multiplanar images and not superimposition structures [201]. Ideally, the application of MRI towards the clinical treatment of PFDs would be standardized, such that the specific needs of a patient would be clear upon review of scans and physical examination. However, this is far from reality for diagnosis and treatment of PFDs. There are several measurements and methodologies that exist in both clinical and research settings, with varying degrees of sensitivity, repeatability, and reliability capabilities. This confuddles the already complex PFDs, for which several factors may contribute to its onset. As with all aspects of healthcare, the creation, collection, and organization of information is necessary towards the development of standards that ultimately improve patient outcomes and quality of care. Given the natural variations within the human population, it is even more critical that information acquired towards to the development of standards is inclusive of these possible variations.

The first section of this Chapter will draw from a historical perspective to support the necessity of developing a female pelvic MRI database, as well as challenges and recommendations associated with its use and development. The second section of this Chapter demonstrates an application of the acquired database, through an exploration of the hymenal ring, a common anatomical landmark applied clinically, with respect to age and parity.

2.2 Towards the Development of a Female Pelvic Anatomical Reference Database

2.2.1 Introduction

Scientific inquiry is an iterative process driven by need and/or curiosity and refined by the application of technology to enhance our understanding of the world around us. Our first practical method of collection of information was, (and still is) empirical evidence. Observations can be passive, where information is collected, but not altered, or active, which involves physical interaction with the objects being observed. Both methods of observation are relevant in medicine; as physicians are trained to observe cases and procedures, followed by the practice of medicine. The colloquium “practicing medicine” in many senses is quite literal, because the ability for physicians to treat patients is directly impacted by the amount of experience they have, and the availability of technologies and resources.

Historically, physicians could only rely on knowledge from drawings, or animal dissections due to laws prohibiting dissection of human bodies until the mid-13th to 14th centuries [24], [202]. Galen, a well-renown Greek physician dissected animals to develop and "prove" his observations; many of which were inaccurate and based on speculation. The limitation of dissections, coupled with vast distances between cities and civilizations, contributed to the development of varying medical practices and skills. In some areas, there would only be one physician for an entire town, meaning their "practice" would only be as informed as the ailments suffered by their patients. While far from ideal, these geographic barriers posed an even greater challenge for women—they were forbidden to study medicine, and it was generally not appropriate for male physicians to conduct pelvic exams on women. This suggests that early perceptions of female pelvic anatomy may be riddled with "old wives' tales", some of which linger today. Many of the inaccuracies during Galen's time were not corrected until the publication of Vesalius' *De Humanis Corporis Fabrica* in 1543, an anatomy textbook based on human dissection [202]. The accuracy of Vesalius' descriptions demonstrated that although animal dissections have contributed to significant advances in medicine, the insight provided through physically exploring the intricacies of the human body to understand human anatomy, physiology, and progression of disease is unmatched [200].

The beginning of the industrial revolution propelled advances in transportation and communication, which, naturally, would influence the medical community and patient care. These technological advances enabled physicians to better share unique findings, surgical techniques and medical devices with the wider community. This paved the way for streamlined processes and gold standard methods for diagnosing and assessing progression of disease based on assessment of several patients rather than single anecdotes. During this period, doctor's practices were shifting from in-house medical care to places where patients could go for medical treatment. The practice of medicine, which had been a “solo act”, morphed with the development of hospitals, or central locations designed to facilitate patient care. By proxy, this forced collaborations between medical practitioners from different backgrounds, and the necessity for patient history and medical records became vital [203]. The mass recording of patient data enabled the development of treatments targeted at specific subgroups [204]. Soon thereafter it was found that characteristic variations can exist, even within close family units. Identical twins, for example, could be found to exhibit different phenotypic expressions based on differing environmental factors [205]. When expanded to encompass the larger human population, variations from person to person can be quite large. As a result, our characterization of human health began to shift from a 2-category model of normal or abnormal towards a continuum of characteristics. Naturally, this created a juxtaposition between the standardization of care and the need for targeted treatment.

While many fields have begun, or even completed their shift away from a 2-category model, through the added support and analysis of diagnostic images, the field of urogynecology has yet to quantitatively characterize natural variations in pelvic anatomy [99], [206]–[208]. As demonstrated in the fields of cardiovascular, orthopedic, and neuro medicine, the collection and analysis of diagnostic images of patients with varying demographics and characteristics provide a framework towards defining normal anatomical variations among early developmental years (0-19 years), childbearing years (20-49 years), and post-childbearing years (50-75 years). Thus, the objective of this study was to assemble an expansive database derived from existing UPMC medical records of female patients, who by MRI and clinical diagnosis were deemed to have healthy anatomy, while exploring the benefits and challenges associated with this task.

2.2.2 Methods

The retrospective collection of pelvic MRIs (axial, sagittal, and coronal) volumes of patients at rest and in the supine position were obtained from the UPMC (University of Pittsburgh Medical Centers) database over the last 10 years and was approved by the University of Pittsburgh Institutional Review Board (IRB# PRO 19050362). Table 3 illustrates the inclusion and exclusion criteria used to determine if patients were suitable for our database. Search criteria for possible patients included a review of MRI scans requested by local urologists and urogynecologists. Additional searches were conducted through queries generated by Nuance software based on age groups described in Table 4 and acceptable anatomical abnormalities, summarized at the bottom of Table 3.

Table 3 Summary of Inclusion and Exclusion Criteria for Patients and MRI volumes for the development of a female pelvic MRI database

DATABASE INCLUSION AND EXCLUSION CRITERIA			
PATIENT CRITERIA		**MRI VOLUME CRITERIA**	
INCLUSION	**EXCLUSION**	**INCLUSION**	**EXCLUSION**
Acknowledgement of race and ethnicity	Unidentified race/ethnicity	Multiplanar MRI volumes (Axial, Sagittal, Coronal) for detailed anatomic evaluation of the pelvic floor (levator ani, rectum, vagina, paravaginal attachments to arcus tendineous, bladder, uerus and uterosacral ligaments)	Missing one or more multiplanar views (Axial, Sagittal, Coronal)
Between the ages of 0 and 75 during the time of a scan	Older than 75 during the time of MRI scan	At rest in supine position	Performing Valsalva/any maneuvers that could alter the position of pelvic organs
Acknowledgement of parity status	Undetermined parity status	T2 Fast Spin Echo sequence (TRUE)	Alternative MRI sequences that do cannot demonstrate visualization of pelvic organ borders
Healthy pelvic anatomy (i.e. gastrointestinal, gastrourogenital and reproductive systems are anatomically normal) *	Endometriosis, current pregnancies, Chron's disease, cancers related to/within pelvic region	Scans imaged within the last 10 years	Scans imaged prior to 2005
No indication of pelvic surgery (i.e. hysterectomy)	Indication of pelvic surgery (i.e. hysterectomy)		
***** Acceptable anatomical abnormalities include: non-infected urethral diverticuli < 3cm, uterine fibroids ≤ 3cm, simple or paratubal ovarian cysts ≤ 3cm, uterine polyps, uterus enlargement ≤ 6 weeks' size, IUD, thrombosed pelvic vein, thickened endometrial stripe, bartholin's cyst, hydrosalpinx and similar findings			

After locating and confirming that patients were biologically female and that the scans were imaged within the last 10 years, radiology notes were reviewed for assessment of normal anatomical status. Normal pelvic anatomy was defined as having uncompromised gastrointestinal (gi), genitourinary (gu), and reproductive systems. The following abnormalities that were deemed acceptable for inclusion in the database included: non-infected urethral diverticuli < 3cm, uterine fibroids ≤ 3cm, simple or paratubal ovarian cysts ≤ 3cm, uterine polyps, uterus enlargement ≤ 6 weeks' size, IUD, thrombosed pelvic vein, thickened endometrial stripe, bartholin's cyst, hydrosalpinx and similar findings. The exclusion criteria included: pregnant women, endometriosis, Chron's disease, cancers and related malignancies of female anatomy, vaginal gel that goes beyond the introitus, Mullerian anomalies, autoimmune disorders (sarcoidosis, sjogrens, lupus, etc.), motion artifacts, and any pelvic surgery that could impact organs of interest (ex: hysterectomy). For scans deemed acceptable for the database, patient scans were de-identified and coded with a SIN (Study Identification Number) using MatrixRay Exchange Software to maintain patient privacy. Additionally, patient demographics such as those described in Table 4 were recorded to support subject classification for future studies. Factors such as height, weight, last menstrual period (LMP), and BMI were not collected, since these factors can fluctuate significantly within individuals over short periods of time.

Table 4 Patient Demographics of Interest: this highlights the categories through which subjects could be grouped within the database

Demographic Factors	Possible Categories
Race	Black/African American | White | American Indian/Alaska Native | Asian | Native Hawaiian/Pacific Islander | Other
Ethnicity	Hispanic/Latino | non-Hispanic/Latino
Age during scan	0-19 | 20-49 | 50-75
Parity Status	Nulliparous | Parous
Delivery Method	Vaginal | Caesarian
Number of Vaginal Births	Varies

2.2.3 Results

One thousand scans were reviewed by experts within the laboratory over a period of 4 months. In accordance with the criteria set forth in section 2.2.2, 316 scans were included in the database. All scans were T2 FSE sequences with an average slice thickness of 4.5 mm and an average spacing between slices of 5.4 mm. Given the known biological and physical changes associated with pregnancy, the demographics of selected patients in Table 5 are first categorized by parity status (i.e., nulliparous or vaginally parous), followed by race and age group.

Some racial demographics, such as American Indian/Alaska Native, Asian, and Native Hawaiian/Pacific Islander, were scarce among the reviewed scans, and even scarcer within our database. In fact, only 1 individual within the database was Asian, and no patients were ethnically categorized as Hispanic or Latino, or racially American Indian/Alaska Native, nor Native Hawaiian/Pacific Islander. Thus, the aforementioned database primarily reflects members who racially identify as white or black/African American, with more than 75% of the database including white women, and 4% black/African American women. Patients where race data was unknown were placed in the racial category of Other (6%), and only impacted nulliparous scans of women and girls between the ages of 0 and 19.

Table 5 Demographic Overview of our MRI patient database

	Nulliparous	**Age**			
Race		0-19	20-49	50-75	**TOTALS**
	Black/African American	-	-	-	-
	White	4	32	13	49
	American Indian/Alaska Native	-	-	-	-
	Asian	-	-	-	-
	Native Hawaiian/Pacific Islander	-	-	-	-
	Other	19	-	-	19
	TOTALS	23	32	13	136

*All patients were non-hispanic/latino

	Vaginally Parous	**Age**			
Race		0-19	20-49	50-75	**TOTALS**
	Black/African American	-	13	-	13
	White	-	39	37	76
	American Indian/Alaska Native	-	-	-	-
	Asian	-	1	-	1
	Native Hawaiian/Pacific Islander	-	-	-	-
	Other	-	-	-	-
	TOTALS	-	53	37	180

*All patients were non-hispanic/latino

The largest population subset within the database consisted of white women between the ages of 20-49 (22%). Regarding parity status, our search did not return any patient under 20 years old who was vaginally parous, and the number of nulliparous older women (aged 50-75) within our criteria was lower than anticipated. Overall, the database contains a wider sampling of parous patients with respect to total number of scans, racial, and age distributions.

Although the ideal patient scans for this database would reveal no abnormalities, the most common abnormalities found in several patients included histories of pelvic pain, adenomyosis, and urethral diverticula. As indicated per the inclusion criteria, these abnormalities were deemed admissible for the database, as it was believed that these abnormalities would not compromise future studies. When available, additional notes were included within the database as factors that we felt could be used to further delineate patient groups in future studies. Common factors observed across several patients included the specific number of deliveries and year of deliveries (and difficulties where noted) smoking habits, and obesity diagnoses. While our studies do not directly address these factors, they have been correlated with increasing the risk of developing POP and other PFDs.

2.2.4 Discussion

The goal of this study was to establish a database that targets characterization of female pelvic organs, while providing recommendations to support similar future endeavors. The results described in Section 2. 2.3 suggest that it is indeed possible to identify, compile retrospective MRIs and data regarding female anatomy. A total of 316 scans were selected as a part of the database, all of which included T2 FSE sequences, and an average slice thickness and distance of 4.5mm and 5.4mm respectively. Of the chosen subjects, most racial demographics were not represented, with greatest representation (22%) among white women aged 20-49 of parity <=1, and non-represented groups as 0%. Furthermore, the availability of scans among women aged 50-75 only accounted for 16% of all collected scans. The following discussion explores these percentages further with respect to existing studies to provide context for these results.

Much of the literature exploring female pelvic health suggests that demographics such as age, parity status, mode of delivery and race are important to consider when exploring questions regarding natural history, disease progression, and response to treatment [90], [209]–[211]. The Wang et. al recent longitudinal study exploring anal incontinence (AI) in parous women with respect to race suggested that there may be racial differences in AI when controlling for age, parity, vaginal delivery, and even BMI, in which, based on questionnaire results, white women appeared to have an increased likelihood of AI symptoms than black women [212]. Additional considerations that support delineation of race and other factors for pelvic research is due to challenges experienced by black women regarding complications pre- and post-partum resulting in maternal birth injuries and even deaths that far surpass that of white women [213]. Thus, systems that rely on generalizations that do not account for implications of intersectionality existing within all women will be incapable to provide adequate and equitable care for all.

With regard to the demographic percentages present in this study, the racial breakdown of patients is heavily skewed towards white women between the ages of 20-49 (over 75%). To determine if this was, although not desired, a representation of the local and US population demographics, publicly available census data (2015) data was compiled to compare Pittsburgh’s female population with respect to the US female population while considering age and ethnicity. A summary of this data is illustrated in Figure 16. Pittsburgh’s Hispanic and Latino population is significantly lower than the national level, while the population of whites between the ages of 18 and 64 is approximately 9% higher than at the national level. It is therefore not surprising that there were no Hispanic and Latino women among our database population, as the Hispanic/Latino population (men and women) is only 3.1% of Pittsburgh's population in its entirety with respect to the 2015 Census.

Interestingly, the population of Blacks in Pittsburgh was higher for all age categories (under 18, 18-64 years, 65 and older), indicating that the relative population of Black women in Pittsburgh is higher than the national average, with Blacks (men and women) constituting 23% of the Pittsburgh population. On the surface, it appears that the database created for this study grossly underrepresents the Black female population in Pittsburgh. However, there are several factors to consider before drawing this conclusion. First, the context of this study is important, as the goal was to collect MRI scans and information about healthy patients between the ages of 20 and 75. In 2019, the city of Pittsburgh's Gender Equity Commission published a study entitled, "Pittsburgh's Inequality Across Gender and Race", in which several inequities are reported. Most notably, the average age of death is lower for black women (69.9 years) than for white women (78.2 years) [214]. This indicates a potential challenge in identifying older women for our database, as the cutoff age for the database is higher (75 years) than the average age of death for black women in Pittsburgh. Furthermore, fetal mortality are approximately two times more likely in Black women than White women, and maternal mortality for Black women is higher than in most comparable cities (97%) [214]. Research suggests maternal health can combat fetal mortality, however, there are several factors that contribute to poor maternal health, which, could also be an indicator for other health abnormalities including, but not limited to, obesity, maternal birth injuries/complications, cancer, endometriosis, and stress, each of which directly or indirectly could increase the likelihood of having anatomical characteristics beyond the inclusion criteria for this study.

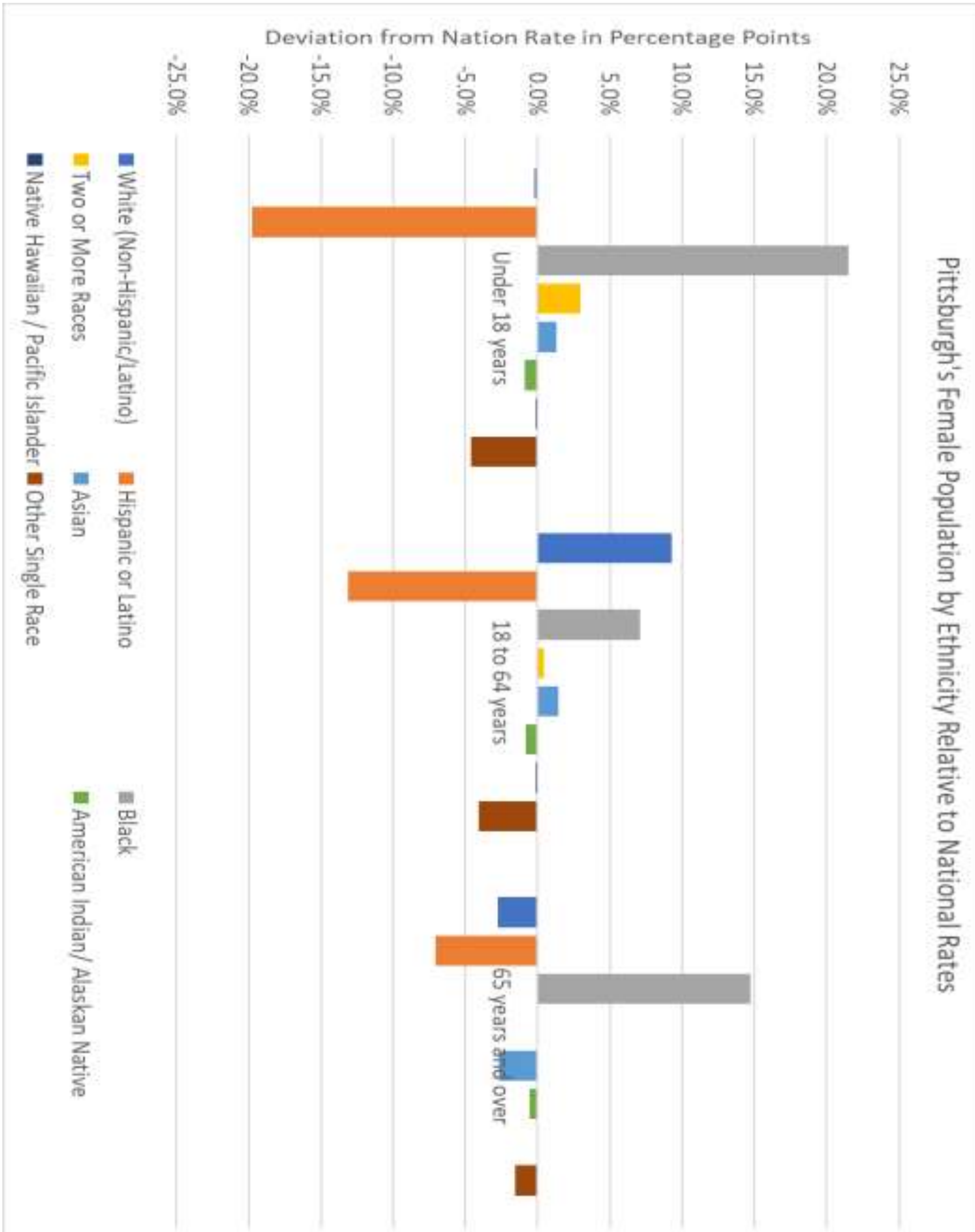


Figure 16 Pittsbrgh's Female Population by Ethnicity Relative to National Rates (2015)

These relative differences are important to consider when drawing conclusions about the population represented within our database, as Pittsburgh holistically does not mirror national demographics, as most cities would not. To truly characterize anatomical variations in different cohorts of women collaborations between several hospital systems would be necessary. Even then, it would be presumptuous to assume that national findings could be extrapolated globally, as the demographics and living conditions in the United States differ drastically from most other countries.

2.2.5 Challenges

While these findings suggest that it is indeed possible to develop a database to study normal female pelvic anatomy from retrospective scans, there are challenges and limitations associated with this process. One limitation is in the use of retrospective scans. Although thousands of MRIs are taken of the female pelvis annually, the availability of resources and cost of MRI operation and maintenance suggests that scans are not routinely performed, but rather on an as needed basis. Thus, only patients with presumed pelvic anomalies or ailments are scanned, and of that subset of patients, only patients that match the inclusion criteria described in Table 3 could possibly be included in the database.

Another common challenge was clarity of scans. We found that T2 FSE sequences were ideal for the visualization of organ borders, which was critical for studies described in each proceeding chapter. Although the sequence is quite common, there were patients encountered that met all patient inclusion criteria but did not have a scan sequence that was adequate for use in future studies. In other instances, patients were excluded as a result of movement during scan sequences was significant enough to impede quality of scans. Scans of women aged 50-75 within our prescribed search criteria proved to be challenging as well. Women within this age group are more likely to experience challenges associated with the biological changes described in Chapter 1.4, as a result of hormonal and structural changes associated with aging. The described challenges further contributed to challenges in acquiring a diverse population of patients. In spite of these challenges, the development of this database provides a foundation from which we can begin to explore methods towards describing the natural anatomical variations within populations of women.

2.3 Characterization of Hymenal Ring Position with Respect to Age and Parity

2.3.1 Introduction

Pelvic Organ Prolapse (POP) is characterized as the unnatural descent of the vagina and other pelvic organs as a result of compromised musculature and/or connective tissue support [127] [11], [67], [84], [215]–[217]. Although the precise etiology of POP is not well defined, much of the existing knowledge supports the theory that aging, and parity are the greatest contributing risk factors towards symptomatic POP. During gestation, women's bodies undergo numerous structural changes. Vaginal deliveries, in particular, induce significant geometric changes to accommodate the high stresses and transfer of forces experienced as the fetus passes through the birth canal [127], [218]. For many women, the dramatic changes to pelvic floor muscles and connective tissues become permanent leading to undue stress on the vaginal walls and a loss of vaginal support, which can result in POP. Such permanent changes to the pelvic floor are made evident by the numerous reports of pelvic floor laxity following vaginal delivery [197], [219], [220]. Aging is accompanied by gradual changes in hormone levels and collagen/elastin ratio content, which permanently alters the mechanical integrity of connective tissues and musculature of the pelvic floor.

The POP-Q, or POP-Quantification exam, is a physical exam performed by clinicians to characterize pelvic support through quantification of vaginal descent [150], [151], [221]. In fact, epidemiological evidence suggests that vaginal descent is most prevalent in menopausal parous women than any other group. As illustrated in Chapter 1 (Figure 10), the POP-Q quantifies descent in the anterior and posterior compartments relative to the hymenal remnant, which is a thin externally visible soft tissue reference point located around the vaginal introitus [150], [151]. Based on these measurements, patients are assigned a stage of prolapse ranging from 0 (no prolapse) to 4 (complete vaginal eversion). Today, the POP-Q is the most widely accepted system for quantifying pelvic organ descent [150], [222], [223].

Given that the vagina, musculature, connective tissues, and other viscera of the pelvic floor are soft tissues, changes in tissue structure and/or composition can significantly influence tissue integrity, and by proxy, tissue morphology. Factors such as tissue hydration, coupled with significant strain on pelvic muscles during delivery, or changes in collagen content ratios and/or subtypes could cause soft tissue locations, and therefore measurements to vary. This suggests that the POP-Q, which is reliant upon only soft tissue landmarks, may not be robust enough to fully characterize subtle changes in Level III support, which, could serve as an early indicator for changes that eventually contribute to symptomatic PFDs. While the POP-Q is widely utilized, the inherent limitations of relying on they hymen, a soft tissue that may be influenced by changes in surrounding organs and tissues, may underestimate the extent of injury present; contributing to prolonged abnormalities that may progress towards symptomatic POP.

Magnetic Resonance Images (MRIs) have proven to be a useful complement to physical examinations of POP. As non-invasive diagnostic tools, they have afforded clinicians and researchers unique insight into the complexity of prolapse, particularly in cases where other pelvic floor disorders (PFDs) occur. Several researchers have proposed methods for quantifying the progression of PFDs, using 2D mid-sagittal MRIs, such as the H-line, Pubococcygeal line, SCIPP line, Perineal line, and Midpubic line, shown in Figure 17, and described in further detail in section 3.1 [193], [195], [224], [225]. While the details and strengths of these measurements differ, they all rely on the pubic symphysis, an amphiarthrotic cartilaginous joint, as a standardized reference point.

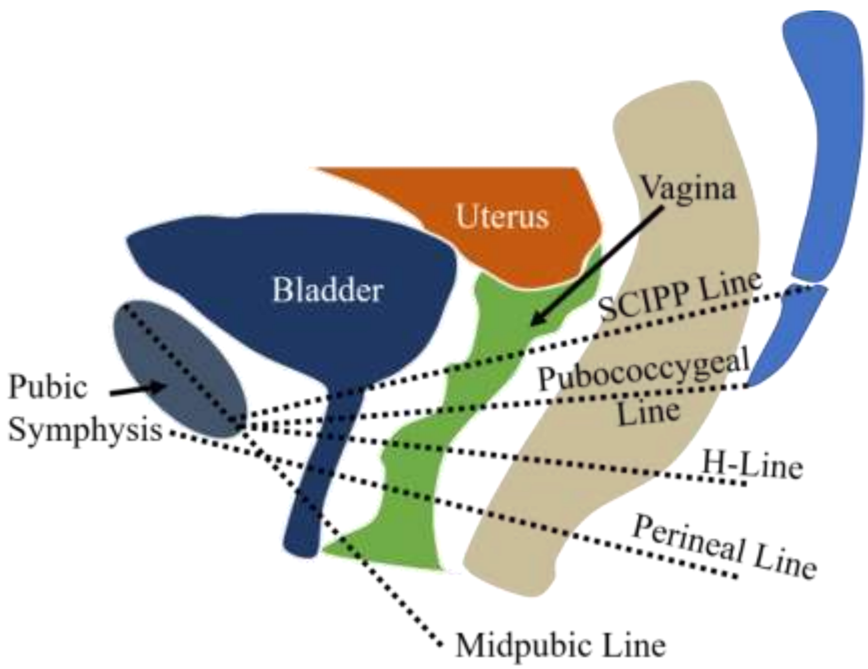


Figure 17 Various 2D Measurement systems

After reviewing hundreds of sagittal scans of women at varying ages and parity status, researchers and clinicians within our laboratory noticed what appeared to be visual differences in the location of the hymenal ring relative to the pubic symphysis on MRI scans. These differences also appeared to differ based on a woman's age and parity status thus leading us to question the assumption that the hymenal ring remains fixed throughout life events and the natural process of aging. Thus, we aimed to determine whether the hymenal ring is indeed a stable landmark that is relatively fixed in its position throughout the lifespan or whether its position changes relative to the pubic symphysis with parity and age. Based on our observations, we predict that the hymenal ring is significantly influenced by age and parity.

2.3.2 Methodology

2.3.2.1 Scan Selection and Subject Demographics

MRIs were selected from the database described in Section 2.2. All acquired scans were collected retrospectively through IRB# PRO19050362 and detailed in Section 2.2. Given that the hymenal ring is soft tissue near the vaginal introitus, it was determined that additional factors required consideration prior to selecting scans for this study. Subjects who had cysts or diverticula near the vaginal introitus were excluded from this study as measurements of the hymenal ring borders are on the order of millimeters. Thus, abnormalities near the measured area of interest could alter the location of soft tissues, thereby confounding potential findings. Additionally, scans that had poor visualization of the pubic symphysis borders in sagittal scans, and/or the vaginal introitus in sagittal, coronal, and axial scans were also excluded from this study due to lack of visualization of required landmarks for measurements. There is reasonable concern that distention of the rectum or urethra could distort the positioning of the vagina and influence its geometry and surrounding structures. Therefore, patients that had gel/contrast manually inserted into the vagina, and rectum were excluded due to the unknown impact that contrast could have on geometries of these structures.

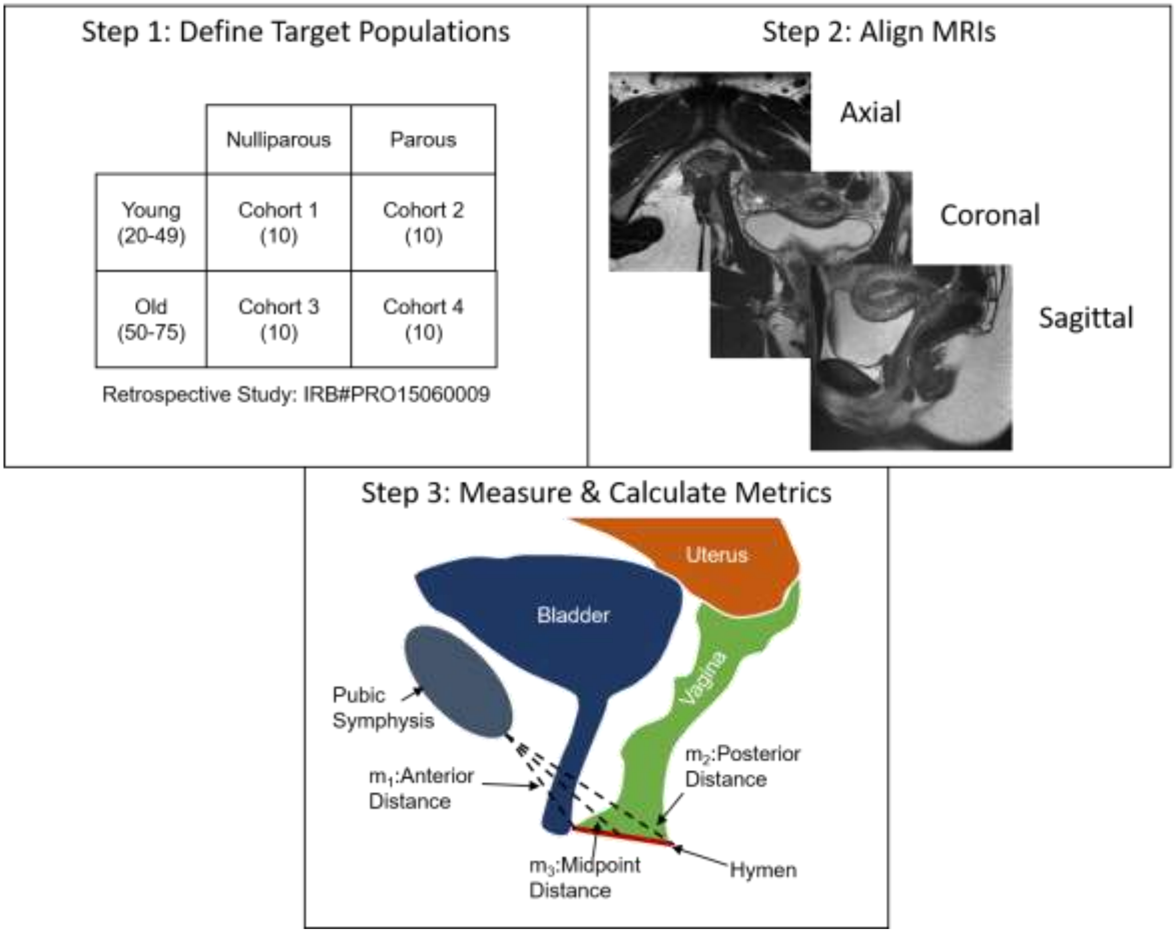
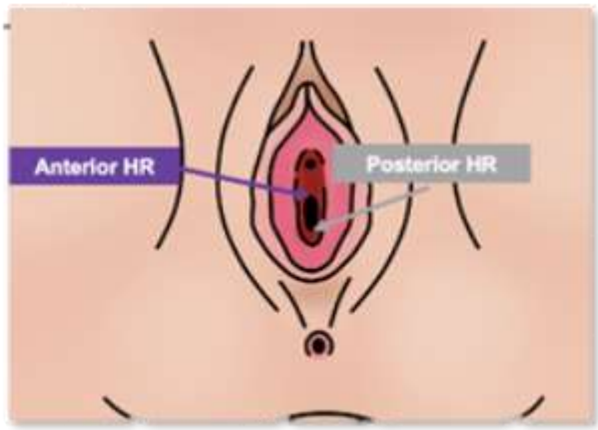


Figure 18 Overview of methods for identifying the position of the Hymenal Ring

2.3.2.2 Scan Alignment

Manual fixed image registration techniques were used to align axial, coronal and sagittal image volumes to improve accuracy of hymenal ring measurements. 3D Slicer (http://www.slicer.org) software was used to perform this alignment[226]. The sagittal volumes were chosen as the MRI fixed volumes, due to the field of view and contrast of bony landmark borders (i.e., pubic symphysis and sacrum). The axial and coronal volumes were moving volumes and aligned individually with respect to the fixed volume through re-slicing each volume sagittally. The spin/rock and fade between volumes enables manual translation and rotation of the moving volume with respect to the fixed volume. Following close alignment of bony landmarks from visual inspection by two observers, the transformation matrices that provide the numerical translations and rotations necessary for alignment were saved. The magnitude of translational movement of the subjects was calculated and used to determine if a lack of alignment impacted the results.



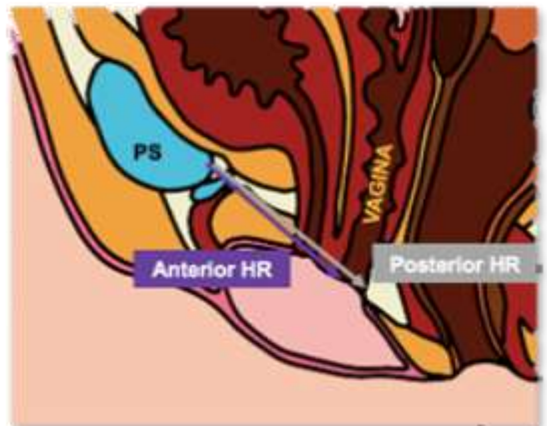


Figure 19 Graphical representation of the anterior and potsterior hymenal ring borders in axial and sagittal view

2.3.2.3 Hymenal Ring Measurement Quantification

A three-by-three slice view and slice intersections were used to visualize coronal, axial, and sagittal scans simultaneously. In the axial view, the most inferior and most anterior and posterior points of the hymenal ring were identified using slicer intersections. The most inferior aspect of the pubic symphysis in the sagittal view was identified. The distance from the pubic symphysis to the anterior hymenal ring (mm), as well as the distance from the pubic symphysis to the posterior hymenal ring (mm) were measured. These values were subtracted to obtain a measure of hymenal diameter (Figures 18 and 19). This is distinct from the genital hiatus which is measured with the labia parted and the patient in lithotomy. In contrast, the hymenal diameter is measured with the patient's legs adducted (thighs apposed) in the supine position at rest. Consequently, while conceptually similar to the genital hiatus, the values will be considerably smaller.

2.3.3 Statistics

SPSS statistical software (version 25) was used for all statistical calculations. To account for potential interaction between age and parity, both parametric ANCOVA and non-parametric ANCOVA (Quade's Test) analyses were conducted as a conservative approach due to our sample sizes and potential variations in measurements within normal populations. Table 6 illustrates the variables and groups for each statistical test that was run. The anterior and posterior hymenal ring measurements served as the dependent variables, and parity and age were used interchangeably as the control variable and group. While parity is tested as a categorical variable (i.e., parous or nulliparous), age was tested as both categorical (i.e., young or old) and continuous to robustly characterize our datasets. The sample size for each statistical test had a total of 40 subjects, with 20 subjects for each control group. Given our achieved sample size, G*Power 3.1.9.4 software was used to determine that a power of .69 can be achieved with our sample size.

Table 6 Overview of the six parametric/non parametric statistical tests to understand interactions of age and parity on the anterior and posterior hymenal ring borders

Statistical Test Variations: ANCOVA and Quade's Test	CONTROL VARIABLE	DEPENDENT VARIABLE	GROUP
1	Parity_cat [nulliparous(n=10)/parous(n=10)]	Anterior	Age_Cat
2	Age_cat [young(n=10)/older(n=10)]	Anterior	Parity_Cat
3	Age_cont [20-49yrs (n=10)/50-75 yrs (n=10)]	Anterior	Parity_Cat
4	Parity_cat [nulliparous(n=10)/parous(n=10)]	Posterior	Age_Cat
5	Age_cat [young(n=10)/older(n=10)]	Posterior	Parity_Cat
6	Age_cont [20-49yrs (n=10)/50-75 yrs (n=10)]	Posterior	Parity_Cat

Histograms were plotted for both the anterior and posterior hymenal ring measurements for each comparison group to better assess if each grouping of data is representative of a normal population. For each test, the raw mean, estimated means, p values for the parametric ANCOVA and nonparametric ANCOVA, Cohn's D, and mean square error were calculated and reported. P values less than p=0.05 were considered significant.

2.3.4 Results

To determine if age and/or parity significantly influence "the position of the hymenal ring with respect to the pubic symphysis, a robust statistical analysis was conducted to characterize subject groups and measurements of interest. The following section will highlight key findings from this study. Age demographics of subjects are described in Table 5. In total, 40 subjects were included in this study. Mean and Median central tendencies are reported for the entire subject group, as well as for subgroups (n=20) and specific subgroups (n=10) with respect to age and parity (Figure 20).

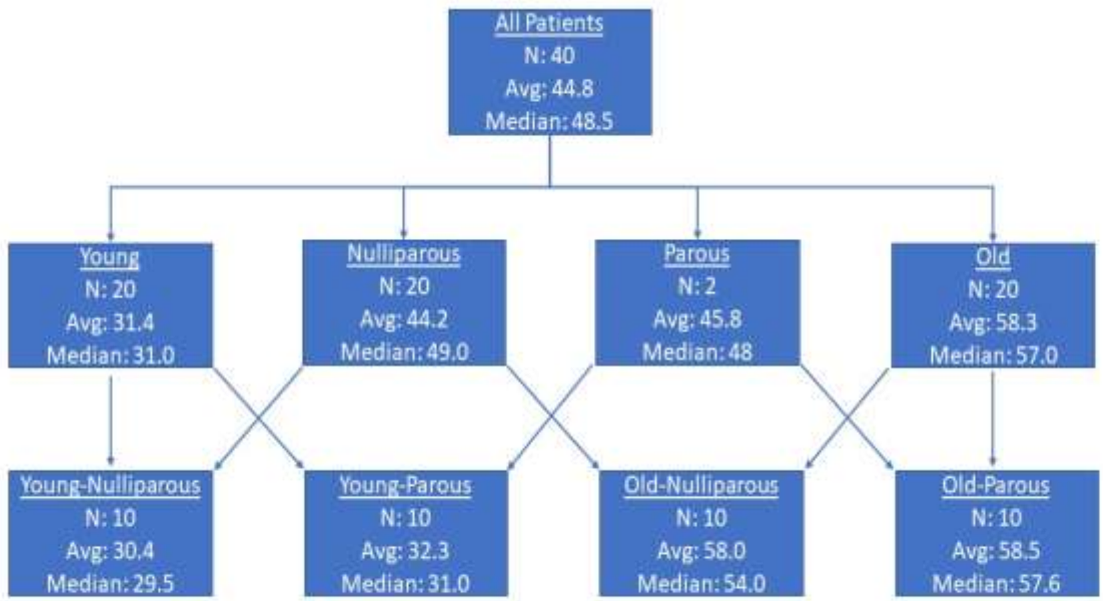


Figure 20 Central Tendencies (Average and Median) for Subject Ages

The median value for older parous women was 1.5, indicating more variation within that population with respect to number of vaginal deliveries. This finding could simply be an indicator that women aged 20-49 may continue to have children beyond the date of their scan within the database. Statistical test results were used to determine if the mean and median values that describe each cohort are significant with respect to visualizing and interpreting our results.

2.3.4.1 Distance from Pubic Symphysis to Anterior Hymenal Ring

The anterior hymenal ring is a point on the anterior border of the hymenal remnant. Thus, we measured the distance from the proximal end of the pubic symphysis, a bony landmark within the pelvis, to the anterior point in all 40 subjects. Figure 21 provides a visual depiction of the anterior hymenal ring measurements for all subjects grouped by their specific category.

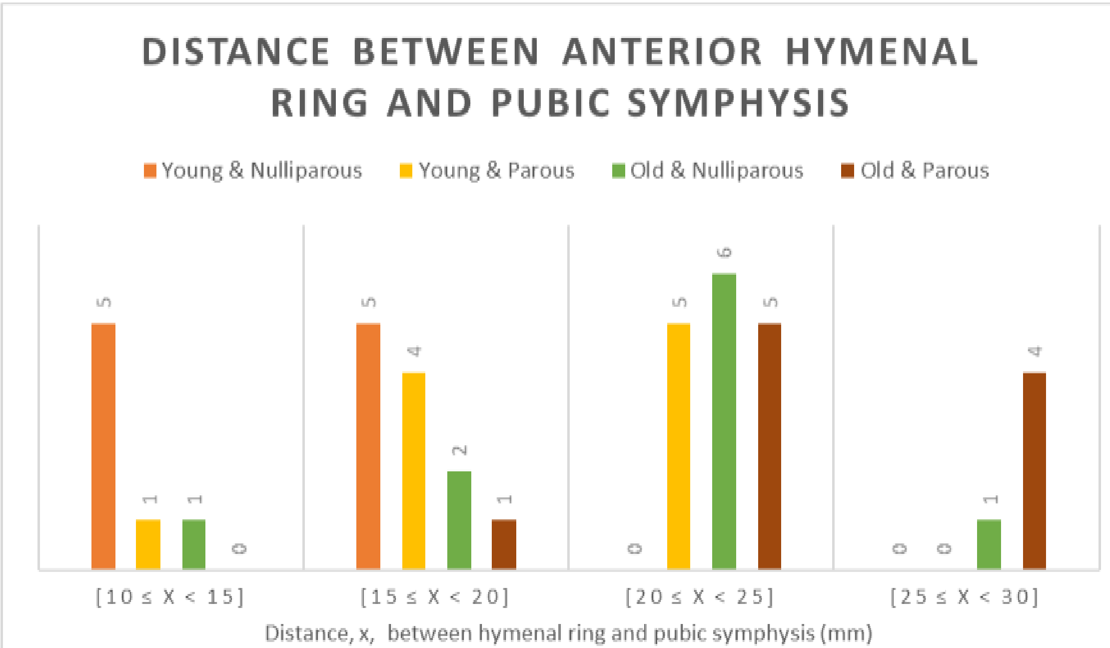


Figure 21 Histogram illustrating the spread of anterior hymenal ring distances from the pubic symphysis. The number of subjects within each bin (which represents the distance in mm) is shown above each respective group.

The histogram visualization of anterior hymenal ring distances with respect to the pubic symphysis suggest, as expected, the means between values obtained from women who were both young and nulliparous, when compared to women who were both older and parous appear to be different. The groupings also suggest that the data is skewed, indicating that outliers may be present, but a majority of the data can be captured effectively. It is important to note that the histogram presented in Figure 21 contains 4 cohorts grouped by age and parity. While the spread of data with respect to the anterior hymenal ring distance appears to have obvious skew, we chose to statistically analyze results based on using age and parity as covariates to one another.

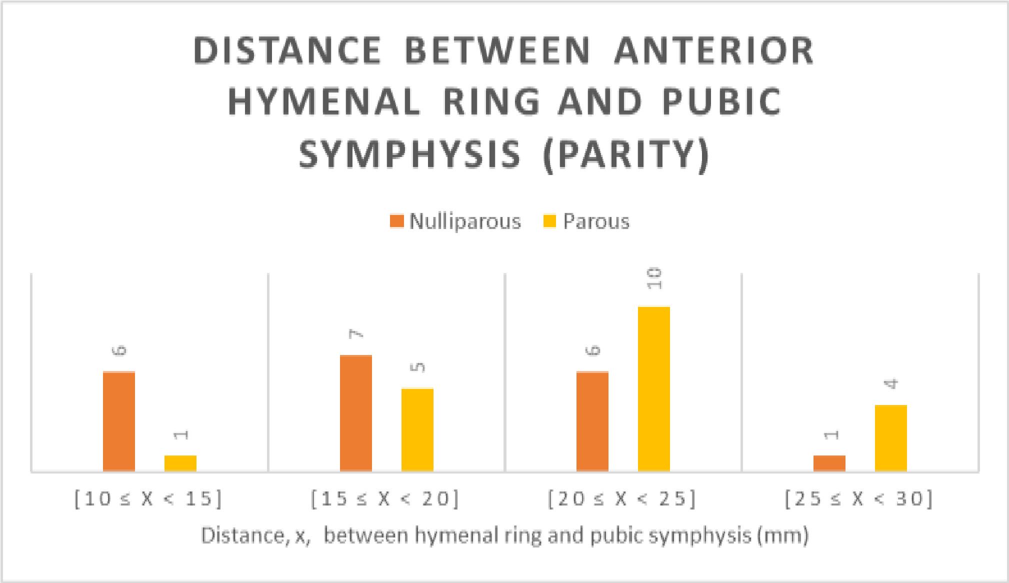


Figure 22 Distance Between Anterior Hymenal Ring and Pubic Symphysis (Parity)

Figure 22 visually depicts the distance found between the anterior hymenal ring and pubic symphysis in nulliparous and parous women. Thus, age serves as the covariate. Although there is overlap in anterior measurement values between the groups, the histogram suggests that the medians between nulliparous and parous women are different. Furthermore, the graph suggest that this particular measurement has opposite skews between nulliparous and parous subjects. These visual indicators suggest that the data may not meet all the assumptions for the parametric ANCOVA Test and will be confirmed through calculations in Table 9.

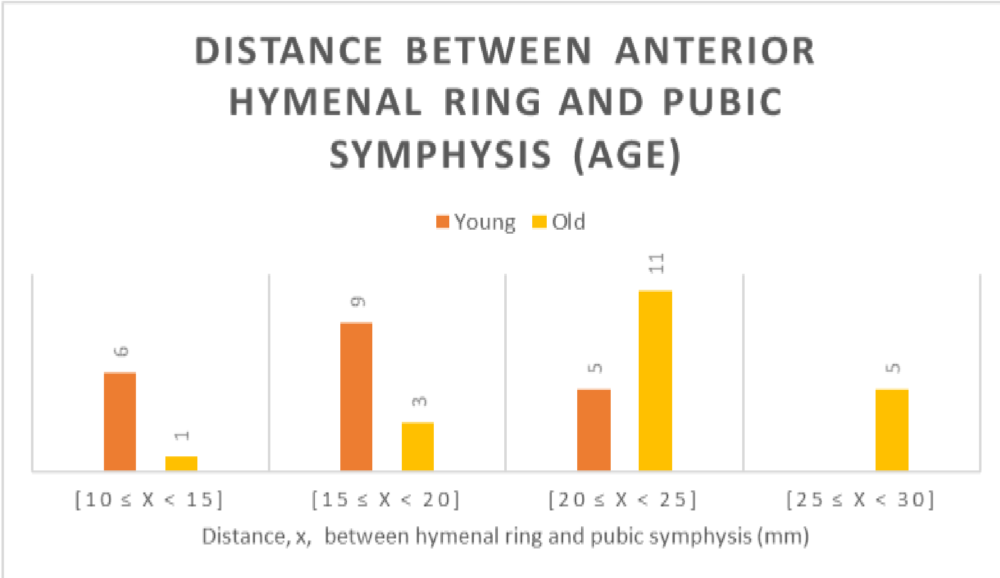


Figure 23 Distance Between Anterior Hymenal Ring and Pubic Symphysis (Age)

Figure 23 demonstrates anterior hymenal ring distance from the pubic symphysis, with parity as a covariate. The spread of values when considering age is less that parity (Figure 22), as no subjects fall within the 25mm-30mm bin. Here, the medians are also clearly different, suggesting potential differences in the anterior measurement with respect to age. To determine if these observed differences are statistically and/or clinically relevant, both parametric and non-parametric statistical analyses were conducted. Results for this analysis are found in Table 7. For all cases, the anterior measurement was the dependent variable, and age and parity were used interchangeably as covariate and grouping variables. An additional case was conducted that categorized age also as a continuous variable, to determine if any additional significance could be determined.

Table 7 Distance from the pubic symphysis to the anterior border of the hymenal ring: ANCOVA and Quade's Test Anlaysis

DISTANCE FROM PUBIC SYMPHYSIS TO ANTERIOR BORDER OF HYMENAL RING			
DEPENDENT VARIABLE N=40	Anterior		
CONTROL VARIABLE N=20	Categorical_Parity	Categorical_Age	Continuous_Age
[Group 1 (N=20) | Group 2 (N=20)]	[Young | Old]	[Nulliparous | Parous]	[Nulliparous | Parous]
Levene's Test of Equality of Error Variances *[p>0.05, indicates that equal variances can be assumed]	*p=0.697	*p=0.251	*p=0.136
Mean ± Standard Deviation (mm)	[17.1±4.0 | 22.1±3.9]	[17.5±4.0 | 21.7±4.3]	[17.5±4.0 | 21.7±4.3]
Estimated Marginal Mean ± Standard Error (mm)	[17.1±0.7 | 22.1±0.7]	[17.5±0.7 | 21.7±0.7]	[17.5±0.7 | 21.7±0.7]
Parametric: ANCOVA *[p<0.05, indicates statistical significance]	*p=3.14*10^-5	*p=3.16*10^-4	*p=3.15*10^-4
Effect Size [0.2-small effect, 0.5-moderate effect, 0.8-large effect]	0.378	0.299	0.299
non-parametric: ANCOVA (Quade's Test)	*p=1.15*10^-5	*p=2.14*10^-4	*p=0.001
Effect Size [0.2-small effect, 0.5-moderate effect, 0.8-large effect]	0.401	0.306	0.272

Levene’s test indicated that equal variances could be assumed for all groups, thus, the impact of parity on age, or age on parity is equal between groups. The Parametric ANCOVA and non-parametric Quade’s test both indicated overwhelming statistical significance, thus supporting the hypothesis that the differences between our groups are not random. More specifically, these data indicate that when controlling for parity status, differences between younger and older women can be detected through measuring the distance from the pubic symphysis to the anterior border of the hymenal ring. Conversely, when controlling for age, difference between nulliparous and parous women can be detected through measuring the distance from the pubic symphysis to the anterior border of the hymenal ring. The effect size for both parametric and non-parametric results were obtained. Overall, the effect was small for all control variables with respect to the hymenal ring. The highest effect size was found when subjects were grouped based on age and parity was considered a covariate (d=0.401). This suggests that grouping subjects by parity status demonstrates that parity has a small to medium effect on the anterior measurement. The lower effect sizes when age was a covariate suggest that age has a smaller effect on the anterior measurement.

2.3.4.2 Distance from Pubic Symphysis to Posterior Hymenal Ring

The distance between the posterior hymenal ring and pubic symphysis is observed through the histogram in Figure 24. Again, we see clear skews in the young and nulliparous and old and parous groups in opposite directions, as expected. Furthermore, subjects that fall within the young and parous categories appear to have the most normally distributed data, while subjects in the young and nulliparous categories appear to have the smallest spread.

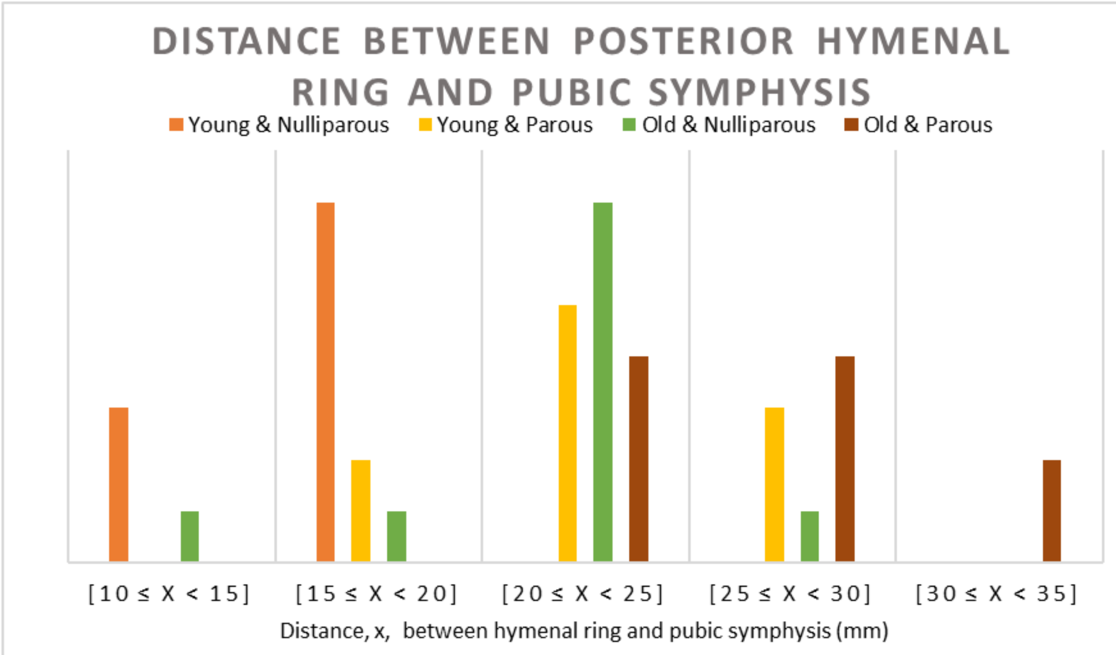


Figure 24 Distance between the Posterior Hymenal Ring and Pubic Symphysis

When controlling for age (Figure 25), we again visualize opposite skews in posterior measurements, with no parous women having a measurement between 10-15mm, and no nulliparous women having a measurement between 25-30mm. Additionally, the median values appear to be further apart, indicating the potential for discernible differences between nulliparous and parous women.

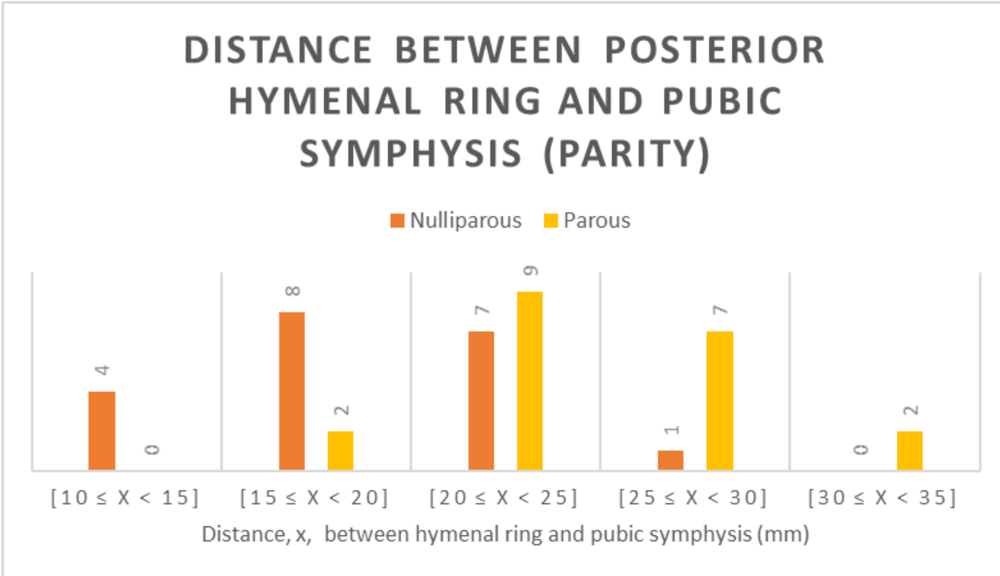


Figure 25 Distance between the Posterior Hymenal Ring and Pubic Symphysis (Parity)

Figure 26 illustrates the posterior distance from the pubic symphysis when parity is a covariate. Here, we also note differences in the median values, suggesting potential statistical significance.

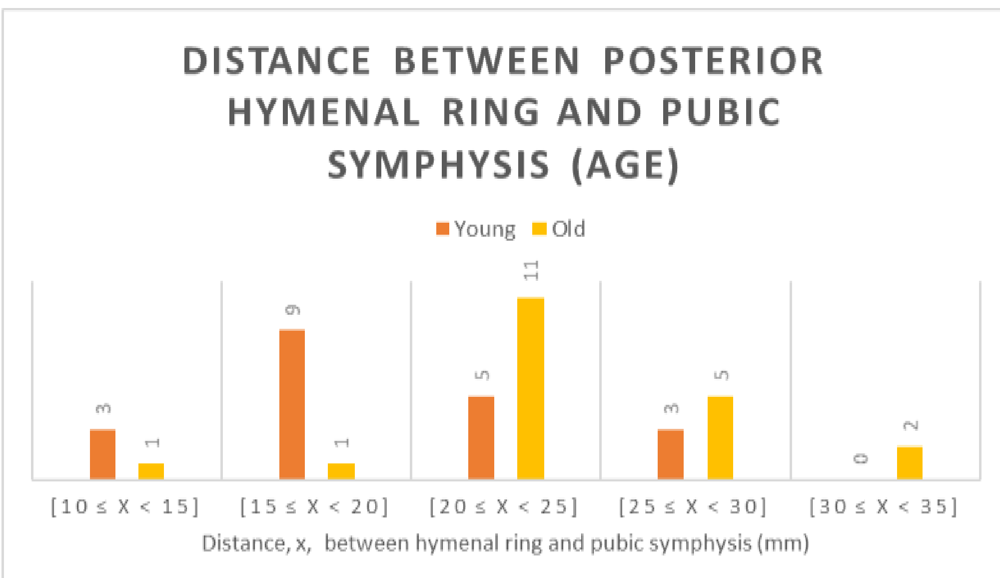


Figure 26 Distance Between the Posterior Hymenal Ring and Pubic Symphysis (Age)

Table 8 displays the statistical analysis associated with the posterior measurements. Similar to the anterior measurement, Levene's test indicated that equal variances can be assumed for age and parity as covariates, and the comparison of mean posterior values between each group provide numerical support for Figures 25 and 26. Both parametric and non-parametric p values for posterior measurements indicate statistical significance. Thus, the posterior measurement is significantly impacted by age and by parity indicate that when grouping by both parity and age, and controlling for age and parity respectively, the posterior measurement is significantly impacted by parity (p=0.003), and even more so by age ($p=3.69*10^{-6}$). Interestingly, the effect size was small to medium for parity when controlling for age (d=0.445), indicating that parity has a greater effect on the posterior measurement.

Table 8 Distance from the pubic symphysis to the posterior border of the hymenal ring: ANCOVA and Quade's Test

DISTANCE FROM PUBIC SYMPHYSIS TO POSTERIOR BORDER OF HYMENAL RING			
DEPENDENT VARIABLE N=40	**Posterior**		
CONTROL VARIABLE N=20	**Categorical_Parity**	**Categorical_Age**	**Continuous_Age**
[Group 1 (N=20) | Group 2 (N=20)]	**[Young | Old]**	**[Nulliparous | Parous]**	**[Nulliparous | Parous]**
Levene's Test of Equality of Error Variances *[p>0.05, indicates that equal variances can be assumed]	*p=0.769	*p=0.099	*p=0.067
Mean ± Standard Deviation (mm)	[20.1±5.0 | 24.0±4.5]	[19.1±4.0 | 25.0±4.3]	[19.1±4.0 | 25.0±4.3]
Estimated Marginal Mean ± Standard Error (mm)	[20.1±0.8 | 24.0±0.8]	[19.1±0.8 | 25.0±0.8]	[19.1±0.8 | 25.0±0.8]
Parametric: ANCOVA *[p<0.05, indicates statistical significance]	*p=1.78*10^-3	*p=1.16*10^-4	*p=8.54*10^6
Effect Size [0.2-small effect, 0.5-moderate effect, 0.8-large effect]	0.235	0.409	0.419
non-parametric: ANCOVA (Quade's Test)	*p=0.003	2.61*10^-6	3.69*10^-6
Effect Size [0.2-small effect, 0.5-moderate effect, 0.8-large effect]	0.213	0.445	0.435

2.4 Discussion

Significant changes in support to the vagina occur over the lifespan but to date, limited quantitative data exists to describe them. In this study, changes in the position of the anterior and posterior borders of the hymen were defined relative to the pubic symphysis, to identify detectable differences in position when considering a subject's age and parity status. Based on existing studies, age and parity continue to be linked to the onset of PFDs as the two leading risk factors; however, the precise etiology is not well defined. Founded in the analysis of existing literature, it was hypothesized that the distance from the pubic symphysis to the hymnal ring would change over the lifespan, with respect to age and parity.

Following the methodology proposed in section 2.3, it was determined that, differences in measurements for both the anterior and posterior hymenal ring border in relation to the pubic symphysis are not random. With respect to parity, the anterior and posterior border distances demonstrated statistical significance at $p=1.15*10^{-5}$ and $p=0.003$ respectively. Similarly, with respect to age, the anterior and posterior border distances demonstrated statistical significance at $p=2.14*10^{-4}$ and $p=2.61*10^{-6}$, respectively. However, the effect sizes with respect to age and parity for these measurements were small to medium. Interestingly, the effect size was greatest for the anterior measurement when subjects were grouped by age and parity was a covariate ($d=0.401$), and the posterior measurement had the highest effect size when subjects were grouped by parity status and age was a categorical covariate ($d=0.445$). At a macro level, these results indicate that the positions of both the anterior and posterior borders of the hymenal ring relative to the pubic symphysis are indeed influenced by age and parity.

The importance of characterizing Level III structural changes through the lifespan and the findings of this study are supported throughout existing literature. Lowder et. al.'s work suggests that larger genital hiatus measurements correlate with loss of apical support; and in fact, the size of the genital hiatus is frequently used as a measure of success for surgical outcomes. While evidence suggests that larger genital hiatus diameters indicate compromised support, Bradley et. al. suggests that the measured point of vaginal descent can increase or decrease with time, and is influenced by age and parity, both of which should be considered when interpreting measurements [138]. Similarly, our study suggests that the anterior and posterior borders of the hymenal ring are not fixed, and can move independently of one another, suggesting that measurements only based on diameter of a hiatus may not be sufficient. Furthermore, this suggests that the position of the anterior and posterior borders of the hymenal ring may also help reveal information about the integrity of surrounding supportive musculature.

Recent work by Routzong et. al. found that the superficial perineal structures (i.e. bulbocavernosus, ischiocavernosus and deep and superficial transverse perinei), which are commonly excluded from finite element and predictive models, may indeed be critical to consider when defining vaginal birth injury, a common risk factor for development of PFDs [227]. In particular, this study revealed that superficial perineal structures may play a significant role in the relative size and position of the genital hiatus; so much so that excluding them could contribute to gross underestimations of the biomechanical events that ultimately result in symptomatic PFDs. Thus, characterizing the relative position and diameter of the hymenal ring relative to the pubic symphysis would be a significant contribution towards mapping structural mechanics of the pelvic floor, as the position may be an indicator of pelvic floor instability. While Routzong's work was based on computer simulations, recent work by Handa et. al. found clinically that hiatal measurements may provide insight into progression of injury, supporting the need for more specific characterization of the pelvic floor [228].

The results of our study indicate that the hymenal ring is not a fixed landmark, and its position relative to the pubic symphysis shifts with respect to age and parity. Therefore, changes to the hymenal ring should be quantified through measurement of both the anterior and posterior borders with respect to the pubic symphysis. Our results indicate that the anterior and posterior hymnal ring border in women between the ages of 20-49 is consistently less than 20mm away from the pubic symphysis. If we assume that young and healthy nulliparous women are a baseline, we also note that the diameter of the hymenal ring, or the difference between the posterior and anterior measurement, ranged from 1mm to 2.7 mm. While 2.7mm is relatively small diameter, it is important to note that seven out of ten subjects who were parous and aged between 50 and 75 had hymenal ring diameters that were less than 2.7mm. These same subjects also had anterior and posterior hymenal ring border measurements that were consistently positioned further away from the pubic symphysis. When comparing younger and older nulliparous women, the lack of significance in hymenal diameter indicates that the position of the hymenal ring moves, but the relative distance between the borders remains the same. These findings indicate that diameter measurements of soft tissues must be coupled with other measurements to provide more context regarding the state of the pelvic floor, as a larger hiatus diameter may not necessarily indicate a structural problem. This finding is of vital importance, as surgical decisions and outcomes are heavily reliant upon genital hiatus diameter measurements and POP Q measurements, neither of which capture the measurements explored in this study.

Tracking the relative movement and position of the hymenal ring over time could serve as early biological indicator that provides insight to changes or damage to muscles and tissues that, if untreated could result in symptomatic PFDs. High-level trends observed through this study indicate that, generally, with vaginal delivery, the hymenal ring widens as a result of the posterior hymenal ring border shifting significantly away from the pubic symphysis, and the anterior border shifting between 2 and 5 mm away from the pubic symphysis shifting 5 mm or more. Changes to the anterior or posterior border further than described above could eventually be used to indicate damage to various pelvic muscles and superficial structures as a result of delivery. Older nulliparous women appear to have comparable hymenal ring diameters to that of young nulliparous women, and in fact, could be smaller. Older nulliparous women also tended to have anterior and posterior hymenal ring borders shifted posteriorly when compared to you nulliparous women. This The small diameter and increased overall distance from the pubic symphysis could indicate tissue atrophy, attenuation of aging muscles, or changes in collagen content as a result of age, or even help detect conditions such as levator hypertonicity, a painful condition that is commonly diagnosed only though exclusion of other possible diagnoses [229]. Thus, characterizing changes in the hymenal ring could serve as a potential indicator for overall pelvic floor health.

Since the position of the hymen changes and is influenced by both age and parity, it then begs the question of whether these changes, while statistically significant, are also clinically relevant, given that POP-Q measurements are typically in cm and our measurements are reported in mm. While the specific clinical relevance of these results is yet to be determined, our ability to detect these smaller, yet significant changes help set the stage for the development of more predictive measures for early detection of PFDs. Most importantly, this study indicates that because the hymenal ring is not a stable landmark, there may be different that the POP-Q is unable to capture, thereby limiting the sensitivity of the POP-Q as the sole method for assessing pelvic support. Studies that require human participation and input are always at risk of bias and error. This study is not exempt from these risks; however, we have made every effort possible to minimize biases and error, and address limitations.

Sample size is a common limiting factor for studies that aim to understand differences within human populations. This was particularly a challenge for this study, as due to the need for clear visibility of the hymenal ring and the precision necessary to collect measurements led to the exclusion of patients who were identified as "healthy" but required the insertion of gel into the vagina or rectum; as gel insertion could have influenced the measurements and results of this study. The use of retrospective scans can also be inherently biased, as only patients who have access to healthcare/resources, or who believe they have an ailment are being scanned. Thus, socioeconomic factors, coupled with the demographics of the Pittsburgh area, suggest that these results may not be generalizable for all populations, races, and ethnicities. At this time, our study does not explore differences in these measurements with respect to race or ethnicity, which is a limiting factor, as it is well-established that race and ethnicity may influence the likelihood of developing prolapse or other PFDs [18], [209].

When interpreting these results, it is important to consider potential sources of error regarding collection of measurements, and the precision of our measurements. To obtain high quality images, patients must remain still for the duration of each scan. Typically, the more slices, the more time required for the scan. Therefore, it is important to balance the quality of the image necessary with the amount of time a patient is expected to remain still. Furthermore, it is virtually impossible to remain completely still for several scan sequences in a row. To help account for this, anatomical views were aligned prior to collecting measurements. Upon tracking the displacement of each MRI volume required, we observed that only 1-2 mm of adjustment was necessary to align most volumes in most cohorts. Interestingly, we found that women within the cohort aged 50-75 typically required the greatest amount of adjustment; suggesting that some patients shift significantly between scan sequences and the alignment of scans should always be considered prior to collecting any measurements. To confirm accuracy and repeatability of our alignments, both alignments and measurements were confirmed by an additional researcher who was blinded to the cohorts, and we found that our results were accurate to 0.5mm. While measurement techniques precision helps supply reliable results, the drawback is the additional amount of time required to confirm alignment.

It is important to consider how the thickness of the MRI slices could impact the precision of our study. The average thickness of MRI slices used in this study was 5mm. This is, in fact why we used multi-planar image volumes and slice intersections to aid in the overall precision of our measurements. To address the question of how slice thickness could impact the validity of our results, we utilized the Pythagorean Theorem. Given that the average slice thickness is 5mm, if we assume a measurement of 15.8mm based on our visual observations, we can conclude that the true measurement would be 15mm. This results in a percentage difference of 5%, which is minimal.

For this study, we chose to use static images. Typically, measurements of pelvic floor stability are done using dynamic images. Given that our assessment was conducted with patients only at rest (no Valsalva maneuvers), we would anticipate that the measured distances could be more pronounced as a result of increased abdominal pressures. Thus, use of dynamic scan measurements may reveal more clear delineations between cohorts. The 2D methodology use for this study only measures anterior/posterior positions, and does not capture inferior/superior movement, or any movement of the apex position, both of which may help further discern differences among the cohorts of women studied.

2.5 Conclusion

The review of literature offered in Section 1.3 supports the notion that both age and parity significantly impact the structure of the pelvic floor, thereby suspected of contributing to the progression of varying degrees of prolapse, prolapse, experienced by women worldwide. While present-day approaches have helped identify correlations, the specific mechanisms that drive these relationships remains unclear. The span of time and events that separates parity from noticeable indicators of POP, reflect a significant challenge that must be tackled to unravel the individual contributions of risk factors towards the progression anatomical pathologies.

In conclusion, the data indicates that the HR is not a fixed landmark and has the potential to change over the lifespan, raising concern about its utility as an independent quantitative measurement. In fact, this study revealed that the position of the hymenal ring (particularly the posterior border) shifts posteriorly and increases in diameter following vaginal delivery and shifts posteriorly but decreases in diameter with age.

3.0 Determining Vaginal Axis and Spatial Position Using a 3D Anatomical Coordinate System

3.1 Introduction

Our review of female pelvic anatomy and physiology in Chapter 1 described the vagina as the “keystone of pelvic support” due to its central location within the pelvis, which by proxy, facilitates support of pelvic viscera (i.e. bladder, rectum, and uterus) [67]. Theories derived from anatomical evidence suggest that the vagina maintains its “keystone” shape, location and orientation through the complex network of connective tissues and ligaments that attach from the perineal body (Level III) to the vaginal apex (Level I) [230], [231]. Thus, compromised integrity of support structures can progress into symptomatic POP.

Chapter 2 examined 2D sagittal images to evaluate subtle changes in the position of soft tissues by measuring movement of the hymenal ring as a proxy for Level III support. This method offered pathways towards the development of quantitative classifications of normal vaginal position, with respect to the greatest risk factors associated with symptomatic POP (i.e., age and parity). However, this approach does not characterize apical (Level I) movement or support, nor describe the orientation of the vagina as it traverses the pelvis. Here, we will justify the need for, and development of, a 3D coordinate system that describes the position and orientation of the vagina with respect to each patient’s anatomy. The development of methods that critically and robustly characterize vaginal position and orientation facilitates improved reliability and interpretation of measurements, thereby enabling clinicians and researchers to more effectively characterize patient anatomy. Ultimately, improved characterization leads to the development of more precise treatments and surgical procedures, and even the possibility of effective preventive measures against the development of POP [232].

3.2 Relevance of Vaginal Axis Measurements

In 1914, British gynecological surgeon Victor Bonney emphasized that characterization of the vagina and its supportive structures was key to successful prolapse repair. In fact, he stated, “The attempt to saddle the onus (for prolapse) on one element of the sustentacular apparatum always appears to me as futile as endeavoring to decide which particular brick supports a wall” [198]. Prior to the advent of medical imaging, knowledge surrounding the shape, position, and interactions of internal organs was obtained through drawings and written descriptions based on cadaver dissections [200]. In fact, cadaver dissections still serve as a method through which medical students can familiarize themselves with anatomy, injury and disease progression, and practice surgical techniques. However, use of cadaver models can be limiting when trying to improve our definition of normal vaginal anatomy, due to muscular rigidity in the pelvic floor, and distention of the rectum; both of which could alter the normal axis of the vagina [198].

The term vaginal axis is used to describe the path, or trajectory of the vaginal organ within the pelvis. The concept of vaginal axis has been discussed at least since the 1950s, and in 1978, Funt et. al. suggests that defining the normal vaginal axis is a critical step towards our ability to successfully restore anatomy through surgical repair [83], [198]. This study utilized images of the vagina captured through x-ray to outline the vaginal border and collect measurements, including a central vaginal axis, and angles between the upper and lower vagina to quantify the relationship of the vagina to other viscera and supports within the pelvis, which is critical towards successful reconstructive surgeries.

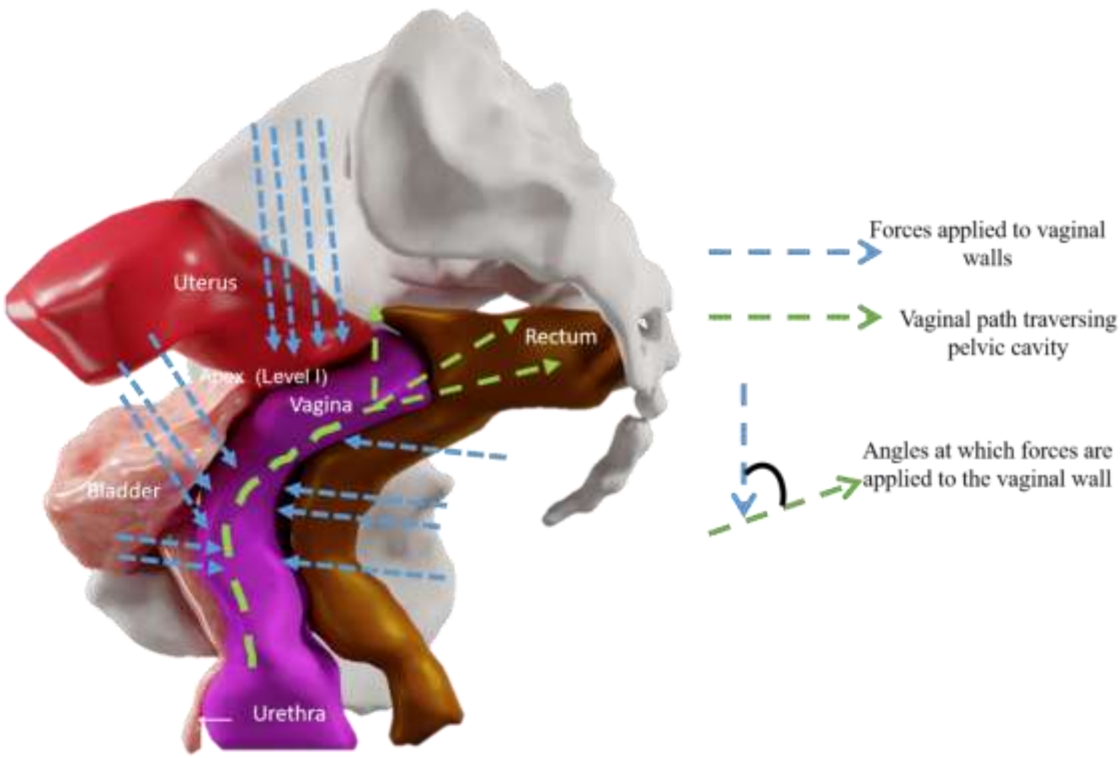


Figure 27 Visual depiction of the vaginal path through the pelvic cavity (green), and potential applied forces (blue). The angle that is formed by the point of contact on the vaginal wall and the vaginal wall impact the net force to the vaginal wall; a soft tissue organ that can be displaced if netforces are not equal to 0.

The concept of a normal vaginal axis, or a normal vaginal angle becomes more relevant when considering pelvic anatomy through a biomechanical lens. All objects in the physical world have mass and influence each other through the application of Newton's Laws. Ultimately, the net forces on an object, which is the sum of all forces or pressures on an object, in tandem with the mechanical properties of the object determine if the object remains at rest or shifts as a result of these forces. When objects are a part of a system, such as a closed link structure, changes to one object can influence changes in another object within that system [233], [234].

Figure 27 illustrates how changes in vaginal axis can lead to redistribution of forces from surrounding pelvic organs and on musculature and connective tissues [235]. For example, a steeper vaginal angle, which is depicted by the vertical green arrow, would result in forces being applied very acutely to the vaginal wall. The change in angle, by definition, will alter the force applied to the soft tissues, which in turn, if there are not forces to counteract it, could result in movement of pelvic organs to less optimal positions. Thus, improvement in our ability to measure the variation in angles formed by the vaginal canal could provide insight towards simulating/postulating specific scenarios that contribute to mechanical failure.

3.3 Existing Pelvic Reference Systems

Non-invasive imaging technologies such as Magnetic Resonance Imaging (MRI) have improved our ability to diagnose complex cases of pelvic floor dysfunctions, and quantify the progression of pathologies [99], [186], [187], [193], [236], [237]. MRI scanners capture axial, coronal, and sagittal image volumes, which aid in the conceptualization of the position and shape of bones, muscles, and pelvic organs. Although there are no universally recognized techniques for quantifying female pelvic anatomy, 2D midsagittal images are commonly used quantify progression of PFDs, through various linear angles and distances based on bony landmarks and vaginal location [193], [238].

To date, there is little consensus among researchers and clinicians regarding standardized methods for quantifying normal and pathologic scans [239]. There are several existing referencing systems used quantify the degree of prolapse. Reference lines such as the pubococcygeal line (PCL), pubosacral line (PSL), sacrococcygeal inferior-pubic point line (SCIPP line), midpubic line

(MPL), the perineal line (PL), and the H line/horizontal line were created to quantify degrees of prolapse, and several additional methods are illustrated in Figure 17 [195]. However, the accuracy and sensitivity of these methods can be significantly compromised due to patient alignment within a scanner, patient position (i.e., supine, lithotomy, etc.), and challenges with obtaining images that capture the exact mid-sagittal plane. These factors, coupled with moderate inter- and intra-observer repeatability when identifying specific anatomical landmarks (i.e. sacral and coccygeal joints), results in similar accuracy to POP-Q examinations [192], [195], [240]–[243]. The compilation of these challenges can contribute to measurement errors of up to 16% (i.e. greater than measurements of interest) which further confounds meaningful interpretations of patient cohort comparisons [241], [244].

When quantifying relatively large changes in anatomical position (i.e., Stage 3 or 4 POP), these metrics seem adequate. However, the method is not sensitive enough with subtler changes in anatomy that may represent an early failure of support, and predisposition to the development of symptomatic prolapse. The lack of sensitivity can lead to errors that are greater than the measurement of interest, thereby confounding any meaningful interpretation [244]. Indeed, changes in a patient's position as low as 20 degrees results in errors in measurement up to 16%. Thus, these methods produce approximately the same amount of accuracy as POP-Q exams, and are subject to poor observer repeatability [192], [195], [241]–[243].

Studies suggest that these methods are generally not superior to a traditional physical examination of the patient due to alignment errors and poor inter- and intra- observer repeatability when identifying anatomical landmarks in the mid-sagittal plane [241]–[243]. This inability to make accurate and repeatable measurements has hindered the development of a gold standard for the reliable quantification of POP based on imaging. For a quantification method to be clinically relevant, the process of quantifying regions of interest must be both repeatable and reliable. To reliability quantify the regions of interest, one must first identify the overall shape of the vagina.

In 2006, Barnhart et. al., utilized MRI to measure baseline dimensions of women in reproductive age [98]. This study revealed significant variations in sagittal 2D measurements of dimensions of the upper and lower vagina, length and width, among patients, with some measurements resulting in a difference greater than 100% between the largest and smallest measurement. One decade later, Luo et. al conducted a supporting study that reconfirmed these findings, and expressed the importance of developing methods to characterize vaginal morphology [99]. These contributions towards defining normal vaginal anatomy illustrate the nuanced complexity and variation of vaginal size and shape within populations. Furthermore, Chapter 1.3 explores limitations of current applications of clinical exams and diagnostic imaging measurement techniques towards the characterization of pelvic organ support, including the lack of standardized, universal methods for characterization of pelvic anatomy, as well as the impact of current limitations on our ability to compare patients.

In 2016, DeLancey, et. al at the University of Michigan developed a method for quantifying vaginal shape and dimension. This is completed through quantifying the dimensions of the vagina with respect to a coordinate system derived from axial and sagittal images of the pelvis. More specifically, the vaginal walls and cervix were traced from axial slices. A point at the middle of the pubic symphysis and two points on the distal and middle regions of the sacrum were used as the bony landmarks for establishing the 3D common coordinate system. Additionally, the vaginal wall length and shape were measured in the mid-sagittal plane. The Pelvic Inclination Correction System (PICS) was then used to implement the coordinate system. For this system, the XY axis view in the sagittal plane is rotated 34 degrees clockwise from the sacrococcygeal-inferior pubic point (SCIPP). It is believed that this rotation aligns the body axis along the direction in which gravity is acting, thus providing a common coordinate system for each subject.

3.4 3D Anatomical Patient Coordinate Systems

Cartesian coordinate systems are used to define n-dimensional spaces. 3D Cartesian coordinate systems describe the location of an object in Euclidian space through the amalgamation of 3 linearly independent unit vectors that share a point of origin. 3D descriptions are particularly useful when trying to define objects with depth, like most things in our physical world, by enabling more accurate descriptions regarding an object. 3D coordinate systems coordinate systems have been applied in several areas of medicine, such as brain imaging, mammograms, and musculoskeletal structures to quantify internal/external and normal/abnormal anatomical features between patients cohorts [245]–[253]. The interpretation of the coordinate system is determined by the orientation of the vectors, and therefore can be positioned an infinite number of ways.

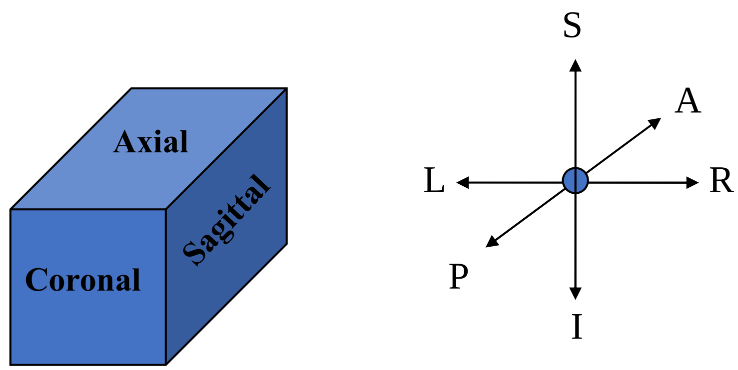


Figure 25 Body planes and anatomical directions matched to a coordinate system

MRI scanners utilize 3D Cartesian coordinate systems to define the position and orientation of patients within the scanner. However, the origin and directions of the perpendicular axes that define each system may differ by manufacturer. Furthermore, patient alignment within the scanner may vary, making the MRI coordinate system ineffective for quantifying comparisons between patients.

Anatomical landmarks are specific points that can be identified and serve as the basis for measurements to compare aspects of biological organisms. Thus, identifying anatomical landmarks within a patient are critical for developing a patient-based coordinate system that accounts for potential misalignment in the MRI scanner and different coordinate systems. Several studies indicate that the most repeatable and reliable landmarks should be static/immovable and similar between patients regardless of their alignment within the scanner [241]. Portions of the bony pelvis are effective as immovable landmarks, as most are not likely change position and location like soft tissues. These landmarks, once selected, can be connected through linear measurements, which can be then applied as the basis of a 3D coordinate system.

Bony Measurement	**Mean difference between examiners, in cm(n=84)**
Acute pubic ligament to left ischial spine	0.0476
acute pubic ligament to right ischial spine	0.025
left ischial spine to right ischial spine	0.0012

Table 6 Select measurements from Stein, et. al.

Common bony pelvis landmarks include the coccyx, sacrum, pubic symphysis, and ischial spines. The selection of landmarks is crucial when determining the coordinate system, especially when the desire is to compare across patients. One must determine static landmarks that are similar enough between patients that regardless of how the patient is aligned in the scanner, the coordinate system is the same in addition to the fact that the points have to be easily and repeatedly identifiable.

A study conducted by Stein et. al reported mean differences for inter-examiner reliability between bony measurement, some of which are summarized in Table 6. The inter-examiner reliability of identifying a line between the left and right ischial spine and found the mean difference between examiners to be 0.0012, with a P value of .98, further justifying the use of these landmarks [254].

3.5 Motivation

Motivated by the limitations of the POP-Q and existing 2D measurement techniques, in 2011, our laboratory began developing our novel 3D measurement system, based on the perception that 3D visualization of female pelvic anatomy provides the opportunity for more detailed and accurate assessments of the complex interactions between pelvic connective tissues, musculature, and viscera, thereby improving our ability to quantify comparisons between subjects and potentially related findings to specific pathologies [192], [241], [255], [256]. Thus, we aimed to develop and evaluate a coordinate system that improves upon previous limitations, such as lack of sensitivity of measurements, patient misalignment in the scanner, improving the inter- and intra-observer repeatability of measurements, and providing a streamline system to quantitatively assess and compare patients. Furthermore, we developed methods for quantifying the spatial position of the vagina with respect to our coordinate system, to serve as a proxy for understanding defects and damage within the network of connective tissue and musculature support. Our hope is that these measures could be utilized to identify subtle changes in pelvic anatomy and help uncover the progression of the degradation of pelvic organ support. utilizing 3D MRI volumes would provide the greatest ability to make comparisons between subjects and potentially relate findings back to a specific pathology.

3.6 Methods

3.6.1 Defining the 3D Anatomical Coordinate System

The proposed 3D anatomical coordinate system is derived from the MRI scanner coordinates of six distinct bony landmarks, summarized in Figure 28. The most medial point of the right and left ischial spines (IS_R and IS_L) are identified in the axial plane of view (figure 28a). The other four landmarks are the superior pubic point of the right and left pubic symphysis (SPP_R and SPP_L) and the inferior pubic point of the right and left pubic symphysis (IPP_R and IPP_L), all of which were identified using axial image volumes resliced for sagittal viewing (figure 28 b, c).

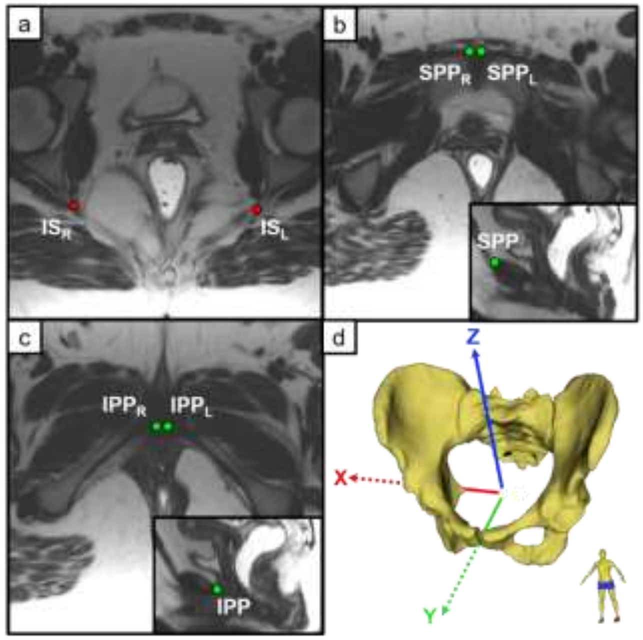


Figure 28 Visual representation of bony landmarks for pelvic coordinate system. a) axial view of right and left ischial spine landmarks (IS_R and IS_L, respectively). b) axial view of right and left superior pubic points (SPP_R and SPP_L, respectively) and sagittal view of the superior pubic point (SPP) location c) axial view of right and left inferior pubic points (IPP_R and IPP_L, respectively) and sagittal view of the inferior pubic point (IPP) location d) 3D visualization of x, y, and z axes of pelvic coordinate system.

The axes were computed from vectors derived from the six landmarks. The x-axis of this coordinate system aligns with the medial-lateral anatomical axis, depicted in red (figure 28 d). The origin of the coordinate system was derived from the mathematical midpoint between the left and right ischial spines and serves as an axis of the coordinate system, and by definition, is mid-sagittal:

$$Origin = \left\{\frac{x_{ISL} + x_{ISR}}{2}, \frac{y_{ISL} + y_{ISR}}{2}, \frac{z_{ISL} + z_{ISR}}{2}\right\}$$ **Equation 1**

The distance from the point of origin to the right ischial spine was normalized by its length to represent the x-axis of the coordinate system:

$$\hat{\boldsymbol{\imath}} = \frac{IS_R - Origin}{\|IS_R - Origin\|}$$ **Equation 2**

This axis is the least susceptible to variations in measurements as a result of misalignment of a patient within the scanner. The y-axis of this coordinate system aligns with the anterior-posterior anatomical axis, depicted in green (figure 28d). Many current methods utilize the sagittal anatomical view to locate the distal middle point of the pubic bone; however, it can be difficult to approximate the exact mid-sagittal location. Thus, our axis is derived from the four pubic points in figure 28 b and c. First, the midpoints between the left and right superior pubic points and inferior pubic points were calculated:

$$Superior\ Pubic\ Point\ Midpoint\ (SPP_m) = \left\{\frac{x_{SPPL} + x_{SPPR}}{2}, \frac{y_{SPPL} + y_{SPPR}}{2}, \frac{z_{SPPL} + z_{SPPR}}{2}\right\}$$ **Equation 3**

$$Inferior\ Pubic\ Point\ Midpoint\ (IPP_m) = \left\{\frac{x_{IPPL} + x_{IPPR}}{2}, \frac{y_{IPPL} + y_{IPPR}}{2}, \frac{z_{IPPL} + z_{IPPR}}{2}\right\}$$ **Equation 4**

This calculation eliminates the potential confounding factor of not locating the mid-sagittal plane as a result of inherent imaging limitations. Figure 29 summarizes how the location of the Levator Insertion Point (LIP) (Equation 5) was determined to be approximately one third of the distance between SSP_m (Equation 3) and IPP_m (Equation 4).

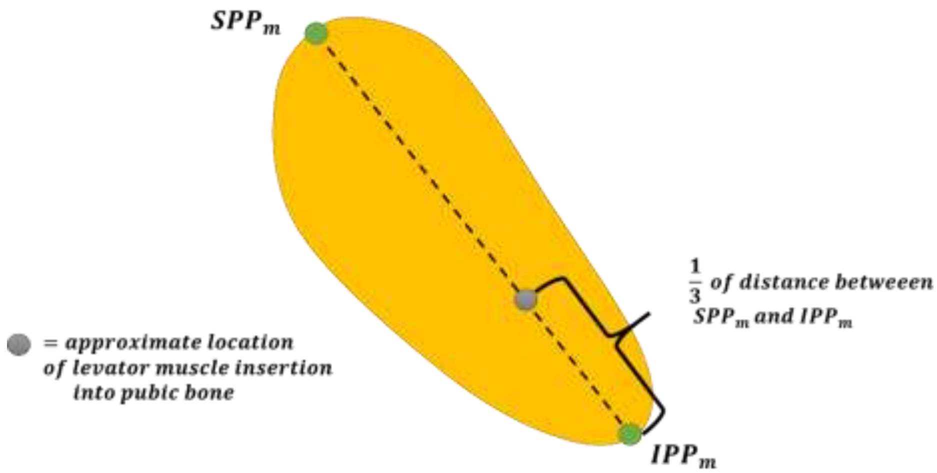


Figure 29 Depiction of Pubic Symphysis measurement for initial y-asis

The distance from the Origin to LIP (Equation 6) was normalized by its length to represent the first iteration of the y-axis of the coordinate system, as the angle relationship between vectors i and j may not be orthogonal, and thus not necessarily linearly independent.

$$Levator\ Insertion\ Point\ (LIP) = \left(\frac{SPP_m - IPP_m}{3}\right) + IPP_m \qquad \textbf{Equation 5}$$

$$\hat{\boldsymbol{j}}^{\boldsymbol{1st}} = \frac{LIP - Origin}{\|LIP - Origin\|} \qquad \textbf{Equation 6}$$

The z-axis of this coordinate system aligns with the superior-inferior anatomical axis, depicted in blue (figure 28d). This axis is defined as the cross product of unit vectors i and j^{1st} in Equation 7:

$$\hat{k} = \hat{\imath} \times \hat{\jmath}^{1st}$$ **Equation 7**

$$\hat{\jmath} = \hat{k} \times \hat{\imath}$$ **Equation 8**

By definition, the cross product of vectors i and j^{1st} result in a vector k, that is orthonormal to the plane containing both vectors. Likewise, determining the cross product of vectors k (z-axis) and i (x-axis) would result in the corrected j vector (y-axis), and satisfy the condition of orthogonality (Equation 8). While the y-axis is similar to the SCIPP Line, commonly used in 2D analyses, this coordinate system eliminates medial-lateral errors with defining the most distal aspect of the pubic bone to keep it in the mid-sagittal plane regardless of orientation of the patient within the scanner.

$$P_{PCS} = T^{-1} \cdot P = \begin{bmatrix} i_x & i_y & i_z & Origin_x \\ j_x & j_y & j_z & Origin_y \\ k_x & k_y & k_z & Origin_z \\ 0 & 0 & 0 & 1 \end{bmatrix}^{-1} \cdot \begin{bmatrix} SCS_x \\ SCS_y \\ SCS_z \\ 1 \end{bmatrix}$$ **Equation 9**

Unit vectors i, j, and k define the orientation of the local 3D anatomic reference system. To map the relationship between the built-in scanner coordinate system and our Pelvic coordinate system, we must calculate the transformation of points defined within the scanner coordinate system (SCS) with respect to our new coordinate system (P_{PCS}), as in Equation 9. Thus, we are now able to quantitatively compare different patients and different scans to one another, as they are all defined relative to a global coordinate system with an origin point of (0,0,0).

3.6.2 Derivation of Vaginal Axis and Position

The vagina is a unique organ, not only for its functions, but its shape. Researchers have found that, unlike the urethra, which resembles a uniformly thin hollow cylindrical tube, vaginal dimensions differ throughout the length of the organ [99]. For example, the width of the introitus is a significantly smaller opening than the apex of the vagina. Additionally, the vagina may not be positioned precisely mid-sagittal, which, depending on the question, could limit the accuracy of 2D calculations [99]. Thus, to capture the deviation from the mid-sagittal axis, we must account for morphological differences in the vagina that could dictate the overall path and positioning in space.

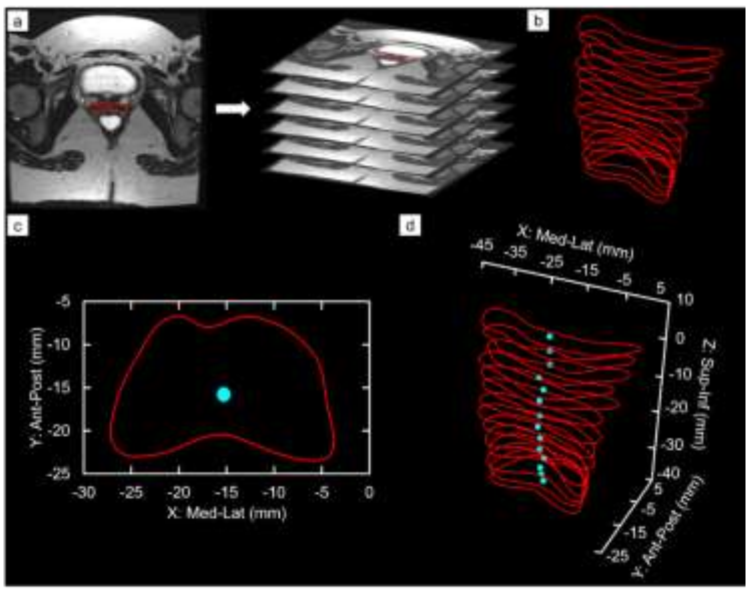


Figure 30 Summary for determinng vaginal axis and position a)Fiducial markers placed around vaginal borders b)Representation of contiguous 2D curves c) slice calculation of centroidal point d)contiguous centroidal points

Axial MRI volumes were used to capture geometric information towards defining the vaginal axis. Fiducial markers were manually placed on the vaginal boundaries using OsiriX, an image processing software (**Version 6**, Pixmeo SARL, Bernex, Switzerland) [257]. The completion of vaginal border segmentation resulted in a set of contiguous 2D curves (Figure 30 a, b), in the SCS. Since the fiducial markers were placed manually and the number of markers used to trace the vaginal border varied throughout the length of the vagina, a closed B-spline interpolation function was applied, and initial sample points were recalculated as 1000 evenly distributed points [258]. This was a critical step towards minimizing biases as a result of non-uniformly distributed points that could influence calculations in Equation 10.

$$C_i = \{\overline{x_1}, \overline{y_1}, \overline{z_1}\} = \frac{1}{1000}\left\{\sum\nolimits_{j=1}^{1000} x_j, \sum\nolimits_{k=1}^{1000} y_k, \sum\nolimits_{l=1}^{1000} z_l\right\}$$ **Equation 10**

$$where\ i = 1 \cdots n^{th}\ contour$$

A centroidal point was calculated for each vaginal trace by finding the mean of the x, y, and z components (Equation 10 & Figure 30c, d). Thus, the central axis of the vagina is defined by the ordered collection of centroidal points, which represents the overall path of the vagina as it traverses the pelvis.

$$V_{sp} = \frac{1}{n}\left\{\sum\nolimits_{i=1}^{n} x_{ci}, \sum\nolimits_{i=1}^{n} y_{ci}, \sum\nolimits_{i=1}^{n} z_{ci}\right\}$$ **Equation 11**

$$where\ i = 1 \cdots n^{th}\ contour$$

The central point calculations were then converted from SCS to P_{PCS} (Equation 9) and stored in an array with respect to the z-coordinate (inferior to superior direction). The spatial position of the vagina (V_{SP}) was calculated through averaging the x y and z components of the centroidal points (Equation 11).

3.6.3 Vaginal Angle Measurements with Respect to Pelvic Coordinate System

While early descriptions of pelvic anatomy dissections described the vagina as a "straight hollow tube extending vertically upwards towards the sacral promontory", 19th century Hadra et. al noted the importance of studying the anatomy of living patients, as well as the possibility that the vagina may not be straight and hollow, but have two distinct axes, separated by the pelvic diaphragm [98], [259]–[261]. Subsequent studies and confirmation through medical imaging further supports this initial claim, and emphasizes the importance of quantifying the upper and lower vagina separately [99], [262].

$$\overrightarrow{\boldsymbol{Vag}} = V_{sp} + t\langle a, b, c\rangle \qquad \textbf{Equation 12}$$

Thus, the vaginal axis centroids that were calculated in section 3.6.2 were divided in half to calculate two lines of best fit. A least-squares algorithm was applied to calculate a line of best fit for the upper/proximal vagina (superior half of centroidal points) and the lower/distal vagina (inferior half of centroidal points). Then, each line of best fit was parameterized (Equation 12), so that the origin of both lines would be defined from the spatial position of the vagina (V_{SP}).

The angles of the proximal and distal vaginal axis were then computed with respect to the pelvic coordinate system by first normalizing each vector, and then calculating the dot product between each vector representing vaginal axis and the axes unit vectors. Thus, angles of elevation, deviation, and sagittal and coronal angles could be calculated.

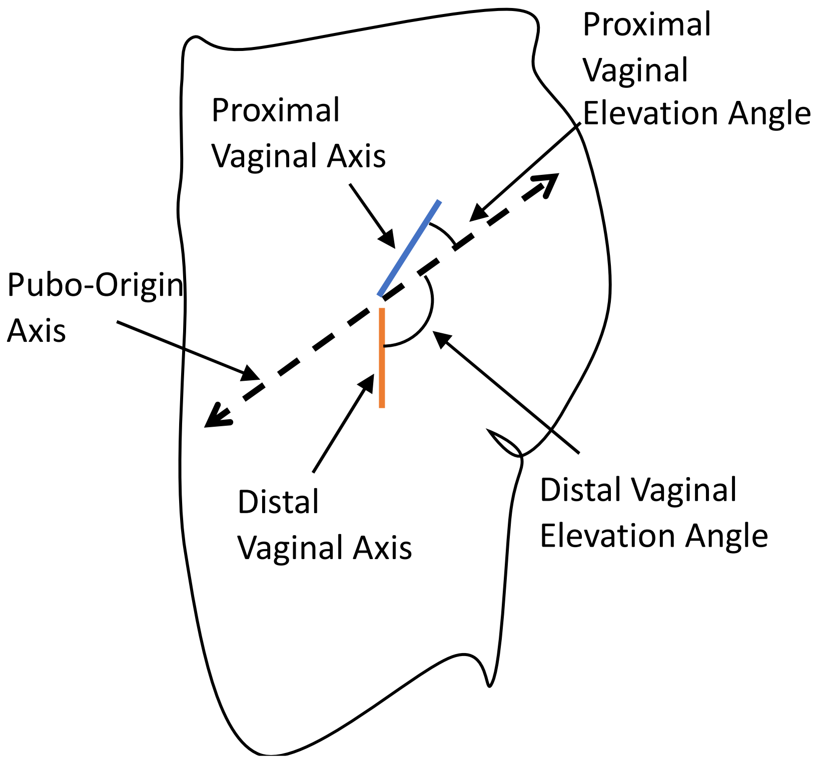


Figure 31 Visual depiction of Calculated Angles of upper and lower elevation

The angle of elevation is the angle formed by the pubo-origin axis (y-axis) of the coordinate system and the vaginal axis. Figure 31 depicts how the proximal angle of elevation (E_{prox}) (Equation 13) and distal angle of elevation (E_{dist}) (Equation 14) were calculated, respectively.

$$E_{prox} = 180 - \cos^{-1} \hat{\boldsymbol{v}}_{upper} \cdot \hat{\boldsymbol{y}} \qquad \textbf{Equation 13}$$

$$E_{dist} = \cos^{-1} \hat{\boldsymbol{v}}_{lower} \cdot \hat{\boldsymbol{y}} \qquad \textbf{Equation 14}$$

$$A_{sag} = E_{prox} + E_{dist} \qquad \textbf{Equation 15}$$

Acute elevation angles indicate posterior deviation (away from the pubic symphysis), while obtuse elevation angles suggest anterior deviation (towards the pubic symphysis). The sagittal angle represents the total angle of the proximal and distal elevation angles (Equation 15). Elevation angles formed by the proximal vaginal axis would provide information regarding the integrity of apical vaginal support, while angles formed by the distal vaginal axis would indicate the quality of distal vaginal support.

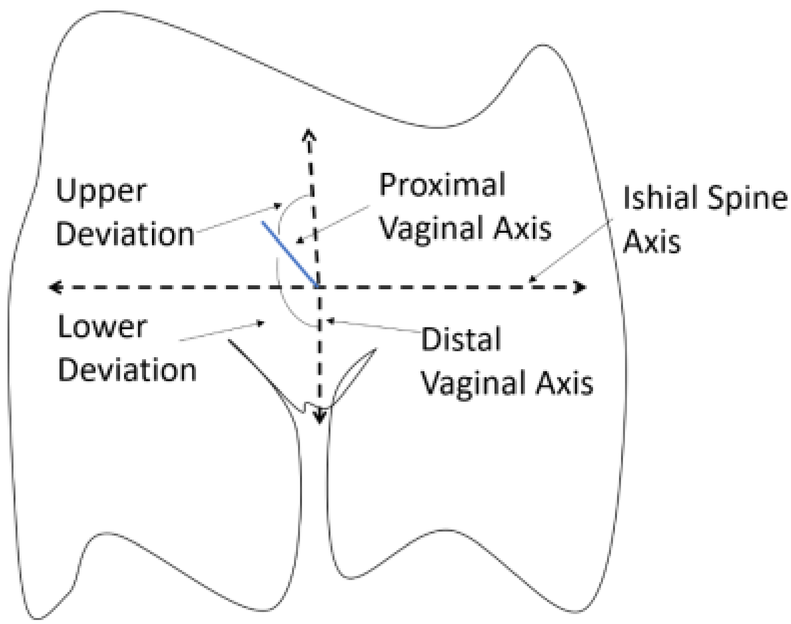


Figure 32 Visual depiction of calculated angles of upper and lower deviation

Angles of deviation, depicted in figure 32, are formed by the z-axis of the coordinate system and the vaginal axis. The proximal angle of deviation (D_{Prox}) (Equation 16) and distal angle of deviation (D_{Dist}) (Equation 17) were calculated, respectively.

$$D_{prox} = 90 - \cos^{-1} \hat{\boldsymbol{v}}_{dist} \cdot \hat{\boldsymbol{z}} \quad \textbf{Equation 16}$$

$$D_{dist} = 90 - \cos^{-1} \hat{\boldsymbol{v}}_{lower} \cdot \hat{\boldsymbol{z}} \quad \textbf{Equation 17}$$

$$A_{cor} = D_{prox} - D_{dist} \qquad \textbf{Equation 18}$$

Acute deviation angles suggest that the vaginal axis is aligned more towards the midline, and obtuse angles suggest lateral deviation of the vaginal axis with respect to the midline. Positive proximal deviation angles signify the proximal vagina is angled towards the right of the patient. Conversely, positive distal deviation angles signify that the distal vagina is angled towards the left. Equation 18 represents the coronal angle, which defines the vaginal axis as being oriented towards the left (negative angle) or right side (positive angle) of the patient. Significant lateral deviation of the vagina may indicate the presence of unilateral defects with respect to vaginal support structures.

3.6.4 Patient Cohort Demographics

De-identified MRI volumes were obtained from the publicly available multicenter Childbirth and Pelvis Symptoms (CAPS) patient database, through the Pelvic Floor Disorders Network (PFDN) [263]. The scans available were initially used as a part of several other studies, and anatomical inclusion criteria for those studies included: primiparous women (gestational age >= 37 weeks), and women who fell into one of the following categories: anal sphincter disruption that was repaired at the time of delivery, anal sphincter disruption that was not recognized and repaired at delivery, or delivery by cesarean prior to active labor. Women were excluded if they had pre-pregnancy anorectal surgery or fecal incontinence, inflammatory bowel diseases, or neurological conditions that would predispose them to fecal incontinence [264]. For the CAPS study, patients were imaged in the supine position on a 1.5T system using surfaced phased array coil [243]. T2-weighted turbo spin echo [SE] images were taken axially. Other imaging parameters included repetition time [TR] 5000 ms, echo time [TE] 132ms, field of view [FOV] 200cmm slice thickness 3mm, gap 0mm, flip angle 180°, and 270x256 matrix [241].

Five MRIs were chosen at random from the aforementioned database for this study and were screened based on visibility of all anatomical landmarks and regions of interest required for the pelvic coordinate system and vaginal axis measurements.

3.6.5 Assessment of Repeatability and Reliability of Pelvic Coordinate System

To robustly characterize our coordinate system, we determined that an evaluation of the repeatability and reliability of our manual and calculated measurements could highlight the strengths and limitations of this method. Thus, we determined that each patient selected for this study should be independently evaluated by multiple observers on multiple occasions.

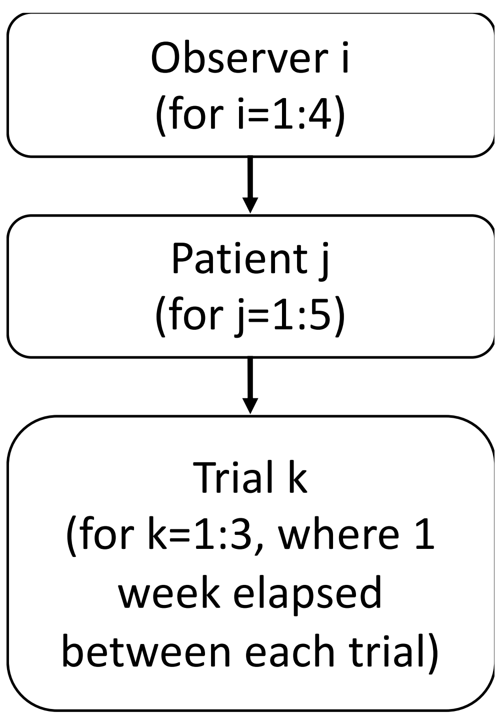


Figure 33 workflow for data collection for inter and intra observer repeatability analysis

Figure 33 describes the process through which four independent observers evaluated five patients on multiple occasions. The data produced for each trial included a vaginal segmentation and 6 bony landmark coordinate points which, upon following the methods in 3.6.2 and 3.6.3 produces several metrics of interest with respect to our coordinate system, including vaginal axis, vaginal spatial position, proximal and distal angles of elevation and deviation, and sagittal and coronal angles.

3.6.5.1 Observer Training

All observers in this study were undergraduate students affiliated with Universities in Western Pennsylvania. Each student was trained in female pelvic anatomy (i.e., organ location, etc.), and how MRI images are constructed and read. The training included the use of 3D printed pelvic models from the human body project, and publicly available medical websites. Following training, students were introduced to the open source DICOM segmentation software Osirix [257] and given a tutorial on the essential functions of the software, including effective methods for segmenting the vagina and identification of pelvic organs via MRI. Observers were walked through manual segmentation examples utilizing the software and then allowed to practice manual segmentation of MRIs not included in the study. Following the completion of at least two successful manual segmentations of the pelvic floor, with assistance, observers were required to complete three manual segmentations unassisted. These geometries were then reviewed, and if correct, the observer was considered trained for the scope of this study.

3.7 Assessment of Vaginal Geometry Segmentation

Motivated by the inaccuracies of current methods, we sought to extend the previously described methodologies to encompass an overall assessment of our ability to repeatedly and reliably segment the vagina. Thus, we aimed to quantify the variability between manual segmentations of MRIs. For this study, we utilized five sets of scans. Five non-medically trained observers were taught pelvic anatomy and trained to manually segment the vagina using OsiriX (© Pixmeo Sarl). Each observer repeated the manual segmentation process of each vagina five times, with no less than one week between successive attempts to minimize bias. Following segmentation, 3D vaginal isosurfaces were generated. Five patient specific average geometries were created based upon five isosurface trials produced by each observer, using Paraview (Kitware, Inc.). Each average vaginal geometry was then compared to observer-specific segmentations for each patient through point correspondences based upon regional distance-mapping. 5 patient specific average geometries from vaginal isosurfacces from all observers. 5000 vertices, 10,000 triangles using Paraview (Kitware, Inc.).

3.8 Statistics

Statistical analysis was conducted using SPSS Version 25 (SPSS, Inc., Chicago, IL, USA). Intraclass correlation (ICC) was used to assess the inter-and intra-observer reliability, or the extent to which measurements can be replicated. Thus, our statistical analysis should reflect the degree of correlation as well as agreement between measurements. The interrater reliability was determined based on the average of the bony landmark coordinates and reference angles produced by each observer. Thus, it is meant to reflect variation between two or more raters who were measuring the same group of subjects. The ICC model was 2-way random effects, type was absolute, and single measure values were reported. [265]. The two-way random effects model allows for randomly selected raters from a larger population of raters with similar characteristics, which allows the reliability to be generalized to any raters. This is also commonly used to evaluate rater-based clinical assessment methods [265]. The intra-rater reliability reflects the variation of data measured by 1 rater across 2 or more trials. The ICC model was 2-way mixed effects, type was absolute, and single measure values were reported. The two-way mixed effects model was used to determine the reliability of specific raters in the study and therefore is not generalizable. Single measure values were reported for both inter-and intra- reliability, as intended clinical application would rely on measurements from one rater. Absolute agreement determines if different raters assign the same score to the same subject, which yields a more conservative analysis than consistent agreement. Reported ICC values range from 0 to 1, and are ranked based on the following scale:

Table 9 ICC Degree of Reliability

Degree of Reliability	ICC Value
Excellent	$ICC > 0.90$
Good	$0.75 \leq ICC < 0.90$
Moderate	$0.50 \leq ICC < 0.75$
Poor	$ICC < 0.50$

An additional analysis was performed to determine variation as a result of manual selection of bony landmarks to form the coordinate axes and segmentation of the vaginal borders. This was done by comparing the vaginal axis, position, and other angular measurement ICCs under the following conditions: (1) a single pelvic coordinate system was used per patient (i.e., vaginal geometries were varied) and (2) a single vaginal geometry was used per patient (i.e., bony landmarks for the coordinate axes were varied).

3.9 Results

The relevance of a quantification system depends upon the clinical relevance of critical points, and that the identification of these points is captured through a repeatable and reliable methodology. To assess the inter- and intra-observer error, statistical comparisons of the bony landmarks and vaginal measurements between and within observers were determined.

3.9.1 Inter-Rater Reliability

Inter-rater reliability is a statistical measure that evaluates consistency or agreement among individuals who collect data. Since observers were trained and then instructed to collect several measurements, it would be rare to have perfect agreement among observers. Thus, this study is a function of disagreement and inconsistency among observers. Results from the inter-rater reliability analysis are reported in Table 10.

Table 10 Inter- and Intra-Rater Reliability for Bony Landmarks and Origin. ISL: Left Ischial Spine; ISR: Right Ischial Spine; IPPL: Left Inferior Pubic Point; SPPL: Left Superior Pubic Point; IPPR: Right Inferior Pubic Point; SPPR: Right Superior Pubic Point. †: $derived\ manually$. ‡: $derived\ computationally$

Parameter		Inter-Rater Reliability ICC			Intra-Rater Reliability ICC											
		All Observers			Observer 1			Observer 2			Observer 3			Observer 4		
Type	Name	X	Y	Z	X	Y	Z	X	Y	Z	X	Y	Z	X	Y	Z
Bony Landmark†	IS_L	0.998	0.992	0.996	0.999	0.997	0.998	0.987	0.982	0.996	0.997	0.976	0.996	0.991	0.964	0.988
	IS_R	0.996	0.975	0.996	0.994	0.967	0.997	0.963	0.972	0.996	0.991	0.971	0.991	0.994	0.967	0.990
	IPP_L	0.996	0.997	0.992	0.993	0.997	0.999	0.991	0.992	0.999	0.989	0.998	1.000	0.996	0.999	0.988
	SPP_L	0.963	0.997	0.932	0.993	0.985	0.999	0.692	0.983	0.580	0.988	0.989	0.595	0.959	0.994	0.999
	IPP_R	0.989	0.998	0.998	0.994	0.999	0.999	0.982	0.998	0.999	0.995	0.995	0.999	0.957	0.997	0.998
	SPP_R	0.992	0.996	0.962	0.994	0.997	1.000	0.981	0.990	0.998	0.995	0.995	0.999	0.991	0.995	0.999
Coordinate System Feature‡	Origin	0.998	0.988	0.998	0.999	0.990	0.999	0.979	0.990	0.999	0.995	0.989	0.997	0.995	0.987	0.997

The ICC was calculated for the x, y, and z components of the six bony landmark measurements required to define the coordinate system, and the ICC of the origin point of the coordinate system was reported. There was excellent inter-rater reliability with respect to the bony landmarks and origin of the coordinate system (median [IQR] ICC, 0.996 [0.989-0.997]).

Table 11 Inter- and Intra- rater reliability for vaginal measurements.

Vaginal Parameter†	Name	Inter-Rater Reliability ICC	Intra-Rater Reliability ICC			
		All Observers	Observer 1	Observer 2	Observer 3	Observer 4
Position (mm)	X	0.808	0.927	0.596	0.57	0.556
	Y	0.841	0.929	0.85	0.796	0.89
	Z	0.314	0.916	-0.086	0.006	0.482
Angle (°)	Proximal Elevation	0.925	0.954	0.823	0.909	0.933
	Distal Elevation	0.767	0.84	0.756	0.902	0.848
	Sagittal	0.582	0.743	0.811	0.729	0.667
	Proximal Deviation	0.594	0.67	0.588	0.223	0.452
	Distal Deviation	0.26	0.713	0.378	0.513	0.134
	Coronal	0.688	0.771	0.653	0.565	0.53

Table 11 reports the inter-rater reliability for each vaginal parameter. The vaginal position coordinates yielded moderate to good ICC values (median [IQR] ICC, 0.808 [0.561-0.825]). The Vaginal angle parameters yielded moderate ICC values (median [IQR] ICC, 0.641 [0.585-0.747]).

3.9.2 Intra-Rater Reliability

Intra-rater reliability provides information regarding individual raters. This measurement is influenced by the finesse of discriminations within the data that the observers were required to make. intra-rater is single collector reliability. These are affected by the finesse of discriminations in data that collectors must make. Thus, we were able to assess how well each observer did compared to themselves. Results from the intra-rater reliability analysis are reported in Table 10. The ICC was calculated for the x, y, and z components of the six bony landmark measurements required to define the coordinate system, and the ICC of the origin point of the coordinate system was reported for each observer. The intra-rater reliability was excellent with respect to the bony landmarks of the coordinate system across all observers (median [IQR] ICC, 0.944 [0.988-0.998]).

Table 11 reports the intra-rater reliability of each vaginal parameter for each observer. The vaginal position coordinates yielded moderate to good ICC values (median [IQR] ICC, 0.696 [0.538-0.897]). The vaginal angle parameters yielded moderate to good ICC values as well (median [IQR] ICC, 0.721 [0.556-0.827]).

3.9.3 Variation Due to Manual Selection

The overall mean for each measurement was calculated and was subtracted from the average measurement of each individual observer (Table 12) [241]. The difference between the overall mean and mean of observer measurements of vaginal position were within 1 mm, while the angle measures were within 1degree.

Table 12 Difference between each observer and overall mean

Name	N	Mean	SD	Difference Between Observer and Overall Mean			
				Observer 1	Observer 2	Observer 3	Observer 4
X	89	0.23	2.07	-0.16	-0.30	0.21	-0.30
Y	89	48.92	3.40	-0.10	-1.99	0.50	1.05
Z	89	-2.65	2.00	0.56	-1.19	-0.40	0.90
Proximal Elevation	89	59.39	7.00	-0.51	2.21	-0.75	-0.62
Distal Elevation	89	100.09	6.63	-0.88	3.05	0.53	-1.10
Sagittal	89	159.31	5.46	0.53	-0.65	-1.11	0.37
Proximal Deviation	89	-0.60	3.01	0.72	0.99	0.70	-1.79
Distal Deviation	89	0.25	3.98	-0.47	0.85	1.28	-1.35
Coronal	89	-0.86	4.57	1.18	0.16	-0.57	-0.45

To better parse the influence of each observer on results was tested by calculating the ICCs for vaginal position and angles under 2 additional conditions: the first utilized the same pelvic coordinate system, but varied vaginal geometries collected by observers, while the second utilized 1 vaginal geometry and varied the pelvic coordinate system. The results of these scenarios are shown in Table 13.

Table 13 Inter-Observer Reliability for a)Variied PCS, Varied Vaginal Geometries b)Single PCS, Varied Vaginal Geometries c) Varied PCS, Single Vaginal Geometry

Vaginal Parameter†	Name	Inter-Observer Reliability ICC		
		Varied PCS, Varied Vaginal Geometries [a]	Single PCS, Varied Vaginal Geometries [b]	Varied PCS, Single Vaginal Geometry [c]
Position (mm)	X	0.808	0.993	0.813
	Y	0.841	0.996	0.864
	Z	0.314	0.994	0.274
Angle (°)	Proximal Elevation	0.925	0.969	0.954
	Distal Elevation	0.767	0.775	0.863
	Sagittal	0.582	0.834	0.958
	Proximal Deviation	0.594	0.421	0.862
	Distal Deviation	0.260	0.567	1.000
	Coronal	0.688	0.707	0.997

This analysis demonstrated that the use of the single coordinate system resulted in higher ICCs with respect to vaginal position, while the single geometry resulted in higher ICCs for vaginal angle measures.

3.9.4 Shape Analysis

Statistical shape modeling is a method by which complex shapes can be used to detect changes in complex morphologies without simplifying the underlying geometry. Given the known complexity of vaginal geometry, and potential challenges in capturing its shape accurately, a statistical shape analysis was performed to detect similarities and differences between the shapes of the vaginal borders between and within observers. Figure 34 depicts how variations among observer tracings could be present on a single trace.

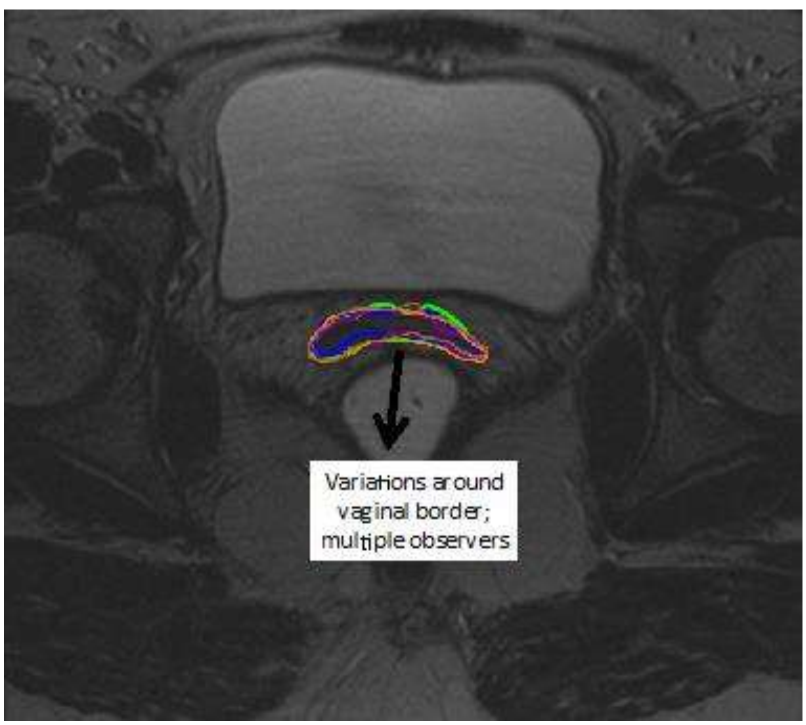


Figure 34 Demonstration of variations we noted around vaginal borders from multiple observers

Qualitative visual observations indicated that there was strong agreement between observers regarding their manual segmentation of vaginal borders. However, statistical shape analysis afforded us the ability to quantify these observations. Figure 35 depicts the statistical differences in shapes captured by observers for two different subjects in mm.

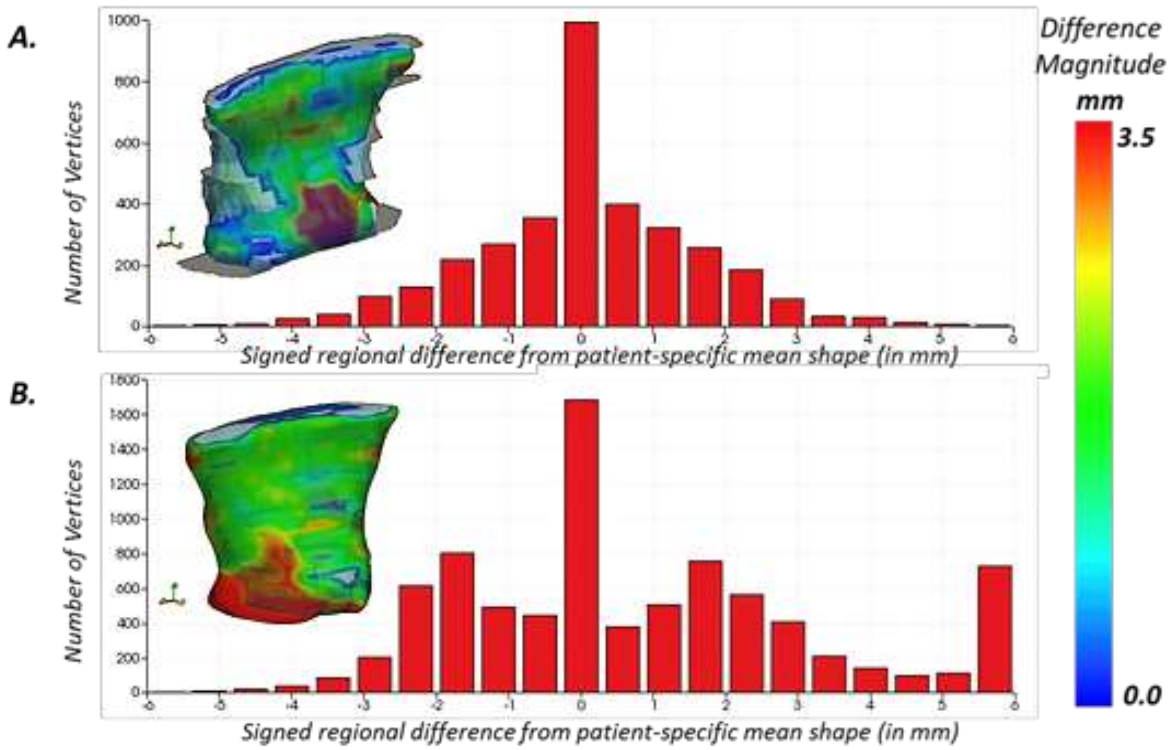


Figure 35 Graph that represents the statistical differencesin shape between observers and within observer

This histogram visually illustrates how segmentations differed for each observer with respect to their patient-specific average geometries. The color map illustrates the geometric differences, with larger differences denoted in warmer colors, and smaller differences as cooler colors. The overall difference between observers was nominal (1.62 +/- 0.43 mm) relative to the average vaginal width of 27.8 mm. Thus, non-medically trained observers can repeatably and reliably trace vaginal borders.

3.10 Discussion

The primary objective for this study was to improve upon existing quantification methods to develop a reliable 3D measurement system that could produce consistent measurements to describe vaginal axis, vaginal spatial position, and vaginal angles with respect to the coordinate system.

3.10.1 The Coordinate System

The importance of defining "vaginal axis" has been widely accepted. The position and orientation of the vagina has been proposed to be an indirect measure of damage to specific levels of support [193], [224]. Intact apical support is thought to "pull" the apex towards the sacrum, while compromised support would enable the apex to rotate anteriorly, such that the vagina assumes a more vertical orientation[266]. Our study in Chapter 2 suggests that the position of the distal vagina is also significant. The nuances of vaginal shape and its nonlinear alignment within the pelvis has been difficult to capture. Thus, previous attempts to mathematically describe the vagina have been limited; either by dimensionality, repeatability of procedure, patient misalignment within the MRI, or the inability to effectively compare patient measurements while accounting for the size and shape of their pelvis [244].

Upon our analysis in section 3.9, we found that our 3D pelvic coordinate system has excellent inter- and intra-rater reliability. The reliability of our proposed coordinate system is minimally influenced by factors such as patient misalignment in the MRI scanner, pelvic shape and size, or even nuances among observers. Thus, our coordinate system methodology improves upon limitations expressed regarding existing pelvic measurement systems while incorporating easily identifiable and relevant bony landmarks, which no doubt contributes to the excellent ICCs reported [231]. Some pelvic reference systems rely in part on a single landmark along sacrum to define measurements or the axis of the system, however, variability in pelvic dimensions and shape could complicate results produced while using this reference point. The shape of the sacrum is known to vary among individuals, and some studies suggest that there may be significant differences in the length of the sacrum with respect to race-all of which contribute to inter- and intra- subject variability [267]. Our coordinate system in part relies on the position of the pubic bone, which we define in 3D space through four bony landmarks to define the length and width of the pubic symphysis. The joining of this anterior-posterior axis at the origin, which is determined as the midpoint of the ischial spines, contributes to minimizing variability in measurements due to pelvic dimensions and shape.

The 3D Pelvic Inclination Coordinate system (PCIS) proposed by Reiner et. al. follows a similar approach but differs from our methodology in several ways: the coordinate system origin is the posterior end of the pubic symphysis, four bony landmarks are used to define the coordinate system, corrected angle of 34 degrees is applied to the coordinate system, and anterior-posterior axis construction relies on the sacrum [268]. Upon review, the inter- and intra-rater reliability results between the two methods are comparable in magnitude. However, the rigor of our analysis with respect to the number of observers and repetition of measurement collection is yet to be matched for 3D pelvic coordinate systems, as there are not specific standards regarding the minimum level of precision necessary for reliable measurements [265], [269]. The methodology for assessing the inter- and intra- rater reliability of the bony landmarks most closely aligns with the methodology followed by Hoyte et. al., where three observers took measurements on two separate occasions, and were trained by the same “expert” [241].

Table 10 summarizes the ICC for the bony landmarks and origin of the coordinate system. While all of the inter observer ICC values were excellent, there were a few interesting results of note among the intra-observer results. Observers 2 and 3 both had moderate ICCs for the z coordinate of the left superior pubic point. Given that the z-axis of the coordinate system corresponds with the location of the axial slices within the MRI volume, we can conclude that these two observers were not as consistent as others in the determination of which slice contained the landmark of interest [241]. This observation could be the result of limited skills of those observers, or an indication of changes in skill level over the five weeks of trials. Since observer 2 also has a moderate ICC for the x coordinate of the left superior pubic symphysis, the aforementioned reasoning may apply. The fact that half of the observers only obtained moderate ICC for that coordinate component may also indicate that interpretation of that point may not be as well-defined for some patients, and instructions for determining that point may need to be refined. Holistically, this analysis demonstrates that the proposed coordinate system has excellent repeatability and reliability.

3.10.2 Vaginal Geometry, Axis, Position, and Orientation

Vaginal borders were manually segmented, and vaginal axis, position, and associated angle measurements were calculated with respect to the patient coordinate system. This methodology captures and utilizes the full 3D vaginal geometry, thus improving upon obvious limitations characteristic of 2D measurements of complex 3D morphology [241]. Thus, in contrast to the bony landmarks discussed in 3.10.1, our parameters of interest are based on the repeatability and reliability of the manual segmentation of soft tissue.

The accuracy of soft tissue segmentation is largely influenced by complexity of shape and sharp contrast between the borders of the organ and surrounding tissues. Increased complexity of shape and noise on or near tissue borders can cause challenges in obtaining observer agreement, thus introducing variability in measurements and an expected decrease in ICC [241]. Our calculated measurements in table 11 demonstrated good repeatability; as intra-observer differences in vaginal position and angle measurements with respect to the overall mean were less than 1 mm and degree, respectively.

Zhang's work in geometric modeling acknowledges that there are challenges associated with segmentation and analysis of complex geometries [270]. Work conducted by Mayeur, et. al. explored the influence of geometry and mechanical properties on simulations of female pelvic anatomy, and found that the accuracy of segmented geometries can significantly influence measurement outcomes [231]. Hoyte et. al, report similar findings and challenges surrounding the repeatability and reliability of soft tissues, and suggests that good repeatability is a function of alignment of both the volume and position of an organ [271]. As we consider the results of vaginal position, it is important to remember that vaginal position is reported as an average of the centroid of each vaginal tracing. Thus, even slight variations in segmentations of the vaginal border are magnified. Our results indicate that there were some variations in observer determination of vaginal border, thus resulting in lower but still good inter-rater ICCs. The lowest ICC for vaginal position was the z component. The vaginal position is mathematically defined as the average of the central vaginal axis, which represents the averages of each vaginal trace which was done in 2D. The z components for each axial MRI volume would be determined by slice thickness and would therefore be the same for all observers. However, variations in slice identification for bony landmarks would alter vector directions, which in turn would make the consistent z component for each axial MRI volume appear to be less repeatable. The intra-observer ICCs, however, demonstrate more variation among segmentations. This is not alarming, and likely a result of skill development over time for most of the observers. As their ability to confidently segment vaginal borders developed, their more recent segmentations likely differed from previous ones, which would result in lower ICCs. However, Observer 1's repeatability demonstrates that it is indeed possible to capture the vaginal borders with only slight variations.

Six angle measures were calculated from the relationship between best fit lines of the central vaginal axis with respect to the coordinate system. The proximal and distal elevation angles yielded the highest ICCs for inter-rater reliability. This indicates that our ability to measure changes in vaginal axis with respect to the y axis, or the pubo-origin axis is quite reliable. Deviation results reflect the relationship between the vaginal axis and the z axis of the coordinate system. These ICCs indicate that deviation is a less reproducible measurement. This is likely because the deviation vector is defined about the z axis, and therefore is derived from x and y coordinate points, which would show more variability than elevation angles, which are defined about the y axis, and therefore has components of x and z, of which z is dictated by slice thickness.

Proximal elevation and deviation measurements had higher ICCs than their distal counterparts. This indicates that observers had higher repeatability towards the apex of the vagina, likely due to clearer vaginal borders as a result of more hydration near the bladder. Thus, we can report comparisons of proximal angles between patients with higher certainty. The distal vaginal borders became increasingly difficult approaching the introitus as a result of the decreasing vaginal width and contrasting structures surrounding the area. Furthermore, slice thickness can complicate interpretation for less seasoned observers, as the shape and size of the vagina and its borders drastically decrease as the hiatus is approached. These findings are reflected in the statistical analysis results as well, where greater variability is observed in the distal vagina.

3.10.3 Sources of Error and Validity

While results indicate that the reliability and repeatability of this method is good to excellent, it is important to recognize random or systematic errors that could influence the accuracy of measurements and interpretation of results. Here, we will focus on random or systematic errors. Random errors are due to incontrollable fluctuations in variables that influence results. Random errors for this study would include variations in exact point selection of bony landmarks, as well as variations in vaginal border segmentation. The influence of random errors was minimized through calculation of the vaginal axis lines of best fit. Coordinate system random errors were minimized through careful selection of bony landmarks that were easily visible, and a calculation that utilized four points instead of one to define the position of the pubic symphysis.

Systematic errors are the result of consistent biases with the execution of methodology such as rounding errors and consistent differences in observer judgement, and calculation assumptions. All coordinate points with respect to the MRI coordinate system were rounded to the nearest hundredth. This level of precision was maintained for all coordinate inputs, with rounding to the nearest tenth occurred only in final reported values. To reduce errors observer judgement, all observers were trained by the same person following a similar protocol, and repetition of segmentations was separated by one week. However, it was not possible for all observers to be trained simultaneously, nor control for the varied skills of observers and their improvements over time. One of the most influential calculated assumptions was that of orthogonality. Other assumptions included dividing the vagina in half to calculate the two lines of best fit and making the pubic point 1/3 of the distance between the averages of the left and right proximal and distal points.

In assessing the validity of this study, we will consider ecological validity and face validity. Ecological validity is an assessment of how closely the testing environment resembles the intended data collection and assessment environment. All data was collected in a standard laboratory setting, using free versions of image viewer software. There were no time limits placed on how quickly or efficiently observers had to complete data collection. This setting would be standard for research purposes but differs from a clinical environment with respect to the lighting, which would be dim to improve screen contrast and visibility of anatomical structures, different software would be utilized, and a radiologist would review several patients scans a day. Additionally, radiologists would be allowed to confer with other experts to gain interactive consensus on measurements. We did not allow interactive consensus for this study to improve our understanding of worst-case scenario outcomes.

Face validity addresses biases or factors that could influence results. One factor to consider is how well defined the users of the method are, or how similar their behaviors are with respect to data collection. In this case, all observers were well defined in that they were all self-nominated students who were interested in research opportunities. Thus, they had a desire to work on the project, and impress those in charge of the project. The users in this study, while less experienced, may have also been more meticulous than someone with several patients to review daily and time pressured deadlines. Also, all observers were trained by the same person, and taught the same methodology. In theory, they would approach evaluation of vaginal borders and bony landmarks similarly. Although there are protocols and methodologies in place, physicians do not receive all of their training from one expert, but many, and are exposed to a wide variation of scan types and complications.

3.10.4 Limitations

One limitation in this study was the population and number of patients examined. While they were all a part of the same population, universal conclusions cannot be drawn based on a very specific cohort of women. In theory, challenges with identifying vaginal borders especially in the distal vagina could be somewhat improved by fine-tuning MRI sequences, however, this would result in the consequence of longer scan acquisition times. The appearance of the vagina in T2-weighted MR images have medium-low signal intensity, although the signal intensity can improve with secretions or the addition of contrast to the vagina. However, it is important to note that the addition of contrast to improve signal intensity could also alter vaginal shape and/or position, therefore compromising the accuracy of results [272].

In comparison to existing vaginal measurement systems, the method proposed here is the most involved, and therefore requires a longer time to collect and process data through several steps. This does expose the method to more potential for gross errors under time constraints. This method, while long, provides many more measurements thereby enhancing our ability to quantify the vagina in 3D space.

A final limitation of this system is that it may not be ideal for patients with prolapse. Our angle measurements and lines of best fit are based on the premise that the path of the vagina has two distinct directions. However, a common characteristic of patients with prolapse is the loss of angulation, especially towards the apex of the vagina. Thus, very severe prolapse cases may produce misleading results.

The outcomes from this study are quite promising, especially given that the observers who collected data for this study had no experience in MRI analysis prior to joining the study. Their minimal training and experience, coupled with the rigor of our analysis with respect to the number of observers and observations present results that demonstrate a worst-case scenario, as we would expect that more experienced observers would demonstrate even higher inter- and intra- rater reliability.

3.11 Conclusion

This chapter detailed the development of a custom software that quantifies anatomical positions and orientations of the vagina with respect to the bony pelvis in 3D space while considering differences in patient size and shape, as well as variations of patient alignment within the scanner. Rigorous statistical analyses were performed to assess repeatability, reliability, and how differences in observer data influences quantitative results. This coordinate system improves upon the limitations of existing clinical methods and demonstrates good to excellent repeatability and reliability to support more robust patient comparisons between patients.

Thus, we contend that using a method such as this over time can provide information about natural changes in anatomical position and the risk for prolapse, thereby enhancing our understanding of the pathogenesis of POP and other PFDs and improve treatment outcomes.

4.0 Female Pelvic Health Literacy: A Pilot Investigation of High School Students' Baseline Knowledge, Comprehension, Retention, and Attitudes Regarding Female Pelvic Health

4.1 Introduction

The preceding chapters of this dissertation explored 2D and 3D mechanisms for improving the characterization of vaginal position and orientation, thereby contributing to the existing "scaffold" of research in the field of urogynecology. While it is crucial to develop techniques, devices and products that ultimately contribute to improved patient care and surgical outcomes, the roles and responsibilities of all stakeholders (i.e., researchers, physicians, patients, etc.) must be considered. We recognize that clinicians and researchers have a responsibility to uphold morals of benevolence via the Hippocratic Oath, but the role of patients is often overlooked [273], [274]. Can patients exercise autonomy over their health decisions by taking the responsibility to be informed? Although intriguing, the scope of this research doesn't directly address this question, but instead, helps us explore critical barriers surrounding the concept of health literacy regarding female pelvic anatomy and disorders.

Health literacy is the ability of individuals to locate, comprehend, and utilize essential healthcare information in order to make informed short- and long-term decisions regarding their health [275]–[277]. The development of competent health literacy skills is strongly correlated with educational opportunities, cultural beliefs, and societal/economic status. Thus, individuals, families, and communities can directly impact health literacy and ultimately health outcomes.

Consider the following scenario: “A 29-year-old African-American woman with three days of abdominal pain and fever was brought to a Baltimore emergency department by her family. After a brief evaluation she was told that she would need an exploratory laparotomy. She subsequently became agitated and demanded to have her family take her home. When approached by staff, she yelled, ‘I came here in pain and all you want to do is an exploratory on me! You will not make me a guinea pig! She refused to consent to any procedures and later died of appendicitis.” [275]. Appendicitis can be treated with antibiotics but is most commonly treated through an Appendectomy (i.e., surgery to remove the appendix), which is one of the most common abdominal emergency procedures performed [278]–[280]. In fact, the risks and complications associated with procedures such as appendectomies, or exploratory laparotomies in cases where the cause of discomfort is unclear, are much lower than the complications and risks of treating a perforated appendix, especially with patients in their 20s [281]. Although no further details were disclosed concerning the case described above, we can hypothesize that gaps in health literacy may have played a role in this unfortunate outcome.

According to a 2004 report released by the National Academy of Sciences, roughly 50% of the U.S. population lacks the necessary and basic literacy skills required to effectively contribute to society [282], [283]. Given that health literacy is a subset of literacy, it can be assumed that health literacy skills are even more compromised for individuals within that 50%, since healthcare is generally more complex than minimal requirements for daily life. Furthermore, deficits in health literacy can contribute to excess healthcare costs totaling over $73 Billion [275].

In the case of the 29-year-old African American woman from Baltimore, although we do not know her background, we can acknowledge that her racial group (i.e., Black) is an at-risk group for literacy challenges, since the U.S. Department of Education reported in 2001 that approximately 77% of Black adults who engaged in a standardized literacy test (NALS) had consistently lower literacy proficiency relative to White adults who completed the same test [283]. Furthermore, years of unauthorized medical experimentation on slaves and Black Americans throughout American history has cultivated fear, apprehension, and mistrust within many Black families and communities [25], [284], [285]. In addition, she was from the city of Baltimore, which has been consistently ranked deficient in terms of literacy. Therefore, her literacy background may have played a key role in the communication breakdown with her physicians. Sadly, stories such as these are all too common and beg the question of what can be done to both encourage preventive care and prevent treatable conditions from becoming deadly.

Studies that will be reviewed in section 4.2 indicate that both men and women, of varying ages, races, ethnicities, and educational backgrounds, have significant literacy gaps and misinformation regarding female pelvic organs and their functions. This is alarming, given that approximately 50% of the U.S. population are women, and the other 50% were possibly raised by a woman, married to or in a committed relationship with a woman, raising a young woman, or caring for an elderly mother or grandmother. Almost all women experience one or more challenges as a result of menstruation, conception, gestation, pregnancy, delivery, cancers, menopause, diseases and abnormities of pelvic organs, and pelvic floor disorders [1]. These challenges not only impact the quality of their lives and physical states, but they also impact the emotional states of women, likely affecting their emotional relationships with others [286].

4.2 Traditional Means of Female Pelvic Health Education and Learning

Section 1.0 provided context regarding the origins of beliefs and medicinal practices surrounding female pelvic health through the centuries. These misguided historical perceptions remain evident globally among all races and ethnic groups, religious establishments, genders, and in several professional fields, including medicine [89], [287]. The theoretical framework of intersectionality suggests that persons who identify with more than one historically excluded social category could be more susceptible to misguiding information and/or subconscious assumptions during treatment that frequently result in negative health outcomes [288]–[291]. Studies suggest that the number of women who experience adverse birth outcomes, such as low birthweight or preterm delivery, and maternal mortality are higher and statistically different for women of color [288], [292]–[295]. Deeper investigation into demographics suggest that these outcomes are far more complex than our social definitions of race. Factors such as environmental stress, genetics, and availability of resources are likely contributing to the number of adverse reported outcomes within specific populations. However, the greatest, and possibly most impactful barrier to overcome is altering attitudes, beliefs and education regarding female pelvic health. Initial perceptions of hygiene and healthy behaviors develop during childhood and are shaped by a variety of factors, including the news/media, familial and social/religious interactions, personal experiences, and established educational institutions [296].

4.2.1 Societal and Cultural Influences

Media, such as television shows, advertisements, podcasts, print media, the internet, and social media serve as a means for people to obtain information. The current availability of resources appears to be metaphorically, and quite possibly, endless. Information ranging from history lessons, current trends and concerns, and predictions of future events are available almost instantly, for better or for worse. In some cases, “clickbait”, or propaganda titles such as “10 ways to lose 10lbs in a week” are used to intrigue followers and spark discussion. Despite the lack of scientific evidence, topics such as the use of vaginal steaming as a detox technique, the use of hygiene products to “clean” the vagina and mask vaginal odor, or the need to surgically “fix” a “loose vagina” or a broken hymen are enticing advertisements. These “wives’ tales” exist because men and women believe and fear that the vagina is fundamentally flawed and that it requires cleansing and fixing. Constant exposure to these ideas, combined with health literacy barriers, further perpetuate inaccurate health information, especially related to female reproductive anatomy [297].

Scientifically informed discussions regarding female pelvic anatomy and function are rare among the general population, and the long-term impact of health decisions are poorly understood. Several research teams have developed assessment tools concerning the location and function of female pelvic anatomy and determined that both men and women demonstrate significant deficits in knowledge, with participants scoring well below 75% in most cases [298], [299]. Participants generally scored higher if their parents worked in the health field, or their parents had open dialogue regarding anatomy, contraception, and sex [300]. Methods of knowledge acquisition can differ by gender and contribute to misinterpretation of facts and misinformation due to informal collections of information based on familial, personal, or cultural experiences. For example, it was found that methods for acquiring gynecological knowledge differ by gender among Chinese college students, with men more likely to research topics independently and women more likely to seek advice from others [300]. This trend was also present in middle school students in Cincinnati [301].

The Eve Appeal © (registered charity no. (England & Whales) 1091708), a cancer research charity, found that 50% of men and 44% of women surveyed could not correctly identify the vagina on a diagram, and 60% of women could not identify the location of the vulva. Studies also suggest that men play a significant role in influencing health decisions of their partners; however, the Eve Appeal reported that 24% of men surveyed felt “slightly uncomfortable” when talking about female pelvic health, and 21% claimed to be “too embarrassed”. The juxtaposition of male influence on female health decisions with a deficit of accurate knowledge is concerning, especially given that even with more sexual experience and partners, men did not score higher than women. This possibly contributes towards unplanned pregnancies and sexually transmitted infections (STIs), both of which can have lifelong physical and emotional implications [300], [302].

4.2.2 The State of K-12 Health Education

A survey developed by Reid et al. found that participants obtained information regarding female pelvic health from family (41.7%), friends (29.9%), and the internet (67.63%) [298]. Two-thirds of the surveyed population reported their primary exposure to female pelvic health concepts was through classroom instruction [298]. Given the challenges described in 4.2.1, educational interventions are logical first steps. National Standards for health information were developed and incorporated into school curriculums for K-12 students, generally through health, physical education, or special elective courses [282], [303]. Topics addressed include nutrition, exercise, safety, substance abuse, prevention and control of disease, reproductive health, and STDs. These standards provide detailed curriculums, objectives, and outcomes that, ideally, are sequential and result in a holistically-health-literate adult. In spite of the development of resources, the lack of uniformity among education systems in different states and countries leads to health curriculums that differ significantly with regard to teaching methods and availability of course content and resources, which, by proxy, is a direct contributor to the abysmal health literacy rates reported [275].

One of the most controversial topics in health education is reproductive anatomy and contraception. In spite of the United States government trying to reduce teen pregnancy since the 1980s, in 2014, the U.S. reportedly had one of the highest rates of teen pregnancy in the developed world, with 82% of the pregnancies being unintentional [304]. In comparison, teens in the Netherlands have the second lowest pregnancy rate in Europe [305]. Two factors that contribute to the difference in rates of teen pregnancy are societal acceptance and education [43]. While many cultures and ideologies discourage sexual interactions between minors and out of wedlock, the common misconception is that learning about anatomy, and facilitation of discussions surrounding reproductive organs, leads to an increase in sexual behavior and pregnancy. This misconception is further complicated by political ideologies, religious institutions, and the lack of regulation surrounding the medical accuracy of information that is presented to students in several states, such as Ohio [304]. In fact, in 2011, the Department of Education found only 7.8% of programs to be evidence based [43]. Social shame and pressure regarding discussions about reproductive topics encourages the use of slang, or “muted” terminology, when referring to reproductive organs, which elicits the perception that reproductive organs, anatomy, and consequently, female pelvic health, are dirty, or inappropriate topics, only to be discussed using alternative terminology and in whispers.

The rising urgency to improve health literacy education among adolescents has led to initiatives spearheaded by healthcare professionals and researchers working with school systems to develop methods of intervention for improving the overall health literacy of students [275]. One intervention was conducted at an inner-city Cleveland middle school to explore student attitudes and knowledge about reproductive health before and after the implementation of a newly designed curriculum [304]. This curriculum spanned 3 days, with two hours of instruction each day given by resident physicians. Topics of focus included male and female reproductive anatomy, pregnancy, STIs, and contraception. Furthermore, lesson plans incorporated a variety of teaching methods, such as lecture, hands on interaction with anatomical models, games, and discussion. Comparisons of pre- and post-intervention test scores suggested significant improvements in knowledge pertaining to anatomy, contraception, and sexual behavior, and a four month follow-up still illustrated overall improvement, although mean total scores decreased for both males and females [304].

In Chicago, a similar study was conducted to understand baseline knowledge of adolescent females in Chicago area schools and compare knowledge gained by a control group, which received the standardized instruction, and an intervention group, which experienced six weeks of 1-hour-per-class interventions [306]. This study also identified significant deficits in basic anatomical knowledge, including inaccurate perceptions of where urine leaves the body.

However, post-intervention results were associated with significant differences in knowledge pertaining to female pelvic anatomy, structure, and function. These studies suggest that even short-term interventions or changes to current curriculums can have a significant and positive impact on knowledge acquisition.

4.2.3 Instruction in Anatomy

The study of anatomy encompasses an understanding of the structure and function of organs, tissues, and organ systems within the body, and the spatial relationships between them. Traditional methods of teaching anatomy entail cadaveric dissections, cadaveric prosection, plastic anatomical models, and 2D methods (i.e., textbooks, chalk drawings, or images) [307], [308].

Spatial awareness is critical in the study of anatomy and can be defined as the ability for students to understand three-dimensional structures when manipulated [309]. In fact, spatial ability has been cited as a predictor for success with regards to anatomy [309]. In fact, models that allow students to manipulate anatomy and observe from multiple points of view have been cited as effective methods in the development of spatial learning ability [307].

Health and biology are required courses in middle and high school curriculums. Instructors for these courses face the challenge of having to cover several complex topics in short periods of time, and with limited resources and support [73], [298], [310]. A lack of resources or money is particularly detrimental in courses that benefit from physical models and activities. Large class sizes present an additional challenge, especially with courses that benefit from student centered learning, hands on activities, and discussions. Thus, instructors must resort to primarily lecture and 2D methods, which present a challenge when trying to fully comprehend complex geometries and interactions of internal body systems. Interestingly, these challenges are not exclusively at the middle school level. In Europe and several other counties several researchers have noticed gaps in the knowledge medical students have with respect to anatomy [311]. Several reasons have been cited as contributing factors, including decline in resources (i.e., anatomy teaching hours, models, etc.), due to increasing interest in other medically related fields that focus on the body at a molecular or genetic level [312]. The shift in resources is particularly concerning due to evidence that suggests the ability to understand anatomical structure, function, and relationships requires significant cognitive effort, with several anatomical structures, including female pelvic anatomy, being difficult to comprehend and visualize without physical models [313].

Significant advancements in rapid prototyping and 3D printing technologies offer alternative solutions to the barriers described above. These physical models can be used to improve spatial awareness of internal organs and associated disorders. As 3D printing gains popularity, the time, effort, and cost of printing continually decreases, making models more accessible. Furthermore, the accuracy of the 3D printer's replication of complicated structures and printing of high fidelity models continues to improve and allow for the replication of unique anatomical structures several times [314]. Thus, 3D printed organs and structures could provide access to the wide range of variation in human populations, including normal and diseased anatomies. This method is a cost effective and ethically-friendly way to approach anatomy and allows models to be shared among various teaching and research institutions [308], [314], [315].

4.3 K-12 Educational Study

Several theories support active learning as an effective method for developing, improving, and maintaining knowledge regarding scientific topics [316]–[321]. Although spatial awareness can be improved through interaction with 3D models [236], there are typically limited opportunities for students to interact with anatomical models, especially those pertaining to female pelvic anatomy. Given the challenges described in sections 4.1 and 4.2, it is imperative that action be taken to increase awareness of female pelvic health. Current literature explores the state of health literacy and sex education for children and adults; however, few focus on female pelvic health in terms of function and dysfunction.

Therefore, as part of this dissertation, a study was conducted to investigate the ability for high school students to comprehend and retain information pertaining to female pelvic anatomy when exposed to educational interventions. These interventions are cost-effective ways to expose students to female anatomy so as to improve health literacy. An additional goal is that this study serve as a model for other educators in beginning to remove the stigma associated with understanding and discussing female pelvic health by educating youth about female pelvic health issues and highlighting the importance of female pelvic health research.

Thus, in this study, we aimed to improve overall understanding, awareness, and appreciation for female pelvic health among a group of high school students using 3D printed models. To measure the effectiveness of the approach, a comprehensive assessment was conducted. This assessment consisted of the following methods:

- Assessment of baseline knowledge about female pelvic health, including anatomy, anatomical functions, the relationship between structure and function, and the effect of compromised structure on function (i.e., incontinence or prolapse).

- Upon instruction with and without 3D anatomical models with two different groups of students, this same knowledge was assessed to determine differences in effectiveness with respect to comprehension and retention.
- Assessment of affective outcomes, including general attitudes and feelings regarding female pelvic health among these students.

4.4 Methods

4.4.1 Application of Evidence-Based Instruction: Identification of Misconceptions, Bloom's Taxonomy, and Backwards Design Theory

Preparation and delivery of scientific lecture is ubiquitous in college and university settings. Evidence-based theories suggest that while lecture-style instruction assists in disseminating loftier quantities of information to large audiences in a controlled manner, the average attention span varies wildly among students, and overall continues to decrease [322]–[324]. As a result, students whose primary method of knowledge attainment is lecture are approximately 1.6 times more likely to fail that course. Several other aspects that influence learning include prior knowledge or misconceptions, organization of information, feedback, and aspects of the affective domain, including emotions, feelings, and motivations [325]. Thus, being mindful of these influences and effective teaching techniques can enhance learning gains.

Evidence suggests that students' self-identity and prior knowledge or exposure to concepts can significantly influence educational outcomes, as previous experiences shape the framework through which new information is processed [326]. If prior knowledge is accurate, this can be a solid foundation to build upon. However, this is often not the case, and even less so with concepts surrounding female pelvic anatomy. Chapter 1 and earlier sections of the present chapter describe influences that contribute to several misconceptions that are common when discussing female pelvic anatomy. Although students can still derive a correct answer through rational, albeit incorrect, reasoning, deeper levels of understanding are not attainable or sustainable if built on a foundation of misconceptions.

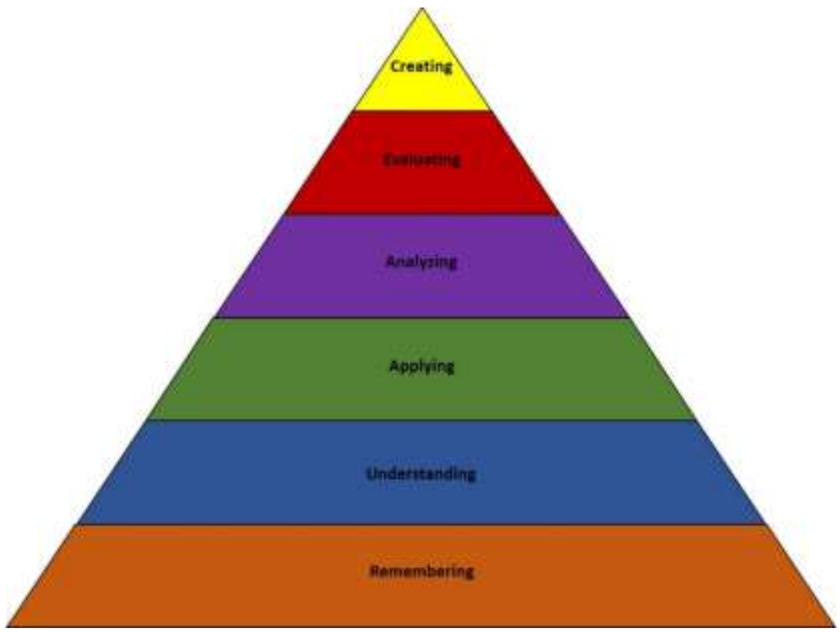


Figure 36 Revised Bloom's Taxonomy

Bloom's Taxonomy, illustrated in Figure 36, is an evidence based theory that categorizes levels of learning such that one level builds upon the other [321]. The lower, or foundational, levels require skills such as identifying, remembering, or defining key concepts (i.e., red level), while effective demonstration of higher order skills, such as creating or evaluation, is built upon the lower-level skills. Thus, misconceptions and incorrect understanding in the lower levels of Bloom's Taxonomy can impede deep or higher-level learning. The consequences of misconceptions can be as benign as failing an assessment in school, but conversely, they can be life altering, or even life threatening, when health literacy is concerned.

Thus, in order to facilitate learning gains, instructors must utilize methods of teaching that help deconstruct misconceptions associated with female pelvic health and provide scaffolding to re-establish or build upon base knowledge.

4.4.2 Investigation of Misconceptions

For this dissertation, approximately 20 informal interviews were conducted with acquaintances of varying educational and cultural backgrounds to uncover specific misconceptions regarding female pelvic health. These interviews were categorized as informal, as the style of interview was casual and had no specific protocol. Participants varied by age, gender, race, ethnicity, education level, and in some cases, religious and cultural practices. Interviews were in person, over the phone, and even occurred in online groups on Facebook and discussion boards. The intent of these interviews was to assess, within my own network, what misconceptions exist and determine if they were consistent with the demographics assessed in the literature.

Interestingly, there were several commonalities among participants, regardless of the factors described above. Almost all participants noted that they are not comfortable discussing female pelvic organs and terminology in public or in private, due to embarrassment and confusion about "what's down there". When asked how they were introduced to these ideas and concepts, most also reported that they were never formally introduced, and for many, they were introduced to concepts through books or movies. Even participants who enrolled in health courses or anatomy and physiology courses felt uneasy discussing details, even when they demonstrated some knowledge of female pelvic organs and their functions. Another common trend among interviewees was the perception of their instructor, parent, friend, or other person they discussed these topics with also showing signs of being uncomfortable or embarrassed when discussing female pelvic health. Findings from these informal interviews indicate that students' perception of female pelvic health topics as embarrassing may correlate with the feelings and beliefs of those providing the instruction, indicating that the classroom or teaching environment plays a critical role in the ability of students to obtain knowledge. If the tone of the room is uneasy and uncomfortable, students may feel uncomfortable participating, which may also enable misconceptions to go uncorrected.

We joined several online groups to talk with active members and gain a better understanding of their attitudes and beliefs when discussing female pelvic health. A trend observed in online groups unfolded as follows: an individual would post a question pertaining to female pelvic health and ask for input and advice from peers within the group. One of the most common questions or themes surrounded appropriate times and effective methods for helping children understand pelvic health and hygiene. Posts would include a variety of responses and opinions, ranging from "they don't need to know until they are grown" to "it's never too early to begin discussing these topics". However, the most alarming posts were from individuals who were suffering from pain, post-partum complications, and several other challenges and were reaching out to their group for advice and support. Review of several questions and challenges posed and the associated responses indicated that, similar to the literature reviewed in section 4.1, many seek advice from the internet and private social groups concerning female pelvic health. However, after reviewing several comments within these groups, it was determined that recommendations and advice posted were frequently incorrect, based on misconceptions, or provided links to resources that were not scientifically based. Similar to the literature reviewed in section 4.1, common topics for which questionable advice was given included vaginal pearls and vaginal rejuvenation. Furthermore, many noted that they wished they had the opportunity to discuss many of these topics and to better understand that pain is not normal and acceptable. In a female discussion group, several noted that they initially thought painfully debilitating menstrual cycles were normal but later found out they were experiencing symptoms of endometriosis or fibroids. Others admitted to having children but had no idea that the urethra and vagina are separate organs. Others expressed frustration with experiencing frequent UTIs but had no knowledge of reasons or habits they may practice that increase the likelihood of developing them. Others exhibited misconceptions surrounding ways to increase or decrease the likelihood of pregnancy, the purpose of menstruation, the purpose of Pap smears, and pelvic floor disorders. Thus, information obtained from reviewing these posts and discussions indicated that there were severe deficits in knowledge and factual evidence regarding female pelvic health among the participants. Also, it's likely that many individuals are lacking information at the fundamental levels of Blooms Taxonomy related to female pelvic health.

As a consequence, the information on misconceptions from this informal investigation inspired the application of the backwards design method for the educational study with high school students. Backwards design is an educational theory by Wiggins and McTighe (1998), which suggests that learning processes are most effective when the desired outcome or result is identified first, followed by identification of assessment practices and ultimately determination of learning techniques and instruction, as illustrated in figure 37.

Figure 37 Flowchart of Backwards Design Method

Following this methodology, it was determined that the desired outcomes of this study were 1) comprehension and retention of basic female pelvic organ anatomy and function and 2) understanding, appreciation, and awareness of normal anatomy and how disorders impact optimal function of anatomy. Further details regarding the big ideas, learning goals, and objectives can be found in the lesson plan (Appendix C.1).

4.4.3 Assessment Development and Scoring

Assessments are used to provide feedback regarding mastery of predetermined objectives. They can be formal, such as a test on a specific unit, or informal, such as a quick in-class survey to have students identify their greatest challenge areas. Assessments can also be categorized as formative or summative, where formative assessments are used to evaluate learning progress to permit changes if needed, and summative assessments are used to evaluate final progress. The depth of knowledge required to complete an assessment is determined by the overall objectives, which can be determined using Bloom's Taxonomy as described in 4.4.1. To measure learning gains in this study, we determined that both formative and summative assessments would be implemented, along with both formal and informal assessment techniques. Formal assessments were developed as summative and included an assessment given prior to classroom instruction to capture baseline knowledge as well as following classroom instruction to capture comprehension and the ability for students to demonstrate their knowledge. To capture the lasting impact of our classroom instruction, or the retention of material, a final assessment was administered several weeks after the classroom instruction.

While considering the learning objectives, question topics and styles were developed by me and a second reviewer who had significant experience with the project and helped develop assessment questions adapted from literature sources. This brainstorming technique is commonly used among design teams to develop solutions that include all possibilities with respect to the challenge being addressed. Furthermore, it allows for new ideas and new approaches to build or surface, which enable exploration of new possibilities that could contribute towards improving our solution. Following the brainstorming process, questions were then sorted by topic, and options were eliminated if they were deemed beyond the scope of our research question or if they were testing the same concepts using different language or methods. Approximately 50 questions were generated during this process, and after sorting and elimination, approximately 30 questions remained.

Questions were then categorized by assessment type, as illustrated in Table 14. Upon reflecting on our intended outcomes in section 4.3 (i.e., determining prior knowledge, attitudes, and beliefs, and changes in these measures associated with our classroom instruction), it was determined that several types of assessment categories were necessary. Demographic questions were included to gain insight into characteristics that may influence our target population and were presented as multiple-choice options, with the exception of grade point average (GPA), which required an open-ended response. To determine baseline knowledge of facts regarding female pelvic anatomy, function, and compromised function, direct assessment questions were used. Question styles for the direct assessments included multiple choice, matching, and open-ended as mechanisms to reveal misconceptions and to produce mixed methods results (i.e., quantitative and qualitative).

Indirect assessment was captured through open-ended and Likert-scale questions to gather students' perceived knowledge and learning, which ideally should strongly correlate with direct assessment findings. However, it is possible for direct and indirect assessment results to differ, which can reveal deeper misconceptions of factual knowledge. Affective questions were included in the form of open-ended and Likert-scale questions to assess attitudes and beliefs held by students and determine whether they changed as a result of the classroom instruction.

The final assessment types were satisfaction-based (i.e., likes, dislikes, suggestions) in the form of open-ended responses to obtain feedback on the structure and style of classroom instruction. Observational assessments were informally conducted to provide additional qualitative data for formative assessment purposes. Qualtrics survey software (Qualtrics, Provo, UT) was selected as the platform for survey dissemination. This software was selected due to being licensed within the University of Pittsburgh and the ability to maintain anonymity of survey participants.

Table 14 Summary of Assessment Types Used to Evaluate Study Participants.

ASSESSMENT TYPE	QUESTION TYPES	EXAMPLES
Demographic	Open ended, multiple choice	*Age, Grade, Gender GPA, race, etc.*
Direct [i.e. testing of factual knowledge]	Multiple choice, matching, open ended	*Organ location, function, defining PFDs, POP risk factors, why is it challenging to understand & diagnose PFDs*
Indirect [i.e. what they thought about material	Open ended, Likert-scale	*What do they believe they learned? Methods of preferredlearning*
Affective [i.e. how participants felt about material/knowledge]	Open ended, Likert-scale	*Importance of understanding female pelvic anatomy, how does it make you "feel", etc.*
Satisfaction Assessment	Open ended	*Likes, dislikes, improvements/suggestions*
Research Observational Assessment	N/A	*Observations loosely based on COPUS protocol*

Rubrics were developed to streamline the grading process. Matching and multiple-choice questions worth one point each were graded for correctness, and the open-ended responses were scored using a rubric developed and agreed upon by two analysts. The rubrics used for grading all assessments can be found in Appendix C.

4.4.4 Development of Instructional Materials: Active Learning Techniques

Active learning techniques are characterized as methods of learning that engage students in their own learning process. Active learning techniques can include active participation by students answering questions in class, working in groups to understand or discover new topics, or physical interaction with tools or models that enable students to experience real-time feedback. Many research studies support the implementation of active learning techniques for promoting student engagement and increasing learning gains, with two examples cited here [316], [317]. Therefore, we decided to incorporate active learning elements within two different instructional interventions that we compared.

The first technique relied on active class participation. Animated lecture slides that contained 2D images of female pelvic anatomy were used as a class discussion tool for anatomical locations and optimal versus compromised function. Students were asked to raise their hands to signify the desire to participate when questions were asked, and generally, questions regarding the material were asked followed by displaying the appropriate answer on the lecture slides. If answers suggested by students were incorrect, the instructor could observe and address misconceptions in real-time, which was an added benefit to this active learning technique. Also, students were told that they could raise their hands and ask questions at any time during the instruction, which could also provide instructors with additional information regarding the attitudes and beliefs students had as well as topics that intrigued them. The second portion of the class time was used to introduce a case study about a woman with POP (i.e., pelvic organ prolapse), (Appendix C) to introduce the concept of dysfunctional anatomy, its impact, and the challenges faced with treating it.

The second active learning technique utilized custom, 3D-printed, female pelvic models (sans photos) to promote the use of spatial awareness to understand functions of optimal and compromised organ function. Figure 38 presents an overview of the methodology used to develop the 3D-printed models. Publicly available images from a female donor from The Visible Human Body Project (NIH) were used to develop our 3D-printed models [327]. The images were generated using a 1.5 Tesla scanner (HarmonyExpert, Seimens ®) as high resolution axial, sagittal, and coronal radiological sections, with .5mm spacing [328]. Each pelvic organ, or regions of interest, (i.e., vagina, bladder, urethra, rectum, bony pelvis, and uterus) were segmented manually slice by slice using Seg3D, an open-source segmentation software. Each segmented region of interest was then exported as a .STL isosurface for smoothing in 3D Coat (V4.2, Pilgway), a robust 3D model sculpting software for surface smoothing. Given the spacing typical for radiological scans, smoothing was necessary due to sharp edge artifacts generated by the interpolation in Seg3D in order to remove artifacts that did not match the respective biological structures. The sculpting tool was utilized to remove all sharp edges from the surface of each organ without altering the correct anatomical shape [329]. Following this process, files were again exported as .STL formats for 3D printing. All prints were done using PLA (Polylactic Acid). Makerbot and a Stratasys Dimension SST 1200es printer were used to print life-size replicas of the segmented pelvic geometries.

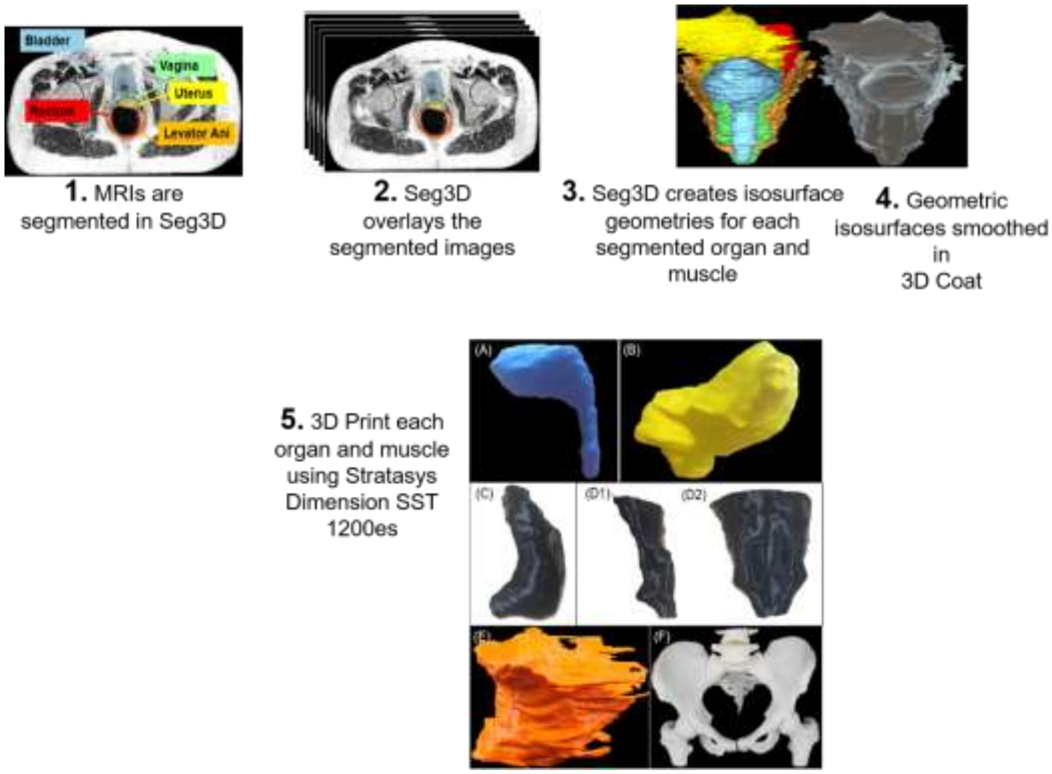


Figure 38 Overview of Process for Development of 3D Printed Models

4.4.5 Classroom Environment and Management

While the implementation of active learning techniques results in improved student outcomes, classroom instructors must establish a classroom environment with clear expectations for student activities to be completed. In addition, research suggests that the most productive learning environments are safe and inclusive spaces, where students feel comfortable offering opinions, theories, and ideas, without the fear of being judged or ostracized by their instructors or peers [330]–[332]. These expectations are most effective when the tone is set early and environmental parameters are established. Environmental parameters are factors that influence student learning and can be related to the instructor, class size, available resources, topics covered, and course objectives. With the knowledge that discussions surrounding female pelvic health and disorders are unsettling for many, it was imperative that our classroom expectations, environment, and research objectives were expressed and implemented immediately prior to our intervention with the high school students.

To maintain student engagement and learning, the instructors created an inviting classroom environment, which encouraged open dialogue and discussion, while demanding respect and sensitivity towards classmates' questions, opinions, and knowledge. Co-instructors were present to provide additional perspective to discussions and to conduct observations and maintain the classroom environment. Students were separated into two groups, with group 1 receiving lecture and active learning and group 2 being exposed to the 3D models and active learning "intervention," as described in figure 39. For method 2, students were randomly assigned to teams of four.

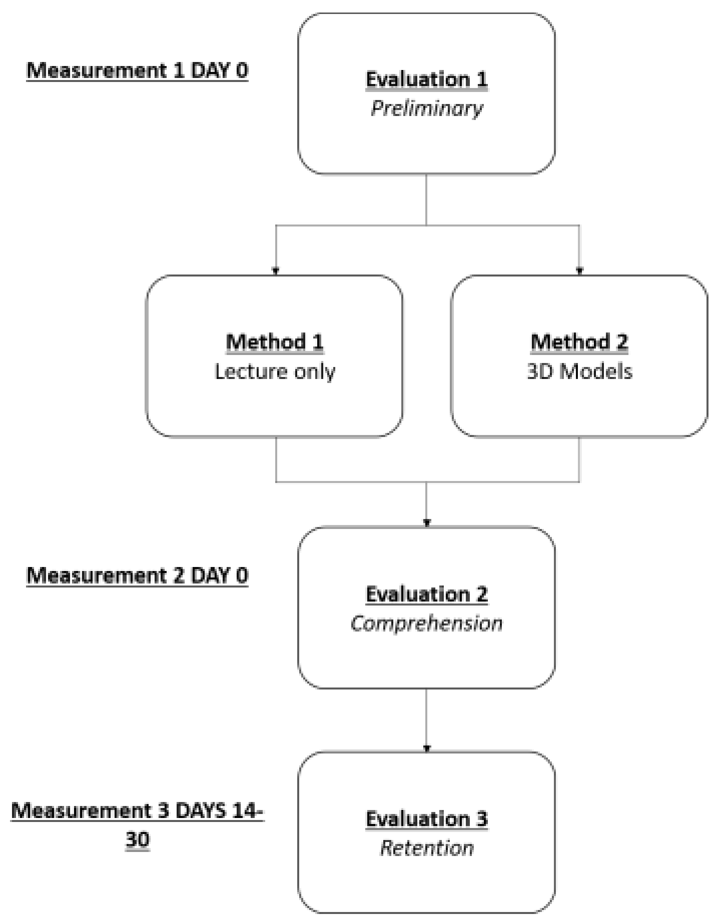


Figure 39 Overview of Intervention Workflow

4.4.6 Validation of Assessments and Instructional Tools

Piloting and testing of the assessment and instructional tools for the study with the high school students involved two iterations. Following the completion of the 3D printing process in 2015, a trial run of each educational method was completed at a local high school. Pre and post tests were administered on paper to collect preliminary data to identify and address pros and cons of the methods of the project. We hypothesized that the incorporation of 3D pelvic models would yield higher learning gains (i.e., post score - pre score) compared to the lecture method. This hypothesis was based on the vast literature that suggests engagement of tactile senses, coupled with auditory and visual aids, helps to reinforce spatial concepts [333]–[336].

Baseline knowledge results during this trial demonstrated gaps in knowledge that were similar to those identified in the literature as well as by our informal interviews and observations. Several students confused basic pelvic organs with regard to their location within the body and their functions. The most common point of confusion was mixed labeling of the urethra and the uterus, possibly due to the misconception that women do not have urethras. Another related point of confusion was found regarding how the body performs functions such as removal of waste, also likely a consequence of being unaware that women have urethras.

During the preliminary tests, the improvement appeared to be greater with the 3D printed model group, and students appeared to be more engaged. However, there were <u>*some positive gains*</u> in the average scores between the pre- and post-tests for the lecture (i.e., non-model) groups of 10^{th} and 11^{th} graders (i.e., 1.6 and 3.0, respectively). The highest variability was seen when students were asked to name each organ, regardless of the group. This was improved for the future by providing students with a word bank. Some students appeared to confuse organs having similar names (i.e., uterus and urethra). However, the best results were seen with the matching of an organ with its function on the post test. This preliminary trial allowed us to improve our assessment and intervention designs. Areas of improvement included the implementation of the assessments using the Qualtrics survey software to ensure completion of questions for an adequate sample size and to minimize confusion with grading.

The second test was completed in 2018 at another local high school with 10 students in a similar manner. The purpose of this second test was to test our improvements, including the integration of Qualtrics software for formal assessments, and to assess overall flow of instructional materials.

4.4.7 Participant Recruitment and Consent

Methods regarding participant recruitment were approved through an exempt IRB, given that no personal identifiers would be collected as a part of this study (#PRO17070047). High schools were recruited through contacting local science, biology and anatomy instructors in public and private schools. Meetings were scheduled with each instructor to define the objectives of the research study and discuss the lesson plan and topical content that would be assessed. Following consent from instructors, permission slips were distributed to notify parents of the research, lesson content, and objectives and to obtain parental consent for students under 18 to be present and participate in the study.

Prior to data collection, an introductory script was read by researchers to the participating students to review the elements of this study and to reiterate the voluntary nature of their participation. Thus, students had the right to withdraw from the study at any time with no repercussions by informing their teacher. In cases involving withdrawn student consent, any data collected from that student was excluded from the study.

4.5 Results

Given the breadth of collected data, results from this study were broken down by assessment types, as described in Table 14, and interpreted as such. All data collected from surveys were summative, as they were not completed while learning. One hundred sixty-one (161) students from three high schools in Western Pennsylvania completed Pre-Tests and Comprehension Tests, and 80 students completed Retention Tests several weeks after the classroom intervention. Approximately 50% of the participant population did not complete Retention Tests due to scheduling conflicts. All students were enrolled in biology, health, anatomy, bioengineering, or medically oriented courses for the duration of this study. Table 15 provides summary details regarding the demographic characteristics of student participants as a whole, and with respect to each intervention test group. Although a significant portion of the student population consisted of white males, the males were approximately evenly spread between the two test groups, as were the females. Ethnic representation was overwhelmingly non-Hispanic or Latino (approximately 95%), and primary English speakers comprised 94% of the study sample. The racial proportions in the sample reflect recent demographic data on the U.S. population [9].

Approximately 90% of the tested population maintained above a 3.0 GPA on a 4.0 scale. Seventy percent (70%) of participants were between the ages of 16 and 19, which indicates the likelihood that most had experienced or were experiencing milestones associated with puberty, as well as some level of sexual activity. This is based on a Resource Center for Adolescent Pregnancy Prevention (ReCAPP) 2015 report, in which 41% of high school students had engaged in sexual intercourse, and 3.9% had engaged in sexual activity prior to age 13 [337].

Table 15 Summary of Student Population Demographics

CHARACTERISTICS		ALL (Pre and Comprehension) n=161 students	LECTURE (Pre and Comprehension) n=79 students	MODEL (Pre and Comprehension) n=82 students	ALL (Rentention) n=80 students	LECTURE (Retention) n=35 students	MODEL (Retention) n=45 students
GRADE							
	9th	42 (26.1%)	7 (8.9%)	27 (32.9%)	14 (17.5%)	5 (14.3%)	9 (20%)
	10th	21 (13%)	8 (10.1%)	13 (15.9%)	17 (21.3%)	5 (14.3%)	12 (26.7%)
	11th	64 (39.8%)	39 (49.4%)	25 (30.5%)	34 (42.5%)	22 (62.9%)	12 (26.7%)
	12th	34 (21.1%)	7 (8.9%)	27 (32.9%)	15 (18.8%)	3 (8.6%)	12 (26.7%)
AGE							
	<14	2 (1.2%)			1 (1.3%)	1 (2.9%)	0 (0%)
	14	25 (15.5%)	16 (20.3%)	9 (11%)	7 (8.8%)	3 (8.6%)	4 (8.9%)
	15	21 (13%)	9 (11.4%)	12 (14.6%)	12 (15%)	3 (8.6%)	9 (20%)
	16	47 (29.2%)	28 (35.4%)	19 (23.2%)	31 (38.8%)	15 (42.9%)	16 (35.6%)
	17	52 (32.3%)	20 (25.3%)	32 (39%)	22 (27.5%)	12 (34.3%)	10 (22.2%)
	18+	14 (8.7%)	4 (5.1%)	10 (12.2%)	7 (8.8%)	1 (2.9%)	6 (13.3%)
GENDER							
	Male	101 (62.7%)	49 (62%)	52 (63.4%)	45 (56.3%)	22 (62.9%)	23 (51.1%)
	Female	58 (36%)	29 (36.7%)	29 (35.4%)	34 (42.5%)	13 (37.1%)	21 (46.7%)
	Other	1 (0.6%)	0 (0%)	1 (1.2%)	1 (1.3%)	0 (0%)	1 (2.2%)
	Prefer not to answer	1 (0.6%)	1 (1.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ETHNICITY							
	Hispanic or Latino	6 (3.7%)	4 (5.1%)	2 (2.4%)	3 (3.8%)	1 (2.9%)	2 (4.4%)
	Not Hispanic or Latino	153 (95%)	73 (92.4%)	80 (97.6%)	77 (96.3%)	34 (97.1%)	43 (95.6%)
	Prefer not to answer	2 (1.2%)	2 (2.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
RACE							
	Asian	7 (4.3%)	4 (5.1%)	3 (3.7%)	7 (8.8%)	4 (11.4%)	3 (6.7%)
	Black or African American	14 (8.7%)	9 (11.4%)	5 (6.1%)	10 (12.5%)	5 (14.3%)	5 (11.1%)
	White	127 (78.9%)	57 (72.2%)	70 (85.4%)	55 (68.8%)	21 (60%)	34 (75.6%)
	Multiraicial	10 (6.2%)	6 (7.6%)	4 (4.9%)	8 (10%)	5 (14.3%)	3 (6.7%)
	Prefer not to answer	3 (1.9%)	3 (3.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ENGLISH 1st LANGUAGE							
	yes	152 (94.4%)	73 (92.4%)	79 (96.3%)	73 (91.3%)	30 (85.7%)	43 (95.6%)
	no	9 (5.6%)	6 (7.6%)	3 (3.7%)	7 (8.8%)	5 (14.3%)	2 (4.4%)
GPA (4.0 scale)							
	1.5-1.99	1 (0.6%)	1 (1.3%)	0 (0%)	1 (1.3%)	1 (2.9%)	0 (0%)
	2-2.49	3 (1.9%)	2 (2.5%)	1 (1.2%)	3 (3.8%)	2 (5.7%)	1 (2.2%)
	2.5-2.99	9 (5.6%)	6 (7.6%)	3 (3.7%)	7 (8.8%)	4 (11.4%)	3 (6.7%)
	3-3.49	43 (26.7%)	18 (22.8%)	25 (30.5%)	17 (21.3%)	5 (14.3%)	12 (26.7%)
	3.5-3.99	82 (50.9%)	39 (49.4%)	42 (51.2%)	34 (42.5%)	19 (54.3%)	15 (33.3%)
	4	22 (13.7%)	11 (13.9%)	11 (13.4%)	11 (13.8%)	4 (11.4%)	7 (15.6%)
	not answered	1 (0.6%)	1 (1.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

4.5.1 Direct Assessment

Direct Assessment questions can be used to measure student knowledge of factual content. Table 16 provides a breakdown of average student scores on several of the direct assessment questions in order to identify misconceptions prior to instruction and determine if identified misconceptions were later found to be resolved. The results from the pre assessment questions revealed that the rectum and bladder were most consistently correct, while the urethra and vagina were commonly mislabeled. Generally, participants performed better when identifying organ function. Also, as expected, most participants were unfamiliar with risk factors for prolapse prior to the teaching intervention.

Table 16 Average Scores for Student Performance on Individual Questions

	Pre Asessment		Comprehension		Retention	
	Lecture n=79 Students	Model n=82 Students	Lecture n=79 Students	Model n=82 Students	Lecture n=35 Students	Model n=45 Students
Label The Following Organs (based on image)	# Correct (%Correct)	# Correct (%Correct)	# Correct (%Correct)	# Correct (%Correct)	# Correct (%Correct)	# Correct (%Correct)
Vagina	44 (55.7%)	40 (48.8%)	63 (79.7%)	70 (85.4%)	29 (82.9%)	36 (80%)
Rectum	62 (78.5%)	51 (62.2%)	70 (88.6%)	65 (79.3%)	29 (82.9%)	34 (75.6%)
Bladder	54 (68.4%)	47 (57.3%)	70 (88.6%)	68 (82.9%)	28 (80%)	34 (75.6%)
Uterus	51 (64.6%)	41 (50%)	69 (87.3%)	58 (70.7%)	29 (82.9%)	29 (64.4%)
Urethra	38 (48.1%)	36 (43.9%)	62 (78.5%)	64 (78%)	29 (82.9%)	30 (66.7%)
Matching Organ Names with Organ Functions						
Vagina	67 (84.8%)	67 (81.7%)	76 (96.2%)	80 (97.6%)	33 (94.3%)	42 (93.3%)
Rectum	68 (86.1%)	66 (80.5%)	75 (94.9%)	77 (93.9%)	32 (91.4%)	41 (91.1%)
Bladder	74 (93.7%)	67 (81.7%)	76 (96.2%)	78 (95.1%)	33 (94.3%)	42 (93.3%)
Uterus	48 (60.8%)	35 (42.7%)	63 (79.7%)	54 (65.9%)	28 (80%)	19 (42.2%)
Urethra	58 (73.4%)	53 (64.6%)	66 (83.5%)	69 (84.1%)	29 (82.9%)	31 (68.9%)
Ovaries	64 (81%)	52 (63.4%)	65 (82.3%)	68 (82.9%)	29 (82.9%)	35 (77.8%)
Fallopian Tubes	58 (73.4%)	49 (59.8%)	63 (79.7%)	72 (87.8%)	28 (80%)	36 (80%)
Levator Ani Muscles	60 (75.9%)	57 (69.5%)	75 (94.9%)	75 (91.5%)	31 (88.6%)	41 (91.1%)
Cervix	45 (57%)	42 (51.2%)	64 (81%)	64 (78%)	26 (74.3%)	30 (66.7%)
Prolapse Questions						
Most Predominant Risk Factor	19 (24.1%)	30 (36.6%)	76 (96.2%)	78 (95.1%)	31 (88.6%)	39 (86.7%)
Can Men Experience Pelvic Floor Disrders	51 (64.6%)	48 (58.5%)	67 (84.8%)	59 (72%)	33 (94.3%)	30 (66.7%)

Student comprehension on all individual direct assessment questions increased following both instructional methods when compared to pre-assessment values, and although fewer students participated in the retention assessment, average scores were still higher than scores obtained on the pre-assessment. Trends such as higher aptitude for matching organ names and functions on the pre assessment were maintained through the comprehension and retention assessments.

A summarized test score was determined by adding the point values of the various direct assessment questions, with 14 points maximum. A summary of average scores can be found in table 17. Interestingly, the average combined score earned on the pre-assessment was lower in the 3D model group. Although the 3D model group's comprehension and retention scores were also lower compared to the lecture group, students exposed to the 3D models actually had the greater learning gains from pre-test to comprehension. Their average retention scores also decreased less from the comprehension score.

Table 17 Average total scores on direct assessment questions.

Group	Pre	Comp	Ret	Difference Pre to Comp	Difference Comp to Ret	Net Impact
Lecture	10.60	13.06	11.80	2.46	-1.26	0.11
Model	8.65	11.46	10.81	2.81	-0.65	0.25

Independent samples t-tests were conducted using SPSS (version 26) to determine if significant differences could be detected in learning gains between students in the lecture group versus the 3D model group. With 95% confidence, it was determined that the differences (between comprehension and pre assessment scores) were significantly different in the lecture versus 3D model groups (p=.042), with an effect size of 0.37 in favor of the 3D model group. Similarly, the differences in retention and comprehension assessment scores were also statistically different between the lecture and 3D model groups (p=0.004), with an effect size of .46 also in favor of the 3D model group. Net impact was calculated by subtracting the pre-ret/ret score values.

4.5.2 Indirect Assessment

Indirect assessments are a method by which students can describe their learning experience and reflect on the impact. This form of assessment was included to collect information on participant beliefs about mastery of concepts within the module.

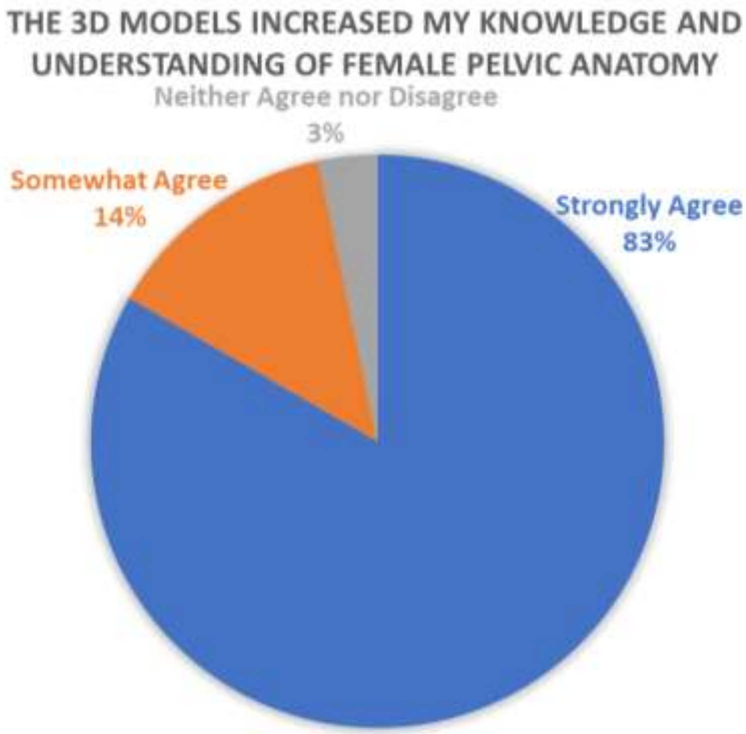


Figure 40 3D Models increased my knowledge and understsanding of female pelvic anatomy.

Figure 40 is an example of one of the indirect assessment questions. 83% of participants strongly agreed that being able to interact with the 3D models as a part of their learning process increased their knowledge and understanding of female pelvic anatomy. In fact, none of the participants reported negative or adverse feelings regarding the use of the models as an instructional tool. Conversely, Figure 41 illustrates the perceived impact of the lecture intervention with regard to an increase in knowledge and understanding.

While a majority of participants strongly agreed that lecture increased their knowledge and understanding, there were a few participants (5%) that did not find this method of learning particularly helpful.

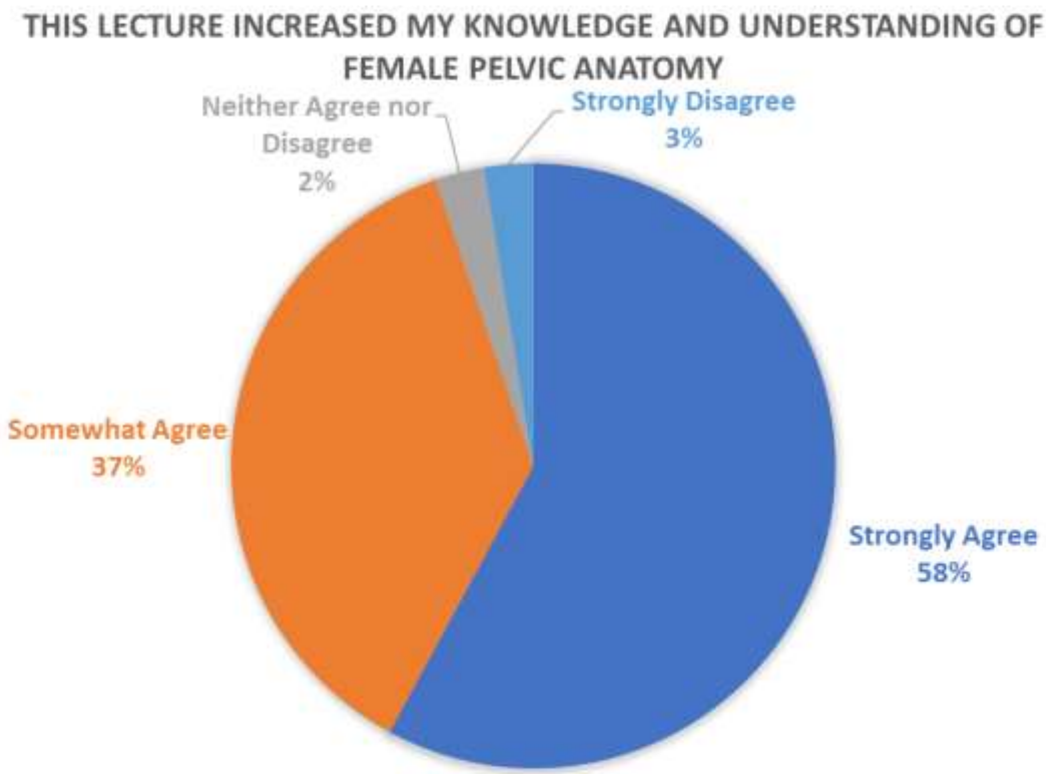


Figure 41 This lecture increased my knowledge and understanding of female pelvic anatomy

These results compliment the direct assessment results, in which the difference in scores was significantly greater for the 3D model group, suggesting that this method was a more impactful method of instruction.

4.5.3 Affective Assessment

To characterize participant attitudes, affective assessment questions were developed. Tables 18 and 19 summarize the impact of each intervention method on interest in pursuing careers in health-related fields. For the majority of participants, there was an increase in interest, with only 3% of all participants indicating a decrease in interest.

Table 18 Summary of increased desire to pursue medical fields

How much did this experience increase your interest/desire to study medicine/anatomy/health related fields?	**Increase in Interest**	**Decrease in Interest**	**No Increase; No Decrease**
Method: Lecture	72%	0%	28%
Method: Model	70%	6%	24%
Both Methods: (Lecture & Model)	71%	3%	26%

The interest illustrated in the table above aligns with the general response of students following each intervention. Several participants from both the lecture and model groups asked additional questions following the comprehension assessments and expressed interest in studying bioengineering or medicine as a future career. Overall, students seemed to be more comfortable with information following our intervention, suggesting that the intervention was also successful in developing awareness and shifting attitudes and perceptions regarding female pelvic health. In fact, Table 19 shows that while some students remained indifferent, more than half of participants felt comfortable discussing female pelvic health with their peers after the intervention.

Table 19 Levels of comfort with material

How comfortable are you in sharing this content information with your peers?	**Comfortable**	**Uncomfortable**	**Indifferent**
Method: Lecture	61%	14%	25%
Method: Model	63%	10%	27%
Both Methods: (Lecture & Model)	62%	12%	26%

Table 20 Summary Statements regarding prior interest in STEM medicine compared to how they felt after experiencing the educational intervention

Statement	**Percentage of Participants**
This lesson had *no impact* on my existing interest in STEM	26
My interest *increased* *a great deal/a lot* as a result of this lesson	20
I was unlikely/indifferent towards pursuing STEM/medical fields prior to this lesson. I am *now less interested as a result of this lesson*.	3
Independent of my initial interest, the lesson had a *moderate to high impact on my interest in STEM*	50
I was somewhat unlikely to entered STEM/medical fields prior to this lesson, but my *interest has increased a little/moderately towards STEM fields*	61
I was extremely unlikely to pursue medical fields prior to this lesson. *I am now slightly/moderately interested*	17

4.5.4 Classroom Observation

During each classroom intervention, observation loosely based on the COPUS observation protocol was conducted to focus attention on the body language, comments, and questions posed by students as a qualitative measure of assessment [338]. Additionally, the body language of students was observed, and interestingly, most girls leaned forward, and most boys leaned backward, which is commonly interpreted as interest and lack of interest, respectively [339]–[341]. Most students were observed maintaining eye contact with the instructors throughout the process, which is another indicator of engagement. Although these observations pertained to the majority of students for all interventions, there were always between 2 and 6 students (depending on class size) who appeared uninterested and/or incredibly uncomfortable, and this was gauged through fidgeting and reluctance to touch or handle the models in the 3D models group.

Prior to the instruction, participants were instructed to complete their pre-assessments. During this time, observers noted several comments made by the students including the following: '"Why are you laughing", "I don't know any of this", "This is so embarrassing", "We all took AP Bio, so we should theoretically know more…but I feel like I know less", "Does anyone even know what a urethra is? "I feel like I got everything wrong", "We still have a lot to learn", and "I don't know what a pelvic floor disorder is"'. This verbal commentary suggests a state of uncomfortableness and lack of knowledge with the topic as well as the realization that their expectations regarding their own level of knowledge were not met prior to this instruction. Further examples of commentary are included within Table 21. During the instruction, students in both the lecture and 3D model groups were engaged in active and interactive learning by answering questions posed by instructors and asking several of their own questions. In the 3D model group, there were discussions among students to contextualize the problems presented as a part of the lesson plan, which is found in Appendix C.

In both the lecture and 3D model instructional groups, engagement increased after students were presented with a case study about a woman who was suffering from prolapse. Many participants expressed empathy for the woman's "emotional pain and distress" and began making connections that explained the woman's condition. One student remarked, "Structure is important for function, so if there is bad structure, function decreases". When students were shown the prolapsed vagina in the 3D model group, they were immediately able to hypothesize reasons for prolapse such as "no support, tearing, menopause, etc." Table 21 demonstrates comments from students among both intervention groups, before, during, and after interventions.

Table 21 Student observational quotes before, during and after interventions

BEFORE	DURING (questions/comments)	AFTER
"Eww"	"Ugh-I'm never giving birth"	"We need to understand if these things will happen to us"
"That's nasty"	"Is there a way to make it better or to fix prolapse?"	"We need to understand our own body"
"This is so embarrassing	Does the bladder go back to normal after delivery?	"if you don't understand your body and when something is abnormal, you may not tell your doctor and your condition could worsen due to delayed treatment"
	"Can you have a missing vagina?	
	How many eggs do women have, and how many are expelled during menstruation?	
	What is the maximum number of pregnancies a woman can have?	

The commentary suggests that as time increased, students became more comfortable in the classroom setting, as they began to show increased interest and a desire to learn more through engagement with their peers and instructors. The quality and thought behind the questions posed throughout the intervention increased as shown in Table 21.

4.6 Discussion

The overall goal of this study was to improve overall knowledge, awareness, and appreciation for female pelvic health among a group of high school students using comprehensive assessments. To determine overall gains, baseline knowledge was assessed prior to each intervention, comprehensive knowledge was assessed immediately after each intervention, and retention of knowledge was assessed at least two weeks following each intervention. I believe the most impactful takeaway from this study is the results in Section 4.5 illustrate that small investments can contribute to learning gains. The results not only demonstrated gains between baseline and comprehension assessments, but overall gain between baseline and retention assessment, which demonstrates an overall positive gain as a result of the intervention, regardless of the instructional method.

Based on my preliminary informal interviews described in Section 4.4.2, and my own experiences during Health class, I anticipated encountering snickering, giggling, lack of participation, off-topic questions, lack of male participation, and overall attitudes of disinterest, apathy, and disgust. Although some students demonstrated a few of the behaviors described (i.e., snickering and giggling), the behavior most demonstrated was lack of comfort regarding the subject area. This was not only observed visually but was overwhelmingly expressed by students on their baseline assessment. Furthermore, males were overall more engaged in the lecture and 3D model interventions than females. In fact, more females demonstrated their lack of comfort relative to the male participants through lack of contact with models and use of slang terminology. Interestingly, some students demonstrated a surprising amount of prior knowledge, although several denied having ever taken anatomy or health courses. This observation could be the result of learning from peers, older siblings, and the internet, which supports findings in literature reviewed in section 4.2.

Results indicated that following the intervention, about 60% of all participants were comfortable with topics surrounding female pelvic anatomy. This was surprising, given that prior to the intervention, many participants had physical reactions (i.e., indirect eye contact, blushing) when asked to identify the vagina verbally, as well as for describing the function of the rectum which was generally articulated as “to help you go to the bathroom. So, at the core, why was there so much anxiety and embarrassment prior to this intervention, versus after, where students expressed increased comfort and understanding of topics after just one hour? Support for this finding can be found in the literature, which suggests that, as discussed in section 4.4.5, classroom environment, which includes educators that are knowledgeable and comfortable with topics can heavily influence comfort and ultimately learning outcomes.

Educators must find ways to make topics relatable to students. As with the student who struggles in math, if the student can relate it to the real world or have a better understanding of how its impact, he/she will feel more passionate about it, and passion is a part of what moves progress. Even in math, students will not ask questions if they feel that their question will be judged or be looked down upon by their peers. This same concept is further exacerbated surrounding topics of health literacy and female pelvic anatomy. Many students were taught, either explicitly or implicitly, that there are certain things that can be asked and discussed, and other things that should not be discussed. This type of learning environment does not enable students to ask questions and gain their own understanding. Some people see doctors, lawyers, scientists, etc. as the “smart ones”, so basically, there is an imaginary line between “us” and “them”. As humans, we seem to have a natural tendency towards these distinctions; however, the truth is the key to society’s progression requires everyone’s participation, and not just an elite few. An example that made concepts more relatable included the breaking of a swing support as a way to help improve understanding of POP. Thus, rather than using complex medical terminology, we employed an example that almost all students and others could picture and relate to in order to help them better understand the significant movement of organs as a result of compromised support. In general, the use of analogies was supported real-time during one intervention, in which a student used a baseball mitt to describe multiparousness. Students were moved by an anecdote that was provided for discussion, which really touched them and made them feel more connected to the issues at hand versus the hard-cold facts. This observation is supported by studies that investigate Generation Z, and their inclination towards societal change.

We found that once students understood that the classroom environment being established was a safe space for teaching and discussing topics that are traditionally taboo, students began asking questions about all kinds of topics related to female pelvic anatomy and health. Questions ranged from generic questions to personal questions regarding birth control, pelvic pain, “breaking” the cervix, etc. Given our purpose and scope of expertise, we refrained from giving medical advice and answering these questions but praised students for being open and willing to ask these questions. While these questions were not necessarily on topic regarding our intervention goals, they were open and honest and showed a need for a safe place for their questions to be discussed. Furthermore, literature suggests that nervous energy from persons in teaching roles can be transferred to their students. In particular, one class instructor thanked our group for coming, saying "Thank you for teaching this so that I don't have to!" This comment suggests relief for not needing to cover the specific topic of female pelvic anatomy with students, even in an anatomy, biology, or medical specialty class.

On the other end of the spectrum, uneasiness felt by school instructors and administrators led to several schools choosing not to host our intervention, and in fact, they would not even meet with us in order to discuss our lesson plans, curriculums, and models. Some adults may struggle with the concept of young women starting to develop and discovering and exploring their own bodies, and unfortunately, they may allow their own embarrassment and shame to impact students. These challenges contribute to barriers towards student comfort and retention of accurate information.

Colloquialism of health terms is also a significant contributor to confusion demonstrated, especially in baseline assessment of female pelvic anatomical location and function, shown in Table 16. The most common point of confusion for many was the fact that the urethra and the vagina are two separate organs, with separate functions. In fact, one student noted that she was unaware that the urethra and vagina were different, because when she went to the restroom her tampon would still get wet. An interesting, yet different interpretation from another student was that "girls pee out of their rectum". These misconceptions stem in part from slang often used to describe the vagina. For example, terms such as "private parts", "lady garden", and "down there" are vague and essentially imply things are lumped together, negating their significance.

Another example was that of “my stomach/tummy hurts” when referring to menstrual cramps. However, this colloquialism was unrealized until the grading of the open-ended responses on the comprehension and retention assessments.

5.0 Conclusions

The field of women's health is of monumental importance, as it aims to understand normal function, as well as abnormal pathologies that significantly impact quality of life, and sometimes, life itself. Due to centuries of bias towards women, a resistance to changing techniques and views, and lack of emphasis placed on these challenges, women are still suffering from disorders that have plagued their quality of life for ages. This body of work, "Shifting and shaping perceptions: Towards the Characterization and Literacy of Female Pelvic Organ Support", was developed to advance our definitions and conversations regarding normal female pelvic anatomy. Thorough an investigation of existing knowledge and challenges in Chapter 1, gaps in knowledge were addressed through completion of the following aims:

Specific Aim 1): To define and assess changes in Level III support with respect to age and parity.

1A) To establish an MRI database derived from local patient populations.

1B) To evaluate the location of the Hymenal Ring position with respect to age and parity.

This study found that there are differences in measurements for both the anterior and posterior hymenal ring border in relation to the pubic symphysis are not random. With respect to parity, the anterior and posterior border distances demonstrated statistical significance at $p=1.15*10^{-5}$ and $p=0.003$ respectively. Similarly, with respect to age, the anterior and posterior border distances demonstrated statistical significance at $p=2.14*10^{-4}$ and $p=2.61*10^{-6}$, respectively. However, the effect sizes with respect to age and parity for these measurements were small to medium. Interestingly, the effect size was greatest for the anterior measurement when subjects were grouped by age and parity was a covariate (d=0.401), and the posterior measurement had the highest effect size when subjects were grouped by parity status and age was a categorical covariate (d=0.445). At a macro level, these results indicate that the positions of both the anterior and posterior borders of the hymenal ring relative to the pubic symphysis are indeed influenced by age and parity.

Specific Aim 2): To establish a 3D pelvic coordinate system that allows for quantification of vaginal angle and spatial position within the pelvis.

2A) To assess the inter-and intra- observer repeatability of the developed 3D coordinate system.

2B) To assess changes in vaginal position and orientation within the pelvis with respect to cohorts of age and parity.

This study developed a 3D anatomic coordinate system that supports longitudinal analysis of changes in the vaginal axis and position. Analysis of the coordinate system demonstrated that our novel coordinate system has superb inter- and intra- rater reliability, and great repeatability with respect to within-observer differences in vaginal position and angle measures, while proving to be less susceptible to variability in pelvic dimensions, shape, and the finessed skill of observers.

Specific Aim 3): To investigate the ability for high school students to comprehend and retain information pertaining to female pelvic anatomy when exposed to educational interventions.

3A) To develop an assessment tool to gage baseline knowledge, comprehension, retention and attitudes following the implementation of active learning techniques to educate high school students about female pelvic health.

3B) To assess the perceived impact each active learning intervention had on the comprehension, retention, and attitudes towards female pelvic health.

This study found that learning gains can be achieved over a short period of time as a result of targeted intervention. Greater learning gains were achieved from participants who were in the 3D model group. Furthermore, these gains can be retained and facilitate positive attitude shifts surrounding topics of female pelvic health.

This work, along with several others, have hopefully made it clear that it is the responsibility of everyone-clinicians, researchers, men, women, children, etc. to bring awareness, normalcy, and acceptance of ordinary functions, such as menstruation, and abnormal functions, such as PFDs, endometriosis, pelvic pain, and many others. Thus, the greatest overall contribution of this work is its unique and multifaceted approach towards improving our conversations towards female pelvic health. It has been demonstrated that increasing our knowledge and ability to treat PFDs is not just a clinical challenge, but an engineering challenge, as public policy and societal challenge. It is my hope that we will continue to unfold the complexities of female pelvic anatomy through continuation of these studies; some of which suggestions are provided below.

5.1 Clinical Implications

Physicians and medical professionals spend several years training to become practitioners of medicine, with significant emphasis on diagnosing and treating ailments and disorders. These professionals are often tasked with addressing immediate or urgent issues to support patients in need. However, in many situations, simply diagnosing and treating disorders does not necessarily push the envelope and expand discoveries and treatments but maintains status quo. This was particularly obvious in womens health, where progress has been slow in our treatment and prevention of PFDs. While some would blame the field’s delayed progress on the insignificance of quality-of-life aliments when compared to life-threatening ailments, this excuse loses validity in the face of the abundance of collaborations among scientists, engineers, and medical professionals to understand and treat ACL injuries, or erectile dysfunction.

One of the most significant gaps in knowledge surrounding women’s health has been the consistent attempt correct anatomical issues without truly understanding and defining the normal conditions under which these systems operate. Furthermore, lack of consensus on measurement systems creates barriers towards developing a comprehensive understanding and basis for quantifying female pelvic anatomy. While the studies within in this body of work are not immediately translatable to a clinical setting, there are several clinical implications of note.

As a whole, this body of work enhances our clinical understanding of the natural evolution of the vagina with respect to age and parity, the two greatest risk factors associated with symptomatic onset of PFDs. The first study in Chapter 2 demonstrates the potential breadth of existing medical scans and patient information accessible to clinicians and researchers. Our finite search was able to produce hundreds of scans that matched our stringent inclusion criteria. Ideally, researchers and clinicians could afford to scan patients in such a manner specific to their research question. However, several practical factors make this an impossible feat, especially when considering the number of studies that still need to be conducted and questions that need to be answered. Our database demonstrates that, among the scans ordered by clinicians every year, there are several with no indications of compromised anatomy that, once reviewed, remain unused in the UPMC database. The second study of chapter two, which uses existing retrospective scans, demonstrates that the hymenal ring, a reference point used in POP-Q measurements changes with respect to age and parity. While the population used in the study was by no means representative of all women, it does suggest that the position of the hymenal ring could, with additional studies, become a biomarker for earlier detection of compromised support. Hence, it may be useful for clinicians to begin collecting measurements of the anterior and posterior hymenal ring with respect to the pubic symphysis as an additional measure while reviewing patient scans. While the H-line, SCIPP, and other measurements are typically applied to patients with prolapse, the additional measurement we propose could be used not only for treatment plans, but towards the development of individualized preventative care for PFDs.

Chapter 3 introduces a 3D coordinate system that improves upon the limitations of existing measurement systems. This system builds on the existing knowledge and strengths of physicians and radiologist with regard to identifying landmarks and meticulous reviews of scans and uses mathematical concepts embedded in a custom code to convert these skills into measurements that may also have clinical relevance. This is relevant because instead of a theoretical coordinate system that is describing random points in 3D space, each aspect of the coordinate system and each point is anatomically relevant, and enables comparisons between patients who may be misaligned, or have different pelvic shapes and sizes. Adopting this method into a clinical setting could serve as a gold standard of measurement and quantify our understanding of how changes in the position and/or axis of the vagina could serve as an indicator of changes in surrounding organs for different populations of women. This would provide valuable insight into the natural variation of vaginal shape and position that is undoubtedly present between and within populations. With enough patients and cohorts, a rubric could be developed and used by clinicians to help them rate their patient’s anatomical measurements with respect to the measurements of women who share distinctive characteristics such as age, parity status, lifestyle habits and race. Ultimately, this measurement would further encourage personalized care, and could even aid clinicians in explaining anatomical changes to their patients.

In fact, the findings in Chapter 4 have clinical implications that support those of Chapters 2 and 3. Chapter 4 demonstrates the need, importance and impact that educating the general public could have on improving attitudes, beliefs, communication, expectations, and outcomes from a patient perspective. Society implies discussing changes in vaginal health are not to be discussed publicly, and in earlier chapters we have outlined how this attitude towards pelvic health is detrimental to patient outcomes. Our inability as a society to provide women effective spaces for asking questions, understanding and learning about pelvic health and anatomy can strain patient physician interactions. The lack of conversation among the general public leaves women without the necessary tools or confidence to share their challenges with their physician, or even the language to describe their fears and challenges. Aim 4 proves that even an hour of directed active learning for high school students can make a difference. This difference was even more apparent with students who had access to the 3D printed models. 3D printed models could be used clinically as well, to help teach patients about general anatomy, or even their specific anatomy. Furthermore, if the geometric data obtained for these models is printed using materials that have similar properties to the organs they represent, they could be used as a much more affordable tool to train medical students, residents, and specialists.

Although the methods discussed in previous chapters are not ready for immediate clinical use, they highlight the need for additional considerations, and quantitative methods for describing pelvic health and could be eventually adapted by clinicians. Ultimately, these methodologies can be expanded in ways that could contribute to early detection/intervention of PFDs through a better understanding of the pathogenesis of PFDs.

5.2 Engineering Significance

Engineers are trained to tackle challenges towards the improvement of quality of life. Given that most PFDs are categorized as non-life-threatening quality of life challenges, the potential impact of engineering is substantial. Here, we demonstrate that many several engineering and concepts and techniques can and should be applied to female pelvic anatomy. Over the last 20 years, engineering and technology have been used to quantify and improve our characterization of female pelvic anatomy. These studies, and several others heavily rely upon magnetic resonance imaging to visualize the complex nature of internal organs that were commonly misidentified with respect to their structure and function. MRIs enable researchers to study these structures in living in patients, and more importantly, develop techniques to quantify the information available through these images.

The study presented in Chapter 2 applies engineering and 3D spatial concepts towards improving the precision with which we can quantify the position and movement of the distal vagina. The information collected in the database coupled with the measurements derived from MRIs led to the conclusion that there may be changes driven by age and parity with respect to the hymenal ring. This information can be applied not only clinically, but towards the improvement of finite element models that help us understand how pelvic organs interact and respond to events such as increases in intra-abdominal pressures, or injuries. The study presented in Chapter 3 adds to existing knowledge through the improvement of methodologies to quantify the position and orientation with respect to a 3D coordinate system. This is enables a means of which, with a large enough dataset, we could reliably quantify variations in patients to incorporate into computer models for assessment. Ultimately, these tools are particularly useful to support the development of patient-specific diagnostics and treatment plans. The study conducted in Chapter 4 utilized 3D printed pelvic organs to improve awareness and health literacy surrounding the structure and function of pelvic organs among high school students. Here, we demonstrated that engineering can be applied towards not only quantifying measurements to improve patient quality of life but can be used towards the development of teaching tools that, in conjunction with evidence-based teaching practices, can change public knowledge and perceptions for the better. The results from this dissertation could aid in the improvement of surgical procedures to help them be more anatomically specific and improve our understanding of mechanisms of disease by starting from normal anatomy and moving forward, rather than working the problem backwards.

5.3 Future Studies

The continued existence of humanity relies upon our ability to adapt to changes around us. Every interaction with the environment initiates a chain reaction; improvements in one area can influence or require changes in another area. Thus, no matter how significant a research study, finding, or adaptation may be, there will always be a need for future studies. As we improved our ability to treat life-threatening diseases and increased the production and access to food, and shelter, the demographics of the world population changed. More specifically, families had fewer children, lifespan increased, and for many, the amount of physical labor decreased. While the aforementioned advancements in society were positive, it led to the introduction of variables that had not yet been explored.

Interestingly, many outcomes of improved society directly impact female pelvic health. Notably, the aging population, childbearing, and sedentary or hard labor lifestyles all contribute to increases in the number of people suffering from PFDs, which emphasizes the importance of this work more than ever. The impact of the Covid-19 pandemic is yet to be seen, but some of the symptoms and long-term effect may exacerbate the need to continue exploring changes in female pelvic anatomy and health. Here, we will explore some direct and long-term future work to advance the field.

Further investigation of changes in the hymenal ring position with respect to age and parity will determine if it could be an effective indicator of pelvic floor injury or degeneration. Future studies should expand this analysis and explore the potential for hymenal ring position measurements to serve as an early imaging biomarker for POP. We plan to expand this work to determine if there are hymenal ring shifts as a result of aging, ethnic backgrounds, as well as patients with prolapse to determine if there is potentially an under appreciation of the clinical presentation of prolapse and other PFDs.

The subsequent step for all of the studies within this dissertation would be expanding the size and demographics of patients within the patient database. Handa et. al. found differences in pelvic anatomy with respect to race, emphasizing the need for expanding subject cohorts and developing a more comprehensive collection representative of several groups of women. Even more importantly, the 3D coordinate system developed now accounts for pelvic size, would not be influenced by the fact that the outlets of white women versus African-American women differ [108]. It would be important to expand beyond patients within the Pittsburgh UPMC network by partnering with other medical systems and universities across the United States. This study, and most others are limited in their findings due to challenges obtaining breadth within the available scan population. Thus, it is critical that we apply methodologies across a wider population, including women under 19, women over 75, black women, Hispanic/Latino women, Asian women, and Pacific Islander women. Additionally, these populations could be further divided based on environmental factors such as parity, smoking status, quality of air in job or living conditions, and BMI. While environmental factors are known to contribute to symptomatic PFDs, we are yet to characterize these factors within different populations and using the methodological contributions from this work.

It is important to acknowledge that race is a social construct, and its applicability must be carefully considered when conducting medical or scientific studies [342], [343]. In fact, categorization of populations based on interpretations of race have exacerbated misconceptions and inequities within the healthcare system-a secondary effect of perceived biological determinism [344]–[346]. Thus, our ability to effectively characterize anatomy, especially as complex as female pelvic anatomy, requires an acknowledgement of disparities and an investigation of causation prior to the implementation of solutions [345].

Differences attributed to race are often caused by environmental differences and availability of resources among individuals within a population. For example, a review of anthropologic literature suggests that variances in pelvic shape and size may be influenced by latitude or differences in climate [347]. Given that environmental factors can significantly influence evolution, anatomical morphology, and consequently the biomechanics of tissues, future studies towards characterizing normal pelvic anatomy should shift to prioritize the influence of environmental factors over race.

Another aspect worth future consideration is the exploration of genetic markers that suggest increased risk for PFDs. A study conducted by Norton et. al. found that within a population of women in Utah, genetics may have contributed to the development of symptomatic POP [348]. Another study by Giri et. al explored genetic markers for Pelvic Organ Prolapse in African American and Hispanic women [210]. Sharma et. al explored female pelvic morphology in twins living in Punjabi [349]. Each study identified genetic markers, however, they all indicated that environment influences genetic factors, and that it can be challenging to parse these specific contributions. Furthermore, research of this nature requires large databases of information to improve interpretation of results. While there are several databases such as Ancestry DNA that contain a wide breadth of information, there are significant barriers for genetic testing; especially among populations who are still coping with post-traumatic stress from eugenics and experimentation without consent [350], [351]. Presently, there are several ethical and legal challenges further complicate the collection, maintenance, and use of genetic information [352]. However, this information coupled with the considerations above and the methods of analysis proposed in Chapters 2 and 3 could further enhance our ability to characterize variations in female pelvic organ support.

The most logical way to develop a large and comprehensive database is to encourage participation from clinicians and researchers across the United States and globally. Participation can be encouraged by requiring contributions to a web-based platform by way of scans, patients, analysis, etc. to the collective database in order to access the information contributed by others.

Centralized access to a database that not only include anonymized patient information and MRI scans, as in Chapter 2, but the addition of anatomical pelvic models developed from scans, will propel research within the field [353]. We propose bringing clinicians, scientists, mathematicians, engineers, and others together through the creation of a centralized location to access important information and discoveries for the field of Urogynecology as it relates to understanding pelvic health, in an effort to reach an understanding of the pelvic floor, comparable to, if not better than what we know about the cardiovascular system, knee biomechanics, etc. As the database is being developed, we can implement “indexical information” in an effort to look for patterns within the data.

The development of reliable 3D quantification of vaginal axis and spatial position is a significant accomplishment within the field. Future studies should apply the methodologies developed in Chapter 3 to a broader population of women to establish ranges of normality within population subgroups. With significantly larger cohorts of women based on the considerations described in section 5.3.1, longitudinal data, effective measurement systems, and database management, applications of predictive medicine can be explored. The impact of such a system would be profound. The Framingham Heart Study is hailed as one of the most robust longitudinal studies to date, and the data collected led to the creation of a risk score that can predict risk of cardiovascular disease over ten years [354]. The possibility of developing a risk score for the onset of symptomatic PFDs could help mitigate the number of cases as well as anatomically correct existing cases. This means of triage will not only save time and money for patients and physicians but minimize unnecessary procedures and treatments. Given the trends observed around hymenal ring position, applying the methodology proposed in chapter 3 could further elucidate subtle changes within populations and explore the possibility of developing additional clinical diagnostic tools to support clinicians and surgeons in offering personalized solutions for patients [355].

5.4 Closing

Although we have a tendency towards holding onto beliefs for generations, there is always opportunity for change. Changes have the opportunity to occur in our beliefs, most commonly through discourse of people who feel passionately about the change in belief-such that not fighting for the belief begins to challenge their moral compass, and they no longer can sit idle [356]. We have witnessed partial evolution of several core beliefs that were justified through religious practices, such as chattel slavery in the Americas; and although not all subscribe to these beliefs, enough of those in power were able enforce laws, provide opportunities, and continue to educate others.

Yes, we must live in the present, but we also must examine our past, in our present, to make changes that impact the future. Reflection is not meant to chastise, or point fingers, but to gain a more comprehensive understanding of why things are the way they are, and how they were shaped. Not everything we dream of and hope for comes to pass; we may desire to live in a world where there is never hunger, people don’t die, etc. But by reaching for the stars, we can fall on the moon; which is improving quality of life for all. Also, the past is what helps shape predictions and groundwork for the future; and with optimism and an open mind, yesterday’s visions of tomorrow become the present. It is an exciting time in science, in that we are experiencing another shift; in which our response to challenges faced will dictate the outcome for humanity. The key to reducing global health burden lies in developing an understanding of the natural history of diseases and disorders and distributing this information to the general public to raise awareness and promote further investigation towards preventive strategies, as well as treatment strategies.

5.5 Postface

From the outside, PhD programs are presented as straightforward paths that are mapped out with specific milestones, with a neatly packaged presentation and thesis to accompany the final stages. The insider experience shows that this couldn't be farther from the truth, and in fact, my experience has been almost entirely the opposite. I struggled to fit the mold that was presented before me. I tried to force myself to fit in the circle and to follow in the footsteps of those before me. The challenge, however, was that I am a square, and I would never quite fit the mold-no matter how hard I tried. I discovered many years later, that the key to successful completion of a PhD is not in forcing yourself to fit into the shape created by others, but through being your own shape. In fact, fitting into a mold forces you to be slightly smaller than the shape you are molded to. I firmly believe that the most effective way to make contributions to a field is to stay true to yourself, because the uniqueness of your own shape, which is built upon the foundation of the original mold, becomes larger, and therefore, rests on top. For anyone reading this body of work who has felt the same way, this message is for you. If I can do this, you can too, and I hope this inspires you to embrace your unique journey and serve as a foundation for your future contributions!

6.0 Shifting and Shaping Lives Through Teaching, Research and Outreach

6.1 Overview

While the goal of any student is to eventually obtain their chosen degree, there are often a myriad of achievements made along the way that play an equally important role in shaping the graduate. For me, these accomplishments can be broken into three categories: teaching, research, and professional service. What follows will highlight these three categories as they pertain to my time as a graduate student at The University of Pittsburgh.

6.2 Teaching

6.2.1 Teaching Assistant

Many graduate programs require students to serve as a teaching assistant (TA) for one to two semesters during their graduate studies. In my case, I was fortunate to experience being a teaching assistant for both undergraduate and graduate level courses. During my first semester as a TA for an introductory Engineering Course, with approximately 85 Freshman, I found myself eager to experiment with different methods and techniques for assessing and approaching the course curriculum. This interest led to a relationship with the Engineering Education Research Center (EERC), which had just begun co-hosting courses with the Center for the Integration of Research, Teaching, and Learning (CIRTL).

In fact, I ended up enrolling and completing every course offered as part of that joint effort. At the time I did not have a plan for this knowledge, but my eyes were opened to a new world of possibilities.

6.2.2 Summer Engineering Academy Instructor

In 2014, I had the opportunity to begin working with the Pitt EXCEL program, which is an undergraduate engineering diversity program towards supporting the recruitment, retention, and transition of traditionally underrepresented students within Engineering. I was particularly excited, because I had been tasked with redesigning the Engineering Problem Solving Course for the Summer Engineering Academy. This academy was a two-week summer “boot camp” to help prepare students for their first semester within the Swanson School of Engineering, and to help build a community between the students. Prior instructor had left a pretty bare bones curriculum for me to work with, so I was immediately able to experiment with the knowledge gained from the CIRTL teaching courses. Ironically, this also gave me the opportunity to implement changes that I felt would enhance the freshman experience for the students within the program. Although the program was only two weeks, it was the first time I truly appreciated how much preparation and planning is necessary for teaching. Over the next four summers, I developed a niche interest in supporting students transitioning from high school to college. This opportunity allowed me the space to experiment with team-based learning techniques, active learning techniques, and incorporating soft skills, such as networking, writing, and presenting, into the curriculum.

6.2.3 Tutoring Business

Starting in 2018, I began financially supporting my graduate studies through private tutoring. I provided tutoring services for students from 5th grade through college level. Through my one-on-one interactions with students, I was able to further develop my teaching philosophies. I realized, once again, that I could use my learned experiences, both the successes and the failures, to serve as a role model for the students I worked with. For me, tutoring was about more than helping students earn an A in a specific course. It was an opportunity to support students in developing confidence, critical problem-solving skills, and study skills with the ultimate goal of getting them to a point where they would no longer need my services.

6.2.4 First Year Engineering Instructor

By 2019, I transitioned into teaching Engineering 0011, Introduction to Engineering Analysis, and Engineering 0012, Introduction to Engineering Computing, which I still teach today. This gave me the opportunity to teach one of the courses I had served as a teaching assistant for in 2014. While I had some teaching experiences prior to this, I had not instructed a large classroom for a full semester while teaching in-sync with several other professors. The first year was definitely a challenge, particularly as the 0012 section was metaphorically derailed by covid, however I was able to iterate on my approach and have been happy with the changes made during my second-year teaching. I have been able to apply the knowledge and theories gathered during my continuing education courses to better connect with students, develop relevant and impactful classwork and examples, and provide input to support and enhance the freshman experience within the Swanson School.

6.3 Research

6.3.1 Bioengineering Research

The work described in Chapters 2-5 of this document have resulted in several abstracts, posters, presentations, and publications in review. This experience allowed me to become immersed within the research field, meet and develop relationships with others outside of the university, and improve my ability to share and disseminate research results through different mediums and for different audiences. Early in my graduate career, I was invited to co-write two book chapters with my dissertation advisor. This work was published within a reference textbook entitled, *Biomechanics of the Female Pelvic Floor*. This text was one of the first created as a resource specifically devoted to the application of biomechanics to Female Anatomy that is accessible to undergraduate students and STEM majors who are not steeped in the research field. I also published a review paper in *Current Opinion in Urology*, an influential journal within my field. This manuscript is often referenced by others within the field. While my dissertation work did not include any animal model studies, I engaged in animal studies with my other colleagues, and served as a surgical assistant for several primate surgeries, necropsies, and mechanically tested several tissue samples. These contributions were included in works published by the lab in journals such as *Acta Biomaterialia*.

The nature of my bioengineering research also afforded me the opportunity to mentor over 20 students during my graduate studies. This included training students on completing projects in the lab, and many helped collect data or participated in the work described in previous chapters.

I also began connecting with researchers within the field, but outside of the University of Pittsburgh by participating in a newly developed society, the Society for Pelvic Research (SPR), for which I served as secretary of the trainee board from 2016-2018, and vice president of the trainee board from 2019-today.

6.3.2 Diversity Graduate Program Research

In 2019, while serving as a first-year instructor, I also immersed myself in diversity research. I joined the internal evaluation team for the AGEP Pitt STRIVE program (Award #1434012). I have always been an active member within the historically underrepresented populations within the Swanson School. However, this gave me the opportunity to explore assessment development and qualitative research, both of which contributed to perspectives and findings throughout my dissertation work, and especially with the work completed in Chapter 4. Furthermore, this experience resulted in three conference papers and the opportunity to serve as a reviewer for the Journal of Engineering Education. I am also looking forward to publishing a paper with two undergraduate who have been working under my mentorship for the last year to analyze qualitative data regarding the culture and climate within the Swanson School of Engineering.

6.4 Outreach & Professional Service

Finally, I have spent every single year of my graduate career committed to outreach. I spent six years attending conferences and visiting my alma mater to help recruit historically underrepresented students to the University of Pittsburgh. I also served as a student leader for EDGSA (the Engineering Diversity Graduate Student Association), by creating more office positions within the organization, building community among members within the organization, and fostering connections between graduate students and corporations. I have facilitated and created several graduate and undergraduate workshops, served on panels, and informally mentored several graduate and undergraduate students during my free time. I have given over 12 motivational speeches and moderated research presentations for six years for the Engineering Office of Diversity.

In addition to my contributions within the Swanson School, I have participated in other outreach programs. I have served as a guest lecturer for Summer programs and in high school classrooms to discuss topics ranging from biomechanics, an introduction to citation software, conducting literature reviews, being an effective mentor, engaging in community outreach, and ethics with respect to science and engineering.

Appendix A 3D Coordinate System for Defining Vaginal Axis and Spatial Position

This code was implemented in chapter 3

CENTROIDAL COORDINATES, ELEVATION & DEVIATION ANGLES CODE (6-29-18)

```
(*Includes .vtk print out, angles of elevation,
deviation print out, centroidal splines and coordinates*)

In[ ]:= (*****************************************************************************
 RUN CODE
 HERE**********************************************************************************
  *****************)

(*Entering patient number for later use: to be included with excel file names*)
Print["Enter patient number here as /####"]

PatientNum = InputString[]

Enter patient number here as /####

Out[ ]= /47_KO
```

Printed by Wolfram Mathematica Student Edition

In[ ]:=
```
(*!!!!!RUN CODE HERE!!!!!*)

(*First browse is for locating the folder with the xml data files.  The second browse is
 setting the output folder where all Mathematica calculated data will be stored*)
SetOptions[$FrontEnd, DynamicEvaluationTimeout → 30 * 10]
Print["Select Your Directory with your DCM files and ROI file:"];
directoryA =
 Grid[{{FileNameSetter[Dynamic[directory], "Directory"]}, {Dynamic[directory]}}]
Clear[filename, datafiles];
Print["Select Your Your Exisiting ROI file Files to Import"];
Dynamic[If[StringQ[directory],
  SetDirectory[directory];
  datafiletype = "xml";
  files = FileNames[];
  datafiles = Select[files, FileExtension[#] == datafiletype &];
  Grid[{{PopupMenu[Dynamic[filename], datafiles]}, {Dynamic[filename]}}]]]
Print["Is data reversed: Check if 'yes'; uncheck if 'no' - "];
Checkbox[Dynamic[checkx]]
Share[];


Print["Select your data output folder"]
directoryB =
 Grid[{{FileNameSetter[Dynamic[directory2], "Directory"]}, {Dynamic[directory2]}}]

CoordinateData = Import["/Users/deannasinex/Google\ Drive/Translational\
      Biomechanics\ Laboratory/Dissertation/Aim\ 2\ 3d\ coord\
      system/3D\ Coord\ system\ data\ 9_26_18.xlsx", "Data"][[8]];
```

Select Your Directory with your DCM files and ROI file:

Out[ ]= Browse...
directory

Select Your Your Exisiting ROI file Files to Import

Out[ ]=

Is data reversed: Check if 'yes'; uncheck if 'no' -

Out[ ]=

Select your data output folder

Browse...

Out[ ]=

```
In[ ]:= (*****************************************************************************
 Then RUN CODE
 HERE*************************************************************************************
  *****************)

Clear[pic, thumbpic, data, data2];

(*defining type of image as DICOM files*)
imagefiletype = "dcm";
Clear[jjj, i]

(*This is importing dcm files, or the filetype for the images,
as well as information from the metadata within the pictures*)
picfiles = Select[files, FileExtension[#] == imagefiletype &];
(*This identifies the number of.dcm files that are
 saved in the folder chosen above.  Ex: 01.dcm, 02.dcm...*)

(*metafirst and metalast allow for the MetaInformation to be called,
and each is locating a specific piece of meta data*)
metafirst = Import[picfiles[[1]], "MetaInformation"];
(*This identifies the starting image of the .dcm
 files and pulls up the metainformation for that patient*)
metalast = Import[picfiles[[Length[picfiles]]], "MetaInformation"];
(*This identifies the length of the dataset,
so it indicates how many .dcm files in total for the patient and the metainformation*)

(*The built in function Position gives a list of positions at which
 a particular thing occurs.  Thus, loccenterfirst & loccenterlast are
 looking for the position of the phrase "ImagePosition" within the first
 and last .dcm files  Both return a position in the form row by column*)
loccenterfirst = Position[metafirst, "ImagePosition"];
loccenterlast = Position[metalast, "ImagePosition"];

(*centerfirst and centerlast output a coordinate point.  It is looking at the first and
 last .dcm images.  The x and y coordinate will more than likely be the same.  The
 z coordinate will differ.  The z position is showing position in the z spacing,
or the distance between slices.  This is the primary thing that would chnage.  If
 you take the z outputs from centerfirst and centerlast to find the total span and
 divide that by the number of images total, you should get approximately 2.9 or 3,
which is the spacing between slices for most of the scans*)
centerfirst = metafirst[[loccenterfirst[[1, 1]], 2]];
centerlast = metalast[[loccenterlast[[1, 1]], 2]];
```

```
locpixelspacing = Position[metafirst, "PixelSpacing"];
(*Locating the line in the Meta Data that contains the prhase "PixelSpacing"*)
pixelspacing = metafirst[[locpixelspacing[[1, 1]], 2, 1]];
(*This prints the value of the actual pixel spacing pulled from the meta data*)

(*These calculate the dimension of voxels in the x and y direction.  The
 funciton ImageDimensions gives the pixel dimensions of the raster
 associated with an image.  Those dimensions are then multiplied by
 the pixel spacing for the x and y direction.  The pixel spacing is
 "the physical distance between the centersf of each 2D pixel.  generally shown as row
   spacing/column spacing, and this is also how it is displayed in the metadata*)
voxeldimx = ImageDimensions[Import[picfiles[[1]], "Image"]][[1]] * pixelspacing;
voxeldimy = ImageDimensions[Import[picfiles[[1]], "Image"]][[2]] * pixelspacing;

zdistance = centerfirst[[3]] - centerlast[[3]]; (*This is calculating the
 actual distance between the first image and last image in the z direction,
so it is only looking at the z portion of the coordinate outputs from
 centerfirst and centerlast.  I believe the subtraction is because of
 the  predefined coordinate system.  The center last value is negative*)

aspectratio = voxeldimx / voxeldimy;
(*Proportional relationship between the width and height of an image*)
numberoffiles = Length[picfiles]; (*Identifies the number of images for the patient*)
file = Import[filename, "CDATA"];
(*CDATA is the character data from the ROI .xml files.  The points associated with those
 files on each image are being imported from the selected file.  This includeds
 the slice on which the points were found as well as the name of each ROI*)
xmldata = ToExpression[file]; (*ToExpression gives the expression obtained
 by interpreting strings or boxes as Mathematica input.  So basically,
this is what allowing Mathematica to actually read the imported strings from
 the previous line of code.  It is important to note that this is 2D data,
and not 3D data, as the images are 2D where the ROIs are drawn*)
posroidata = Flatten[Position[xmldata, ROIPoints]];
(*This tells you the position of the phrase "ROIPoints" within the xml data set,
after flattening*)
posslicedata = Flatten[Position[xmldata, Slice]]; (*This tells you the
 posiiton of the phrase "Slice" within the xml dataset after flatening*)
(*The following is a data table that produces a table displying the values
 between the phrases "ROIPoints" and "Slice".  The plus 1 says to go 1
 past the prhase until you have completed the length of that particular
 array.  This table contains 2D information from the ROI tracings*)
data = Table[{xmldata[[posroidata[[n]] + 1 ;; posslicedata[[n]] - 1]]},
   {n, 1, Length[posroidata]}];


(*This section determines if the scan is FFS (feet first supine) or HFS
 (Head first supine) in order to ensure geometric surface plots upright*)
PatPosition = Position[metafirst, "PatientPosition"];
```

```
(*This determines where the phrase "PatientPosition" is located in the META DATA*)
PatPosition2 = metafirst[[PatPosition[[1, 1]], 2]];
(*This shows what's actually in that position -Either FFS or HFS*)
(*The following IF statments are telling the code once
 it has found the position in which FFS or HFS would be located,
to look at the value.  The slices are defined differently
 depending on the way in which the patient was imaged*)
If[ PatPosition2 == "FFS",
  slice = Table[
    numberoffiles - xmldata[[posslicedata[[n]] + 1]] + 1 , {n, 1, Length[posroidata]}]];
If[PatPosition2 ≠ "FFS",
  slice = Table[xmldata[[posslicedata[[n]] + 1]] , {n, 1, Length[posroidata]}]];
(*If PatPosition2 is FFS, that means that a table is generated where
 the slice numbers go from largest to smallest (so it has to flip stuff),
but only that of the ones that have ROI traces.  Otherwise,
a table is generated vice versa.*)

If[checkx == True, slice = Reverse[slice]];
roistartframe = slice[[1]];
(*once the slices are organized from "top to bottom" for our purposes,
we can identify which slice is considered the starting slice of the ROIs*)
metaroi = Import[picfiles[[roistartframe]], "MetaInformation"];
(*Importing data from the image in which the ROIs were said to start*)
loccenterroi = Position[metaroi, "ImagePosition"];
(*Locating the position of the phrase "ImagePosition" on the starting image*)
centerroi = metaroi[[loccenterroi[[1, 1]], 2]];
(*This is a point.  It is the location of the center of
 the image that contains the middle of the set of drawn ROIs??*)
slicezcoord = Table[0 &, {i, 1, Length[picfiles]}];
(*This creates a table with a z coordinate for each slice*)

(*taking image position for each slice,
finding the z coordinate and entering that in -this is taking actual data,
instead of determining based on the distance between slices*)
Do[
  metaall = Import[picfiles[[all]], "MetaInformation"];
  (*Imports MetaInformation*)
  loccenterall = Position[metaall, "ImagePosition"];
  (*Locates the position of the string "ImagePosition" within metadata*)
  centerall = metaall[[loccenterall[[1, 1]], 2]];
  (*locates the xyz data corresponding to ImagePosition*)
  slicezcoord[[all]] = centerall[[3]];
  (*Takes the 3rd number of the xyz coorindate for each image*)
  , {all, 1, Length[picfiles]}];

(*pic2 represent the actual data per slice based on the ROI images;
in the MRI coordinate system*)
pic2 = pixelspacing * data;
(*multiplies the 2D data table from the ROI tracings by the pixel spacing *)
slicedistance = Abs[zdistance] / numberoffiles;
(*This should probably be around 3...it's the distance between image slices z distance
```

```
 is based on the z coordinate of first and last image locations summed together*)
Clear[clusters];

(*Clusters mean number of objects; for this particular purpose,
there is just one cluster or 1 object*)
nnncurrent = 1;
countb = 0;
count2b = 1;
count3b = 0;
nnn = 1;
clust = 1; (*Assigning some variables*)
splinefunctionarray = Array[0 &, Length[pic2]];
(*Sets an array full of 0's with the length of the data, or the number of ROIs*)
fitdataarray = Array[{} &, Length[pic2]]; (*2D data points,
is an array where the data values for each roi are present.  There
  number of "sets" of data in this variable = the number of ROIs?*)
check = Array[{} &, Length[pic2]]; (*This is probably
 not necessary b/c it's updated late*)


findcuts[sf_, n_] := Module[{ti, tf, length, sol, times}, {{ti, tf}} = sf["Domain"];
   length = NIntegrate[Norm@D[sf[t], t], {t, ti, tf}];
   {{sol}, {times}} = Reap@NDSolve[{r'[t] == Sqrt[sf'[t].sf'[t]], r[0] == 0,
       WhenEvent[Evaluate[Mod[r[t], length / n]], Sow[t]]}, r, {t, ti, tf}];
   sf@# & /@ times];


Do[
  clusters = pic2[[nnn]];
  numclusters = Length[clusters]; (*Would be 1 in our case*)
  check[[nnn]] = Array[0 &, numclusters];
  (*A zero array with a dimention of 1. I don't think
   I need the variable check because it is redefined later???? *)
  splinefunctionarray[[nnn]] = Array[0 &, numclusters];
  fitdataarray[[nnn]] = Array[0 &, numclusters];
  decimation = 1000;

  (*Do statement is looking to make sure there is data in the file and if there is,
  then it can perform the following operations,
  such as setting the spline to the data.  We need to set the spline
   partially because we do not know where the ROI files start/finish,
  and also so we can have the same number of points in each slice*)
  Do[
   If[clusters[[clust]] ≠ {},
     (*If there is data stored in the variable clusters aka if it is not empty*)
     splinefunctionarray[[nnn]][[clust]] = BSplineFunction[clusters[[clust]],
       SplineClosed → True]; (*If there is data, then create a spline function
      based on the data in clusterss and close it (they aren't closed by default,
       and the close makes the first and last points connect smoothly*)
     fitdataarray[[nnn]][[clust]] = findcuts[
```

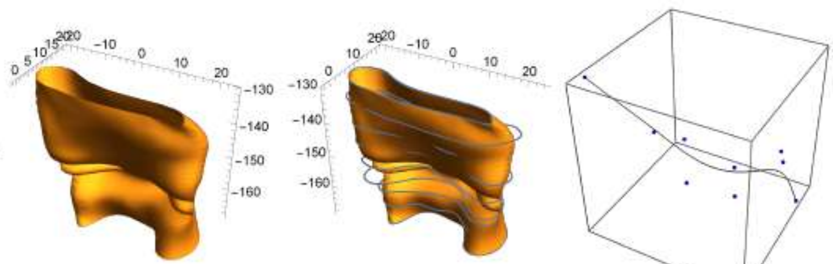
```
  splinefunctionarray[[nnn]][[clust]], decimation];
elimarray = Array[{} &, Length[fitdataarray[[nnn]][[clust]]]];
(*This separates out all of the empty arrays within the dataset*)
len = 1;
cnt = 2;
found = False;
elimarray[[1]] = fitdataarray[[nnn]][[clust]][[1]]; (*This is noting that the
 first position of the sorted array equals the original spline function data??*)
max = RankedMax[Table[EuclideanDistance[fitdataarray[[nnn]][[clust]][[k]],
     fitdataarray[[nnn]][[clust]][[k + 1]]],
    {k, 1, Length[fitdataarray[[nnn]][[clust]]] - 1}], 1];

While[len < Length[fitdataarray[[nnn]][[clust]]] - 1,
 val = len + 1;
 While[found == False,
  If[EuclideanDistance[fitdataarray[[nnn]][[clust]][[len]],
      fitdataarray[[nnn]][[clust]][[val]]] ≥ max,
    elimarray[[cnt]] = fitdataarray[[nnn]][[clust]][[val]];
    cnt++;
    len = val;
    If[val == Length[fitdataarray[[nnn]][[clust]]],
     len = Length[fitdataarray[[nnn]][[clust]]]];
    found = True;,
    val++;
    If[val ≥ Length[fitdataarray[[nnn]][[clust]]],
     len = Length[fitdataarray[[nnn]][[clust]]];
     found = True;];
   ];
 ];
 found = False;
];

(*Start deleting empty slices that did not have ROIs associated with them,
and calculate centroids for the ROI slices*)
splinefunctionarray[[nnn]][[clust]] = BSplineFunction[DeleteCases[elimarray, _{},
   1], SplineClosed → True]; (*Deletes things that don't match the pattern ???*)
centroid = Sum[splinefunctionarray[[nnn]][[clust]][j],
   {j, 1 / decimation, 1, 1 / decimation}] / decimation;
check[[nnn]][[clust]] = centroid;
rotatearry = Array[0 &, decimation + 1];
fitdataarray[[nnn]][[clust]] = Table[
  splinefunctionarray[[nnn]][[clust]][(z - 1) / decimation], {z, 1, decimation}];
maxval = {}; (*Table with x, y values ????*)


(*Basically taking every point and subtracting the centroid from it,
and then normalizing those values.  Then multiply by a vector that
  corresponds to the y-axis.  The point that is closest to one becomes
  the starting point.  Then the array is reordered in "posarray".  This
  is so that all of the starting points can correspond for each slice.*)
Do[rotatearry[[(z + 1 / decimation) * decimation]] =
```

```
      Normalize[splinefunctionarray[[nnn]][[clust]][z] - centroid].{0, -1}, {z,
      0, 1, 1/decimation}];
    maxval = Select[rotatearry, # ≥ (1 - 10 * 1/decimation) &];

    If[maxval == {},
     Do[rotatearry[[(z + 1/decimation) * decimation]] =
       Normalize[splinefunctionarray[[nnn]][[clust]][z] - centroid].{0, 1}, {z,
       0, 1, 1/decimation}];
     maxval = Select[rotatearry, # ≥ (1 - 10 * 1/decimation) &];];
    posarray = Table[Flatten[Position[rotatearry, maxval[[rt]]]][[1]] /
       (Length[rotatearry] - 1), {rt, 1, Length[maxval]}];
    pos = Flatten[Position[Table[splinefunctionarray[[nnn]][[clust]][
          posarray[[rt]]][[2]], {rt, 1, Length[posarray]}],
       RankedMin[Table[splinefunctionarray[[nnn]][[clust]][posarray[[rt]]][[2]],
         {rt, 1, Length[posarray]}], 1]]];

    If[Length[pos] > 1, pos = {pos[[Round[Length[pos] / 2]]]}];
    fitdataarray[[nnn]][[clust]] = RotateLeft[
      fitdataarray[[nnn]][[clust]], Flatten[posarray[[pos]] * decimation - 1]];

    If[Sum[(Normalize[fitdataarray[[nnn]][[clust]][[k]] - centroid])[[1]],
       {k, 1, Round[Length[fitdataarray[[nnn]][[clust]]] / 3]}] < 0,
     fitdataarray[[nnn]][[clust]] = Reverse[RotateLeft[
        fitdataarray[[nnn]][[clust]], 1]]];
    splinefunctionarray[[nnn]][[clust]] = BSplineFunction[
      fitdataarray[[nnn]][[clust]], SplineClosed → True];
    test = Table[fitdataarray[[nnn]][[clust]][[k]] - centroid,
       {k, 1, Length[fitdataarray[[nnn]][[clust]]]}]
      If[nnn ≠ nnncurrent, Print["Processed Frame #: ", nnn];
       nnncurrent = nnn;];
     ];
   , {clust, 1, numclusters}];
  , {nnn, 1, Length[pic2]}];
mmm = 1; nnn = 1; jjj = 1;
numclusters = Length[pic2[[1]]];
count2b = 1; count3b = 1;
splinedata1 = Array[{} &, {Length[pic2], numclusters}];

For[nnn = 1, nnn ≤ Length[splinefunctionarray], nnn++,
  count3b = 1;
  mmm = 1;

  If[Not[IntegerQ[Total[splinefunctionarray[[nnn]]]]],

   For[mmm = 1, mmm ≤ numclusters, mmm++,

    If[Not[IntegerQ[splinefunctionarray[[nnn, mmm]]]],
      splinedata1[[count2b, count3b]] = Table[Append[splinefunctionarray[[nnn, mmm]][
            tttt], slicezcoord[[slice[[nnn]]]]].{{1, 0, 0}, {0, 1, 0}, {0, 0, 1}} +
```

```
        {centerfirst[[1]], centerfirst[[2]], 0}, {tttt, 0, 1, 1/decimation}];
      count3b++;, count3b++];];];
  count2b++];
splinedata2 = Array[{} &, {Length[pic2], numclusters}];
obscountarray = Array[{} &, numclusters];

Do[
  framescount = 1;
  obscountarray[[obs]] = 0;

  Do[If[DeleteCases[splinedata1[[frames, obs]], _{}, 2] ≠ {},
    splinedata2[[framescount, obs]] = DeleteCases[splinedata1[[frames, obs]], _{}, 2];
    framescount++;
    obscountarray[[obs]] = framescount - 1;]
   , {frames, 1, Length[splinedata1]}]
  , {obs, 1, Length[splinedata1[[1]]]}];
splinedata3 = Array[{} &, {numclusters}];

Do[splinedata3[[inc2]] = DeleteCases[splinedata2[[All, inc2]], _{}, 1];,
 {inc2, 1, numclusters}]
deletedups2 = DeleteCases[splinedata3, _{}, 1];
splinedata2 = deletedups2;
centroidarray = Array[{0, 0, 0} &, {Length[splinedata2[[1]]]}];

Do[
  Clear[splinesum];
  If[NumberQ[splinedata2[[1, j, 1, 1]]], splinesum = Mean[splinedata2[[1, j]]]];
  If[NumberQ[splinesum[[1]]], centroidarray[[j]][[1]] = splinesum[[1]]];
  If[NumberQ[splinesum[[2]]], centroidarray[[j]][[2]] = splinesum[[2]]];
  If[NumberQ[splinesum[[3]]], centroidarray[[j]][[3]] = splinesum[[3]]];
  , {j, 1, Length[splinedata2[[1]]]}];
Share[];
Print["Generating 3D Geometry..."];
splinesurfacefunction = Array[{} &, Length[splinedata2]];
rr = 1;

While[rr ≤ Length[splinedata2], splinesurfacefunction[[rr]] =
   BSplineFunction[splinedata2[[rr]], SplineDegree → Automatic, SplineClosed → False];
  rr++];
rr = 1;
pointplot = ListPointPlot3D[Flatten[splinedata2, 2], BoxRatios → 1];
Grid[{{surfaceplot = ParametricPlot3D[
     Table[splinesurfacefunction[[rr]][u, v], {rr, 1, Length[splinedata2]}],
     {u, 0, 1}, {v, 0, 1}, Mesh → None, PlotRange → All, Boxed → False, AspectRatio → 1],
   Show[surfaceplot, pointplot],
   Graphics3D[
    {BSplineCurve[centroidarray[[All]], SplineDegree → 100, SplineKnots → "Clamped"],
     Blue, Point[centroidarray[[All]]]}, AspectRatio → Automatic, BoxRatios → 1]}}]
Share[];
```

```
Processed Frame #: 2
Processed Frame #: 3
Processed Frame #: 4
Processed Frame #: 5
Processed Frame #: 6
Processed Frame #: 7
Processed Frame #: 8
Processed Frame #: 9
Generating 3D Geometry...
```

Out[ ]=



In[ ]:=

```
(******************************************************************************
 Then RUN CODE
 HERE*********************************************************************************
  *****************)


(*This part of the code allows for manipulation of the 3D surface
 within the context of the parent MRIs.  It is doing this through the
 manipulate function which allows you to slide through MRI slices*)
thumbpic = Array[0 &, numberoffiles];
(*An array of 0's as long as the total number of images for the patient*)
geo = True;
Print["Generating 3D Reconstruction..."];
(*This for statement says go from 1 to the number of images,
and go up in increments of one.  Begin filling array that had 0's with
 an an array that matches the ImageData, from each imported .dcm file*)
For[q = 1, q ≤ numberoffiles , q++,
  thumbpic[[q]] = ImageData[
    ColorConvert[Thumbnail[ImageAdjust[Import[picfiles[[q]], "Image"]]], "RGB"]]];
Print["Finished. Rendering Image..."];
Share[]; (*Share minimizes the memory used to store all expressions*)


Manipulate[If[geo, Show[Graphics3D[{Glow[White], Texture[thumbpic], EdgeForm[None],
     (*This sets details for the actual MRI images as they will show here*)
     (*The Polygon function allows you to define a polygon based on
```

```
  an ordered list of vertices in the x y and z directions*)
 Dynamic[{Polygon[{{slicex, 0 + centerfirst[[2]], 0 + slicezcoord[[1]]},
     {slicex, voxeldimy + centerfirst[[2]], 0 + slicezcoord[[1]]},
     {slicex, voxeldimy + centerfirst[[2]], slicezcoord[[Length[slicezcoord]]]},
     {slicex, 0 + centerfirst[[2]], slicezcoord[[Length[slicezcoord]]]}}, (*These
     are defining the vertices of the polygon for slices in the x direction*)
    VertexTextureCoordinates → {{slicex / voxeldimx - centerfirst[[1]] / voxeldimx,
       0, 0}, {slicex / voxeldimx - centerfirst[[1]] / voxeldimx, -1, 0},
      {slicex / voxeldimx - centerfirst[[1]] / voxeldimx, -1, 1},
      {slicex / voxeldimx - centerfirst[[1]] / voxeldimx, 0, 1}}],

   (*Defining vertices in the y direction *)
   Polygon[{{0 + centerfirst[[1]], slicey, 0 + slicezcoord[[1]]},
     {0 + centerfirst[[1]], slicey, slicezcoord[[Length[slicezcoord]]]},
     {voxeldimx + centerfirst[[1]], slicey, slicezcoord[[Length[slicezcoord]]]},
     {voxeldimx + centerfirst[[1]], slicey, 0 + slicezcoord[[1]]}},
    VertexTextureCoordinates → {{0, -slicey / voxeldimy + centerfirst[[2]] / voxeldimy,
       0}, {0, -slicey / voxeldimy + centerfirst[[2]] / voxeldimy, 1},
      {1, -slicey / voxeldimy + centerfirst[[2]] / voxeldimy, 1},
      {1, -slicey / voxeldimy + centerfirst[[2]] / voxeldimy, 0}}],

   (*Defining vertices in the z direction *)
   Polygon[{{0 + centerfirst[[1]], 0 + centerfirst[[2]], slicez},
     {voxeldimx + centerfirst[[1]], 0 + centerfirst[[2]], slicez},
     {voxeldimx + centerfirst[[1]], voxeldimy + centerfirst[[2]], slicez},
     {0 + centerfirst[[1]], voxeldimy + centerfirst[[2]], slicez}},
    VertexTextureCoordinates → {{0, 0, slicez / -zdistance - slicezcoord[[1]] /
         -zdistance}, {1, 0, slicez / -zdistance - slicezcoord[[1]] / -zdistance},
      {1, -1, slicez / -zdistance - slicezcoord[[1]] / -zdistance},
      {0, -1, slicez / -zdistance - slicezcoord[[1]] / -zdistance}}]}]},
 Background → Black, RotationAction → "Clip"], surfaceplot],


Graphics3D[{Glow[White], Texture[thumbpic], EdgeForm[None],
 Dynamic[{Polygon[{{slicex, 0 + centerfirst[[2]], 0 + slicezcoord[[1]]},
     {slicex, voxeldimy + centerfirst[[2]], 0 + slicezcoord[[1]]},
     {slicex, voxeldimy + centerfirst[[2]], slicezcoord[[Length[slicezcoord]]]},
     {slicex, 0 + centerfirst[[2]], slicezcoord[[Length[slicezcoord]]]}},
    VertexTextureCoordinates → {{slicex / voxeldimx - centerfirst[[1]] / voxeldimx, 0, 0},
      {slicex / voxeldimx - centerfirst[[1]] / voxeldimx, -1, 0},
      {slicex / voxeldimx - centerfirst[[1]] / voxeldimx, -1, 1},
      {slicex / voxeldimx - centerfirst[[1]] / voxeldimx, 0, 1}}],

   Polygon[{{0 + centerfirst[[1]], slicey, 0 + slicezcoord[[1]]},
     {0 + centerfirst[[1]], slicey, slicezcoord[[Length[slicezcoord]]]},
     {voxeldimx + centerfirst[[1]], slicey, slicezcoord[[Length[slicezcoord]]]},
     {voxeldimx + centerfirst[[1]], slicey, 0 + slicezcoord[[1]]}},
    VertexTextureCoordinates → {{0, -slicey / voxeldimy + centerfirst[[2]] / voxeldimy,
       0}, {0, -slicey / voxeldimy + centerfirst[[2]] / voxeldimy, 1},
```

```
{1, -slicey / voxeldimy + centerfirst[[2]] / voxeldimy, 1},
{1, -slicey / voxeldimy + centerfirst[[2]] / voxeldimy, 0}}],


Polygon[{{0 + centerfirst[[1]], 0 + centerfirst[[2]], slicez},
  {voxeldimx + centerfirst[[1]], 0 + centerfirst[[2]], slicez},
  {voxeldimx + centerfirst[[1]], voxeldimy + centerfirst[[2]], slicez},
  {0 + centerfirst[[1]], voxeldimy + centerfirst[[2]], slicez}},
 VertexTextureCoordinates -> {{0, 0, slicez / -zdistance - slicezcoord[[1]] /
      -zdistance}, {1, 0, slicez / -zdistance - slicezcoord[[1]] / -zdistance},
   {1, -1, slicez / -zdistance - slicezcoord[[1]] / -zdistance},
   {0, -1, slicez / -zdistance - slicezcoord[[1]] / -zdistance}}]}]},
Background -> Black, RotationAction -> "Clip"]], {{slicex,
0.5 * voxeldimx +
 centerfirst[[1]], "depth"},
0.01 * voxeldimx + centerfirst[[1]],
.99 * voxeldimx +
 centerfirst[[1]]},
{{slicey, 0.5 * voxeldimy + centerfirst[[2]],
  "thickness"},
0.01 * voxeldimy + centerfirst[[2]],
.99 * voxeldimy +
 centerfirst[[2]]},
{{slicez, 0.5 * slicezcoord[[Round[Length[slicezcoord]]]], "height"}, slicezcoord[[1]],
 slicezcoord[[Length[slicezcoord]]]}, {{geo, True, "Geometry"}, {True, False}}]
Share[];(*Share minimizes the memory used to store all expressions*)
Generating 3D Reconstruction...
Finished. Rendering Image...
```

```
In[ ]:= PositionofData = Position[CoordinateData, "47_KO_NP"];
CoordinateInformation = CoordinateData[[PositionofData[[1, 1]], ;;]];

risx = CoordinateInformation[[5]];
risy = CoordinateInformation[[6]];
risz = CoordinateInformation[[7]];
rightischial = {risx} ~ Join ~ {risy} ~ Join ~ {risz}

lisx = CoordinateInformation[[8]];
lisy = CoordinateInformation[[9]];
lisz = CoordinateInformation[[10]];
leftischial = {lisx} ~ Join ~ {lisy} ~ Join ~ {lisz}

dpplx = CoordinateInformation[[11]];
dpply = CoordinateInformation[[12]];
dpplz = CoordinateInformation[[13]];
distpostpubptleft = {dpplx} ~ Join ~ {dpply} ~ Join ~ {dpplz}

ppplx = CoordinateInformation[[14]];
ppply = CoordinateInformation[[15]];
ppplz = CoordinateInformation[[16]];
proxpostpubptleft = {ppplx} ~ Join ~ {ppply} ~ Join ~ {ppplz}

dpprx = CoordinateInformation[[17]];
dppry = CoordinateInformation[[18]];
dpprz = CoordinateInformation[[19]];
distpostpubptright = {dpprx} ~ Join ~ {dppry} ~ Join ~ {dpprz}

ppprx = CoordinateInformation[[20]];
pppry = CoordinateInformation[[21]];
ppprz = CoordinateInformation[[22]];
proxpostpubptright = {ppprx} ~ Join ~ {pppry} ~ Join ~ {ppprz}

Out[ ]= {-47.74, 44.79, -130.68}

Out[ ]= {61.15, 46.85, -116.28}

Out[ ]= {22.21, -53.58, -154.99}

Out[ ]= {22.21, -3.97, -172.13}

Out[ ]= {3.01, -52.85, -156.71}

Out[ ]= {3.01, -4.56, -174.67}

In[ ]:=

(*(*INSERT DATA POINTS BELOW*)
(*Data points that help define coordinate
 system.  These have to be manually put in every time.*)
rightischial={-34.72,57.86,4.24};
leftischial={75.62,58.22,7.24};
```

```
distpostpubptleft={11.31,-37.88,-25.09};
proxpostpubptleft={11.31,-4.09,-41.51};
distpostpubptright={27.72,-37.21,-23.97};
proxpostpubptright={27.72,-5.06,-41.37}; *)
(****************************************************************************
                                          Then RUN CODE
                                          HERE*************************************
                          ****************************************************
 *******)

(*Defining the axis*)
proxpostpubpt = (proxpostpubptleft + proxpostpubptright) / 2;
(* Determining the midpoint of the proximal pubic bone*)
distpostpubpt = (distpostpubptleft + distpostpubptright) / 2;
(*Determining the midpoint of the distal pubic bone*)
Needs["VectorAnalysis`"]
origin = (leftischial + rightischial) / 2;
Print["Origin is:  ", origin];(*This is calculating the origin of the
 coordinate system.  The midpoint between the left and right ischal spines*)
pubicbonept = (proxpostpubpt - distpostpubpt) * .333333333 + distpostpubpt;
(*go about 1/3 the distance from the most distal point.  This is somewhat arbitrary,
but there is some literature to support the fact that
 muscle attachments seem to be most present at this marker*)
midlataxis = (rightischial - origin) / Norm[((rightischial - origin))];
(*unit vector for medial/lateral axis*)
antpostline = (pubicbonept - origin) / Norm[((pubicbonept - origin))];
(*unit vector for anterior/posterior line???????*)
proxdistaxis = (CrossProduct[midlataxis, antpostline]);
antpostaxis = (CrossProduct[proxdistaxis, midlataxis]);
rotationm = Orthogonalize[{midlataxis, antpostaxis, proxdistaxis}];
Print["Rotation Matrix is {midlat,antpost,proxdist}: ", rotationm // MatrixForm];
eulers = EulerAngles[rotationm] * 180 / Pi;
Print["Euler Angles in Degrees (z-y-z) or (proxdist-antpost-proxdist):  ", eulers];
(*Must create empty arrays that are the same
 length as the array created with the MRI centroidal data*)
centroidsnewcoord = Array[{} &, Length[centroidarray]];
(*empty array with a length of ??? for the patient coordinate conversion*)
centroidsnormcoord = Array[{} &, Length[centroidarray]];
(*empty array with a length of ?? for the normalized coordinate conversion*)


(*These Do statements fill the arrays with
 patient coordinates and normalized coordinates *)
Do[centroidsnewcoord[[kk]] = rotationm.(centroidarray[[kk]] - origin);,
  {kk, 1, Length[centroidarray]}];
Do[centroidsnormcoord[[kk]] = {{-1 / Norm[rightischial - origin], 0, 0},
      {0, -1 / Norm[pubicbonept - origin], 0}, {0, 0, 1 / Norm[pubicbonept - origin]}}.
     centroidsnewcoord[[kk]];, {kk, 1, Length[centroidarray]}];
zvaltofit = Select[centroidsnewcoord[[All, 3]], # ≥ 0 &];
centtofit = Array[{} &, Length[zvaltofit]];
```

```
count3 = 1;

numberofcentroids = Length[centroidsnewcoord];
halfvagina = numberofcentroids / 2;

centtofit = centroidsnewcoord[[1 ;; Round[halfvagina]]];

(*Do[If[centroidsnewcoord[[num,3]]≥0,centtofit[[count3]]=centroidsnewcoord[[num]];
   count3++],{num,1,Length[centroidsnewcoord]}];*)
totalcent = Sum[centtofit[[inc]], {inc, 1, Length[centtofit]}] / Length[centtofit];
xpest = FindFit[
   Table[centtofit[[i]][[1]], {i, 1, Length[centtofit]}], totalcent[[1]] + t xp, {xp}, t];
ypest = FindFit[Table[centtofit[[i]][[2]], {i, 1, Length[centtofit]}],
   totalcent[[2]] + t yp, {yp}, t];
zpest = FindFit[Table[centtofit[[i]][[3]], {i, 1, Length[centtofit]}],
   totalcent[[3]] + t zp, {zp}, t];
parallelvect = {xpest[[1]][[2]], ypest[[1]][[2]], zpest[[1]][[2]]};
bestfitline[t_] = totalcent + t * parallelvect;
zvaltofit2 = Select[centroidsnewcoord[[All, 3]], # ≤ 0 &];
centtofit2 = Array[{} &, Length[zvaltofit2]];
count3 = 1;
(*Do[If[centroidsnewcoord[[num,3]]≤0,centtofit2[[count3]]=centroidsnewcoord[[num]];
   count3++],{num,1,Length[centroidsnewcoord]}];*)
centtofit2 = centroidsnewcoord[[Round[halfvagina] ;; numberofcentroids]];
totalcent2 = Sum[centtofit2[[inc]], {inc, 1, Length[centtofit2]}] / Length[centtofit2];
xpest2 = FindFit[Table[centtofit2[[i]][[1]], {i, 1, Length[centtofit2]}],
   totalcent2[[1]] + t xp, {xp}, t];
ypest2 = FindFit[Table[centtofit2[[i]][[2]], {i, 1, Length[centtofit2]}],
   totalcent2[[2]] + t yp, {yp}, t];
zpest2 = FindFit[Table[centtofit2[[i]][[3]], {i, 1, Length[centtofit2]}],
   totalcent2[[3]] + t zp, {zp}, t];
parallelvect2 = {xpest2[[1]][[2]], ypest2[[1]][[2]], zpest2[[1]][[2]]};
bestfitline2[t_] = totalcent2 + t * parallelvect2;
p1 = ListPointPlot3D[centtofit, PlotStyle → {Green, PointSize[Large]}];
p2 = ListPointPlot3D[centtofit2, PlotStyle → {Green, PointSize[Large]}];
p3 = ParametricPlot3D[{bestfitline[t], bestfitline2[t]}, {t, -50, 50}];
intersection = Mean[centroidsnewcoord];

Show[Graphics3D[{(*{Thickness[.03],Pink,Line[centroidsnewcoord]},*)
   {PointSize[Large], Red, Point[intersection]},
   {Thick, Dashed, Yellow, {Arrowheads[Large], Arrow[{{0, 0, 0}, {60, 0, 0}}],
     Arrow[{{0, 0, 0}, {0, 60, 0}}], Arrow[{{0, 0, 0}, {0, 0, 60}}]}}},
  Background → Black, RotationAction → "Clip"], p1, p2, p3]


elevation = -ArcCos[Normalize[parallelvect].{0, 1, 0}] * 180 / Pi;
deviation = 90 - (ArcCos[Normalize[parallelvect].{1, 0, 0}]) * 180 / Pi;
elevation2 = 180 - ArcCos[Normalize[parallelvect2].{0, 1, 0}] * 180 / Pi;
deviation2 = 90 - (ArcCos[Normalize[parallelvect2].{1, 0, 0}]) * 180 / Pi;
(*Rounding values for vaginal with respect to coordinate axes*)
intersectionfinal = Round[intersection, .001];
```

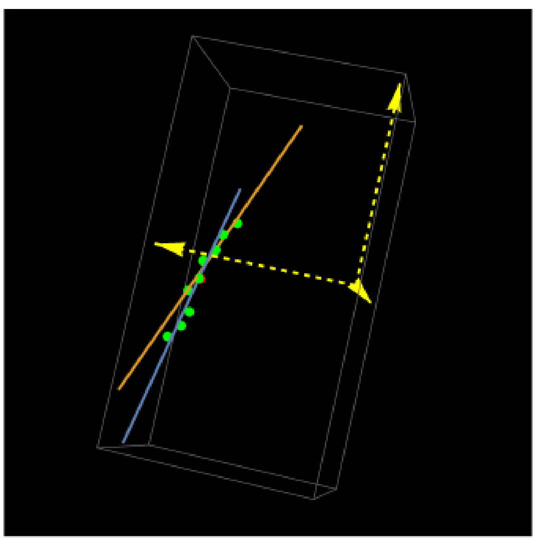
```
Print["vaginal position in mm (midlat, antpost, proxdist):  ", intersectionfinal];
elevation2final = Round[elevation2, .1];
Print[
  "elevation of upper vagina from negative antpost axis (degrees): ", elevation2final];
deviation2final = Round[deviation2, .1];
Print[
  "elevation of upper vagina from postive proxdist axis (degrees): ", deviation2final];
elevationfinal = Round[elevation, .1];
Print[
  "elevation of lower vagina from negative antpost axis (degrees): ", elevationfinal];
deviationfinal = Round[deviation, .1];
Print[
  "elevation of lower vagina from postive proxdist axis (degrees): ", deviationfinal];
changeelevation = Round[elevation2 - elevation, .1];
Print["Angle between upper and lower vagina in saggital plane: ", changeelevation];
changedeviation = Round[deviation2 - deviation, .1];
Print[
  "Angle between upper and lower vagina in coronal plane: (negative = angle towards
    the right of patient, postitive = angle towards
    the left patient):  ", changedeviation];
```

```
Origin is:  {6.705, 45.82, -123.48}
```

Rotation Matrix is {midlat,antpost,proxdist}: $\begin{pmatrix} -0.991195 & -0.0187516 & -0.131079 \\ 0.0723549 & -0.905764 & -0.417559 \\ -0.110897 & -0.423367 & 0.899145 \end{pmatrix}$

```
Euler Angles in Degrees (z-y-z) or (proxdist-antpost-proxdist):  {-107.428, 25.954, -75.3217}
```

Out[ ]=



```
vaginal position in mm (midlat, antpost, proxdist):  {6.966, 46.132, -6.927}

elevation of upper vagina from negative antpost axis (degrees): 68.7

elevation of upper vagina from postive proxdist axis (degrees): 4.9

elevation of lower vagina from negative antpost axis (degrees): -102.8

elevation of lower vagina from postive proxdist axis (degrees): -2.3

Angle between upper and lower vagina in saggital plane: 171.5

Angle between upper and lower vagina in coronal plane: (negative = angle
   towards the right of patient, postitive = angle towards the left patient):  7.2
```

```
In[ ]:= (*Joining data strings together to prepare for export to excel:   intersectionfinal,
elevation2final, deviation2final, elevationfinal,
deviationfinal, changeelevation, changedeviation*)
Z = {elevation2final}~Join~{deviation2final}~Join~{elevationfinal}~
   Join~{deviationfinal}~Join~{changeelevation}~Join~{changedeviation};
Y = origin~Join~Z;
X =  Y~Join~intersectionfinal;
W = X~Join~eulers;


(*Exporting Centroidal Data*)
If[StringCount[filename, "Vagina"] == 1,
  Export[StringJoin[ToString[directory2], {PatientNum, "vaginacentrodialdata.xls"}],
   {"MRI coordinates (mm)" → centroidarray, "Patient coordinates (mm)" →
     centroidsnewcoord, "normalized patient coordinates" -> centroidsnormcoord}]];
If[StringCount[filename, "Vagina"] != 1,
  Export[StringJoin[ToString[directory2], {PatientNum, "vaginacentrodialdata.xls"}],
   {"MRI coordinates (mm)" → centroidarray, "Patient coordinates (mm)" →
     centroidsnewcoord, "normalized patient coordinates" -> centroidsnormcoord}]];

(*Exporting elevation and deviation data*)
If[StringCount[filename, "Vagina"] == 1,
  Export[StringJoin[ToString[directory2], {PatientNum, "angleoutputs.xls"}],
   {"angleoutputs" → W}]];
If[StringCount[filename, "Vagina"] != 1,
  Export[StringJoin[ToString[directory2], {PatientNum, "angleoutputs.xls"}],
   {"angleoutputs"  → W}]];

(*Portion of code for average geometry of geometries*)
vagnewcoordpts = Table[{}, {u, 0, 1, .01}, {v, 0, 1, .01}];
vagnormalcoordpts = Table[{}, {u, 0, 1, .01}, {v, 0, 1, .01}];


Do[Do[vagnewcoordpts[[u * 100 + 1, v * 100 + 1]] = {midlataxis, antpostaxis, proxdistaxis}.
      (splinesurfacefunction[[rr]][u, v] - origin);, {v, 0, 1, .01}], {u, 0, 1, .01}];

Do[Do[vagnormalcoordpts[[u, v]] = {{-1 / Norm[leftischial - origin], 0, 0},
       {0, -1 / Norm[pubicbonept - origin], 0}, {0, 0, 1 / Norm[pubicbonept - origin]}}.
     vagnewcoordpts[[u, v]];, {u, 1, 101}], {v, 1, 101}];
```

```
(*Exporting normalized vaginal Data*)
If[StringCount[filename, "Vagina"] == 1,
  Export[StringJoin[ToString[directory2], {PatientNum, "vaginanormalizeddata.xls"}],
   {"MRI coordinates (mm)" → vagnewcoordpts,
    "Patient coordinates (mm)" → vagnormalcoordpts}]];

If[StringCount[filename, "Vagina"] != 1,
  Export[StringJoin[ToString[directory2], {PatientNum, "vaginanormalizeddata.xls"}],
   {"MRI coordinates (mm)" → vagnewcoordpts,
    "Patient coordinates (mm)" → vagnormalcoordpts}]];

(*Export vagina as a .vtk file*)
Export[StringJoin[ToString[directory2], {PatientNum, "surfaceplot.vtk"}], surfaceplot]
"/Users/deannachristinemac/Desktop/p3surfaceplot.vtk"

MessageDialog["3 excel files, and one .vtk files of HAVE BEEN
    EXPORTED TO your folder.  PLEASE CHECK EXPORT FOLDER TO CONFIRM."];
```

```
Out[•]= /Users/deannasinex/Google Drive/Translational Biomechanics Laboratory/Dissertation/Aim
  2 3d coord system/MyDatabaseVagCoordSystemoutputs9_26_18/47_KOsurfaceplot.vtk

Out[•]= /Users/deannachristinemac/Desktop/p3surfaceplot.vtk
```

Appendix A.1.1 Example of Excel file setup that works with the code

	Excel Row1, Column B	*Excel Row2, Column C*	*Excel Row3, Column D*	*Excel Row 4, Column E*	**Right Ischial**	**Right Ischial**	**Right Ischial**
Excel Row 2, Column A	**Label**	**Observer**	**Patient**	**Trial**	**X**	**Y**	**Z**
Excel Row 3, Column A	Patient1_vagina	Deanna	1000	1	-76.43	52.58	-38.2
Excel Row 2, Column A	Patient1_vagina	Deanna	1000	2	-77.31	52.3	-38.2
Excel Row 3, Column A	Patient1_vagina	John	1000	1	-76.43	52.58	-38.2

Left Ischial	Left Ischial	Left Ischial	distpostpubptleft	distpostpubptleft	distpostpubptleft	proxpostpubptleft
X	Y	Z	X	Y	Z	X
34.76	55.58	-47.2	-29.15	-46.87	-72.91	-29.15
35.25	56.38	-47.2	-31.89	-46.06	-74.41	-31.89
34.76	55.58	-44.6	-29.15	-46.87	-72.91	-29.15

proxpostpubptleft	proxpostpubptleft	distpostpubptright	distpostpubptright	distpostpubptright
Y	Z	X	Y	Z
-16.01	-91.89	-9.23	-45.73	-72.91
-7.35	-90.86	-8.84	-45.15	-74.64
-16.01	-91.89	-9.23	-45.73	-72.91

proxpostpubptright	proxpostpubptright	proxpostpubptright
X	Y	Z
-9.23	-6.89	-91
-8.84	-6.44	-90.18
-9.23	-6.89	-91

Appendix B Materials for Health Literacy Intervention

Appendix B.1 Lesson Plan

	FEMALE PELVIC ANATOMY
Big Idea	The idea of "Structure = Function" is an important concept in anatomy. It can be applied to female pelvic floor organs and their support (connective tissue and muscles). When that structure is comprised, the function is compromised. Students should be able to relate the structure of organs and musculature in the female pelvic floor to its function. They should then be able to apply this knowledge to various case studies/scenarios of compromised structure or compromised function.
Learning Goals	Students will: • Learn about the structure, location, and function of female pelvic organs • Recognize major components of internal and external genital organs • Explore various scenarios with compromised anatomy • Be exposed to challenges in diagnosing and understanding pelvic floor disorders

Objectives	Students will be able to: • Identify and label the names female pelvic organs/genitals based on relative location and structure • Match organ/genital names with their respective functions • Identify risk factors for pelvic floor disorders • Identify pelvic floor disorders (i.e. urinary/fecal incontinence, prolapse) based on described scenarios, or predict how compromised pelvic support can affect function • Explain challenges with assessing and diagnosing pelvic floor disorders
Materials	ALL GROUPS • Computer w/internet access for pre- and post-assessments • Note taking guides LECTURE (individual, teacher centered) • In-class worksheet 3D MODEL (group interaction, student centered) • 3d printed organs (1 set per 3-4 students) • 3D model activity worksheet
Model Group Procedure	**PRE-TEST** **EXPLORE:** Students will complete the first two parts of the activity and study guide on their own in groups of 3-4. They will each be given a model to complete this. After they put the model together, they must sketch and label a picture. The teacher will check that the model is correct, if it is, they may continue on. They may use the internet and their textbook to help them with the rest of part 1.

	DISCUSS & EXPLAIN: Discuss part 1 and part 2 of the activity as a class. Then the teacher will go over what compromised anatomy looks like etc. Students will explore sample models and try to predict what is different about the anatomy. **POST-TEST**
Non-Model Group Procedure	**PRE-TEST** **EXPLAIN** Teacher lectures through Pelvic Floor Anatomy and Function. **ENGAGE**: Teachers review **EXPLAIN**: Teacher goes over compromised anatomy **POST-TEST**

****Test (10 minutes) was administered between 2-4 weeks after the intervention to assess retention****

Appendix B.1.1 Participant Permission Slip

October 4, 2018

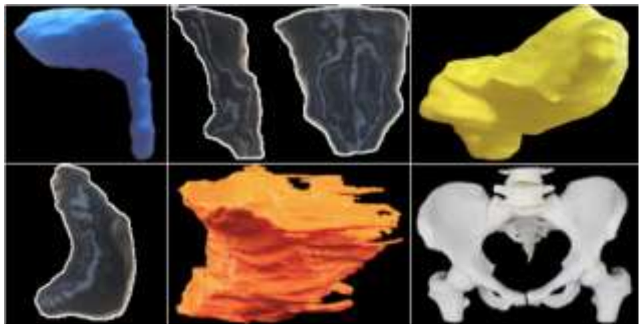
Dear Parent/Guardian,

My name is Deanna Easley, and I am a Ph.D. graduate student researcher from the University of Pittsburgh. My research focuses on understanding effective ways of helping high school students comprehend and retain information about the basic structure and function of female pelvic anatomy. This letter provides background for the study, learning objectives, and the specific procedures that will take place.

Background:

Previous research studies and current social media groups have demonstrated that adult men and women have significant gaps in comprehending and retaining information about female pelvic anatomy and function. This gap in knowledge may seem insignificant, however, over 50% of women experience some level of pelvic floor dysfunction (i.e., incontinence, prolapse) during their lifetime, and much of the stigma that surrounds these pelvic floor disorders is rooted in the gap in knowledge that developed decades prior. Interestingly, research reports that 1/3 of adults in the US received their education regarding female pelvic anatomy during high school. Therefore, we propose a study to investigate the ability for high school students to comprehend and retain information pertaining to female pelvic anatomy when exposed to either lecture or 3D pelvic models (examples shown below), to determine if there are cost-effective and retention- effective ways to expose students to female anatomy.

We believe this research is impactful by addressing the stigma associated with understanding and discussing female pelvic health, helps educate the general public (i.e., future generations) about female pelvic health and concerns, all while highlighting the importance of female pelvic health research.



Examples of 3D printed organs that will be studied

Learning Objectives:

- Identify and label the names of female pelvic organs/genitals based on relative location and structure
- Match organ names with their respective functions
- Identify risk factors for pelvic floor disorders
- Identify pelvic floor disorders based on described scenarios and predict how compromised pelvic support can affect function
- Explain challenges with assessing and diagnosing pelvic floor disorders

Research Procedures:

- Students will be assigned a 4-digit code by their teacher that will be used to match pre- and post-assessment responses
- Students will take a pre-assessment to gage their baseline knowledge regarding female pelvic anatomy. They will be asked to provide demographic information such as gender and GPA in order to help us conduct statistical tests based on characterization of the general population.

- Students will be randomly broken into 2 groups:
  - Lecture Only group
  - 3D Pelvic Model Group
- Students will be taught using one of the 2 teaching styles shown above for 45 minutes -1 hour
- Students will be given a post-assessment following all activities to gage comprehension of material
- Two weeks later, students will be given another post assessment to gage the retention of the material
- The researchers will observe class sessions but will not record information about individual students
- Results from all assessments will be provided to the researchers for comparisons between groups
- Results from this research may also be shared with others researchers conducting similar or related research studies, however, because no identifying information is collected, all results will continue to remain anonymous and untraceable to the students.

No identifying information (i.e. name, birthday, etc.) will be collected and used for research purposes. There are no payments/compensations provided for participation in this research study.

Your child's participation is completely voluntary, and they can discontinue participation at any time. There are no foreseeable risks associated with this research study. **Individual student responses are confidential.** All research results published from this study will be done without student/school identifiers. Questions regarding the research study can be answered by Ms. Deanna Easley via email at [redacted]

PERMISSION SLIP: Please return to your classroom teacher by **MM DD, YYYY**

I, ________________________________ give my child __________________________

permission to participate in this research study.

I, _________________________________DO NOT give my child_______________________ Permission to participate in this research study.

Date___________________

Appendix B.1.2 Introductory Script

Researchers from the Bioengineering Department in the Swanson School of Engineering (University of Pittsburgh) are conducting a research study to investigate the use of various teaching techniques to understand female pelvic health in high school classrooms. In this study, the following will be done:

- You will be assigned a 4-digit code by your instructor that will be used to match pre- and post-assessment responses
- You will take a pre-assessment to gage your baseline knowledge regarding female pelvic anatomy.
- You will be asked to provide demographic information such as gender and GPA.
- You will randomly be broken into 2 groups:
    - Lecture Only Group
    - 3D Pelvic Model Group
- You will be taught using one of the 2 teaching styles for 45 minutes to an 1 hour

- You will be given a post-assessment following all activities to gage comprehension of the material
- Two weeks later, you will be given another post assessment to gage your retention of the material
- Researchers will observe class sessions, but will not record information about you as individuals
- Results from all assessments will be provided to the researchers for comparisons between groups
- Results from this research may also be shared with others conducting similar research, however, because no identifying information is collected, all results will continue to remain anonymous and untraceable to you.

Again, no identifying information (i.e., name, birthday, etc.) will be collected and used for research purposes. If you do not want your assessment or other results data to be used as a part of this research study, let your instructor know so that your results can be excluded from research data. Your participation is completely voluntary, and if you choose to participate, you may discontinue at any time. There are no foreseeable risks associated with this research study. All research results published from this study will be done without student/school identifiers. Questions regarding the research study can be directed to your teacher or classroom instructor, who will then contact researchers to make sure your questions are addressed.

Appendix B.1.3 Breakdown of Intervention

The table below provides an overview of the number of classrooms attended, which schools were visited, who was the instructor, and which intervention method was used. Letters and numbers are used to protect the identity of schools and participants within the study.

Table 22 Layout of Intervention location, instructor, and method

Class	Where	Who Taught	Which intervention
1	A	1 & 3	Models
2	B	1& 3	Lecture
3	B	3	Lecture
4	B	3	Models
5	B	3	Models
6	B	1	Models
7	A	1	Models
8	A	4	Lecture
9	B	2	Models
10	C	1	Lecture
11	C	2	Models

Appendix B.1.4 Pre-Evaluation

This sub appendix contains a generic version of the questionnaires provided to students through Qualtrics. While the order of question items and verbiage is the same, the format presented here does not directly resemble that of the Qualtrics survey.

1. **Please enter the 4-digit student code provided to you by your instructor for this research study**: ___________________________
2. **Please select your grade level**: 9th 10th 11th 12th
3. **Please select your age**: Less than 11 | 11 12 13 14 15 16 17 18 19 | Greater than 19

4. **Please enter your unweighted GPA on a 4.0 scale (example: 3.4): _____________**

5. **Are you Hispanic or Latino?** Yes No Prefer not to answer

6. **Please indicate your race by selecting one or more categories (mark all that apply):**

   American Indian/Alaska Native || Asian || Native Hawaiian/Pacific Islander Black/African American || Other || Prefer not to Answer

7. **Gender:** Male Female Other Prefer not to answer

8. **Is English your first language?** Yes No

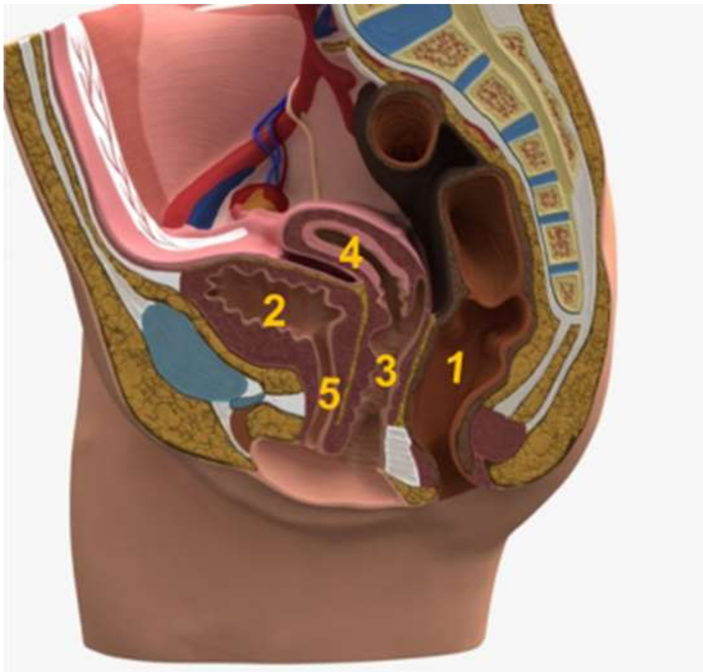
9. **Describe anything that you already know about female pelvic anatomy:**

   ____

   ____

   ____

   Use the following picture to answer the next question.



10. Label each organ with the appropriate corresponding number:

Uterus_____Urethra_____Rectum_____Vagina______Bladder

11. Match each organ with its function (drag and drop items to match descriptions):

Uterus	Provides passage for menstrual flow, and a child during childbirth; Receives the penis during intercourse
Rectum	Carries urine out of the body
Fallopian Tubes	Acts as temporary storage of feces before it is expelled from the body
Vagina	Stores urine
Urethra	Fertilized egg implants into the walls and nurtures maturing fetus
Bladder	Where eggs are created
Cervix	How eggs are transported
Levator Ani Muscles	Provides support to pelvic organs
Ovaries	Connects the vagina and uterus, and plays a role during pregnancy and delivery

12. **Which of these DOES NOT describe a pelvic floor disorder? (Check all that apply):**

    a. A disorder that develops from weakening of support in the pelvic floor that causes the pelvic organs to abnormally descend into the vaginal canal

    b. A disorder that can cause involuntary urinary or fecal leakage

    c. A disease caused by a virus that is characterized by chronic pain in the abdominal and pelvic regions of the body

d. A disorder that can cause the fallopian tubes to be twisted due to the development of a cyst on the ovaries

13. What is the MOST prevalent (predominant) risk factor for the development of Pelvic Organ Prolapse (POP) (i.e., which risk factor is most associated with POP)?

a. Parity (the number of children a woman has had)

b. Age

c. Neurological and connective tissue disorders

d. Obesity

14. A patient visits her doctor complaining of a bulge in her vagina, and trouble defecating (i.e., pooping). What could she be suffering from?

a. Rectocele (prolapse of rectum)

b. Cystocele (prolapse of bladder)

c. Vaginal prolapse

d. She is about to give birth to a child

15. Why can it be challenging to diagnose and assess pelvic floor disorders?

____

____

____

16. Do you think that it is important for YOU to understand female pelvic anatomy? Why or why not?

____

____

____

17. **What are your general thoughts and feelings about discussing female pelvic anatomy and health (i.e., fun, interesting, gross, uncomfortable, unnecessary, etc.)?**

____

____

____

18. **Can men experience pelvic floor disorders?**
    a. Yes
    b. No

Appendix B.1.5 Direct Assessment Rubrics

The following table illustrates the rubric used to score direct assessment open-ended questions within the evaluation survey.

QUESTION	SCORE	DETAILS
Describe what you already know about female pelvic anatomy:	0	no answer, N/A nothing written; or if they just don't answer the question
	1	vague, but claims knowledge (i.e. I know organs, I know bones, etc.)
	2	1 correct fact
	3	2 or more correct facts (organs, functions, etc.)
	0	idk, no answer, totally unrelated

Why can it be challenging to diagnose and assess pelvic floor disorders?	1	incorrect, but attempted answer (because it has many symptoms, vague answer (i.e. there could be many other disorders like it)
	2	1 or more correct facts (lack of info, education, embarrassment, lots of risk factors, etc., overlap of symptoms, difficult to visualize/see what's happening w/o MRI)
Explain how obesity could be a contributing factor to developing pelvic floor disorders:	0	no answer; inappropriate answer
	1	vague, but tried, or incorrect
	2	partially correct (part of a correct answer, but not quite getting to point, or 1 correct fact/1 incorrect fact)
	3	correct (i.e., compression/loads/weight/pressure on pelvic organs/muscles
Describe one fact that you learned, that surprised you, or that you were unaware of prior to this exercise.	0	no answer; inappropriate answer
	1	attempted, but did not list actual fact
	2	listed fact, but incorrect or too vague
	3	listed fact and correct

Bibliography

[1] S. M. Hartigan and A. L. Smith, “Disparities in Female Pelvic Floor Disorders,” pp. 1–6, 2018.

[2] J. Chao and T. C. Chai, “The Future of Research in Female Pelvic Medicine,” *Curr. Urol. Rep.*, vol. 16, no. 2, 2015.

[3] K. Kenton and E. R. Mueller, “The global burden of female pelvic floor disorders,” *BJU Int.*, vol. 98, no. s1, pp. 1–5, 2006.

[4] Y. Peng, B. D. Miller, T. B. Boone, and Y. Zhang, “Modern Theories of Pelvic Floor Support: A Topical Review of Modern Studies on Structural and Functional Pelvic Floor Support from Medical Imaging, Computational Modeling, and Electromyographic Perspectives,” *Curr. Urol. Rep.*, vol. 19, no. 1, 2018.

[5] S. D. Abramowitch, A. Feola, Z. Jallah, and P. A. Moalli, “Tissue mechanics, animal models, and pelvic organ prolapse: A review,” *Eur. J. Obstet. Gynecol. Reprod. Biol.*, vol. 144, no. SUPPL 1, pp. S146-158, 2009.

[6] J. O. L. Umek, Wolfgang H.; Morgan, Daniel M.; Ashton-Miller, James A.; DeLancey, “Quantitative Analysis of Uterosacral Ligament Origin and Insertion Points by Magnetic Resonance Imaging,” *Obs. Gynecol*, vol. 103, no. 3, pp. 447–451, 2004.

[7] D. Borello-France *et al.*, “Fecal and Urinary Incontinence in Primiparous Women,” *Obstet. Gynecol.*, vol. 108, no. 4, pp. 863–872, 2006.

[8] K. L. Burgio *et al.*, “Risk factors for fecal and urinary incontinence after childbirth: The childbirth and pelvic symptoms study,” *Am. J. Gastroenterol.*, vol. 102, no. 9, pp. 1998–2004, 2007.

[9] P. D. U.S. Census Bureau, “Annual Estimates of the Resident Population for Selected Age Groups by Sex for the United States, States, Counties, and Puerto Rico Commonwealth and Municipios: April 1, 2010 to July 1, 2014,” 2015.

[10] A. Baah-Dwomoh, J. McGuire, T. Tan, and R. De Vita, “Mechanical properties of female reproductive organs and supporting connective tissues: A review of the current state of knowledge,” *Appl. Mech. Rev.*, vol. 68, no. 6, 2016.

[11] J. M. Wu, C. a Matthews, M. M. Conover, V. Pate, and M. Jonsson Funk, “Lifetime risk of stress urinary incontinence or pelvic organ prolapse surgery,” *Obstet. Gynecol.*, vol. 123, no. 6, pp. 1201–6, 2014.

[12] H. P. Drutz and M. Alarab, “Pelvic organ prolapse: Demographics and future growth prospects,” *Int. Urogynecol. J.*, vol. 17, no. SUPPL. 7, pp. S6–S9, 2006.

[13] M. A. T. Bortolini, H. P. Drutz, D. Lovatsis, and M. Alarab, “Vaginal delivery and pelvic floor dysfunction: Current evidence and implications for future research,” *Int. Urogynecol. J.*, vol. 21, no. 8, pp. 1025–1030, 2010.

[14] P. A. Moalli, S. Jones Ivy, L. A. Meyn, and H. M. Zyczynski, “Risk factors associated with pelvic floor disorders in women undergoing surgical repair,” *Obstet. Gynecol.*, vol. 101, no. 5, pp. 869–874, 2003.

[15] a L. Olsen, V. J. Smith, J. O. Bergstrom, J. C. Colling, and a L. Clark, “Epidemiology of surgically managed pelvic organ prolapsed and urinary incontinence,” *Obs. Gynecol*, vol. 89, no. 97, pp. 501–506, 1997.

[16] C. Ghetti, J. L. Lowder, R. Ellison, M. A. Krohn, and P. Moalli, “Depressive symptoms in women seeking surgery for pelvic organ prolapse,” *Int. Urogynecol. J.*, vol. 21, no. 7, pp. 855–860, 2010.

[17] J. L. Lowder, C. Ghetti, P. Moalli, H. Zyczynski, and T. F. Cash, “Body image in women before and after reconstructive surgery for pelvic organ prolapse,” *Int. Urogynecol. J.*, vol. 21, no. 8, pp. 919–925, 2010.

[18] G. C. Dunivan, S. B. Cichowski, Y. M. Komesu, P. S. Fairchild, J. T. Anger, and R. G. Rogers, “Ethnicity and variations of pelvic organ prolapse bother,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 25, no. 1, pp. 53–59, 2014.

[19] C. L. Mandimika *et al.*, “Knowledge of pelvic floor disorders in a population of community-dwelling women,” *Am. J. Obstet. Gynecol.*, vol. 210, no. 2, pp. 1–9, 2014.

[20] I. Nygaard, C. Turvey, T. L. Burns, E. Crischilles, and R. Wallace, “Urinary incontinence and depression in middle-aged United States women,” *Obstet. Gynecol.*, vol. 101, no. 1, pp. 149–156, 2003.

[21] R. Beck, “Pelvic relaxational prolapse,” in *Principles and practice of clinical gynecology*, N. Kase and A. Weingold, Eds. New York: John Wiley & Sons, 1983, pp. 677–85.

[22] S. Li, M. Ji, and Z. Zhao, “The effectiveness of two different laparoscopic surgeries for apical support of pelvic organ prolapse,” *Eur. J. Obstet. Gynecol. Reprod. Biol.*, vol. 188, no. May 2013, pp. 74–78, 2015.

[23] D. Mazloomdoost, L. B. Westermann, C. C. Crisp, S. H. Oakley, S. D. Kleeman, and R. N. Pauls, “Primary care providers’ attitudes, knowledge, and practice patterns regarding pelvic floor disorders,” *Int. Urogynecol. J.*, vol. 28, no. 3, pp. 447–453, 2017.

[24] R. A. Leonardo, *History of gynecology*. Froben Press, 1944.

[25] R. Porter, *The Greatest Benefit to Mankind: A Medical History of Humanity*, vol. 75, no. 2. New York: W.W. Norton & Company, Inc., 1997.

[26] K. T. Downing, "Uterine Prolapse: From Antiquity to Today," *Obstet. Gynecol. Int.*, vol. 2012, pp. 1–9, 2012.

[27] W. J. S. McKay, *The History ofAncient Gynaecology*. London, UK: Balliere, Tindal and Cox, 1901.

[28] C.P.Bryan, *Ancient Egyptian medicine : The Papyrus Ebers*. Chicago, Ill, USA: Ares Publishers, 1974.

[29] J. V. Ricci, *The Genealogy of Gynaecology: History of the Development ofGynaecology Throughout the Ages, 2000 B. C.- 1800 A. D.* 1950.

[30] C. C. Nezhat, F. Nezhat, and C. C. Nezhat, "Endometriosis: Ancient disease, ancient treatments," *Fertil. Steril.*, vol. 98, no. 6 SUPPL., 2012.

[31] "Leviticus 15," in *The Holy Bible, King James Version*, Cambridge., 1769.

[32] T. Bahrampour, "The hidden medical epidemic few women have been willing to talk about, until now - The Washington Post," *The Washington Post*, 2015. [Online]. Available: https://www.washingtonpost.com/local/social-issues/a-hidden-epidemic-millions-of-women-suffer-pelvic-floor-disorders-silently/2015/12/22/f5997966-a6d5-11e5-b53d-972e2751f433_story.html?noredirect=on&utm_term=.7b07f4052f47.

[33] J. D. Enderle, S. M. Blanchard, and J. D. Bronzino, *Introduction to Biomedical Engineering*, Second edi., vol. Academic P. Elsevier Academic Press, 2005.

[34] C. J. Brim, *Medicine in the Bible*. New York: Froben Preti, 1936.

[35] T. A. Wue, *Commentary on the Hindu System of Medicine*. Calcutta, 1845.

[36] "The Qur'an, Al-Baqarah 2:222." .

[37] C. K. Wieslander *et al.*, "Misconceptions and Miscommunication among Women with Pelvic Organ Prolapse," *Int Urogynecol J*, vol. 33, no. 2, pp. 557–573, 2016.

[38] T. Ravenel, A. Erpelding, and L. R. Pathak, "Listening to " Felt Needs ": Investigating Genital Prolapse in Western Nepal Linked references are available on JSTOR for this article : Listening to " Felt Needs ": Investigating Genital Prolapse in Western Nepal," vol. 12, no. 23, pp. 166–175, 2018.

[39] G. Nonjinge, "Talking Openly About Menstruation Remains A Major Taboo." The Huffington Post, 2017.

[40] J. Gettleman, "Where a Taboo Is Leading to the Deaths of Young Girls - The New York Times," *The New York Times*, 2018. [Online]. Available: https://www.nytimes.com/2018/06/19/world/asia/nepal-women-menstruation-period.html.

[41] M. Zelaya and I. Bickis, "Nepalese women suffer stigma and pain of fallen wombs | Magally Zelaya and Ian Bickis | Global development | The Guardian," *The Guardian*, 2014. [Online]. Available: https://www.theguardian.com/global-development/2014/may/07/nepalese-women-stigma-fallen-wombs-prolapsed-uterus. [Accessed: 01-Aug-2018].

[42] "Abstinence Curriculum in Black Churches: A Critical Examination of the Intersectionality of Race, Gender, and SES," 2009.

[43] V. Millner, M. Mulekar, and J. Turrens, "Parents' Beliefs Regarding Sex Education for Their Children in Southern Alabama Public Schools," *Sex. Res. Soc. Policy*, vol. 12, no. 2, pp. 101–109, 2015.

[44] R. L. Roudsari, M. Javadnoori, M. Hasanpour, M. M. Hazavehei, and A. Taghipour, "Socio-cultural challenges to sexual health education for female adolescents in Iran," vol. 11, no. 2, pp. 101–110, 2013.

[45] "CULTURE-Oscar-winning documentary spotlights stigma of women's periods in India," *Business Insights: Global.*, 2019. [Online]. Available: https://bi.gale.com/global/article/GALE%7CA579232188?u=upitt_main&sid=summon.

[46] E. F.-L. Gabriella, "Women's Pollution Periods in Tamilnad (India)," *Anthropos*, vol. 69, no. 1/2, pp. 113–161, 1974.

[47] S. J. Parish *et al.*, "Female Sexual Health: Barriers to Optimal Outcomes and a Roadmap for Improved Patient–Clinician Communications," *J. Women's Heal.*, vol. 00, no. 00, pp. 1–12, 2019.

[48] Y. Benyamini, T. Blumstein, V. Boyko, and L. Lerner-Geva, "Cultural and Educational Disparities in the Use of Primary and Preventive Health Care Services Among Midlife Women in Israel," *Women's Heal. Issues*, vol. 18, no. 4, pp. 257–266, 2008.

[49] D. Zhang, Y. Bi, J. E. Maddock, and S. Li, "Sexual and Reproductive Health Knowledge Among Female College Students.pdf," pp. 118–126, 2010.

[50] F. F. Denny, "What People Don't Tell You About Childbirth: The Realities of Vaginal Tearing," *Bazar*, Jul-2018.

[51] I. Milsom and M. Gyhagen, "Breaking news in the prediction of pelvic floor disorders," *Best Pract. Res. Clin. Obstet. Gynaecol.*, pp. 1–8, 2018.

[52] F. A. Maton, Kenneth I.; Pollard, Shauna A.; McDougall Weise, Tatiana V.; Hrabowski III, "Meyerhoff Scholars Program: A Strengths-Based, Institution-Wide Approach to Increasing Diversity in Science, Technology, Engineering, and Mathematics," *Mt. Sinai J. Med.*, vol. 79, pp. 610–623, 2012.

[53] J. B. Slaughter, Y. Tao, and W. Pearson, Eds., *Changing the Face of Engineering: The African American Experience*. Baltimore, MD: Johns Hopkins University Press, 2015.

[54] C. Verniers and J. Vala, "Justifying gender discrimination in the workplace: The mediating role of motherhood myths," *PLoS One*, vol. 13, no. 1, 2018.

[55] "Crash Dummies Impacted by Additive," *Automotive Design and Production*, 2018.

[56] A. Linder, K. Holmqvist, and M. Y. Svensson, "Average male and female virtual dummy model (BioRID and EvaRID) simulations with two seat concepts in the Euro NCAP low severity rear impact test configuration," *Accid. Anal. Prev.*, vol. 114, no. June 2017, pp. 62–70, 2018.

[57] J. Östh, M. Mendoza-Vazquez, F. Sato, M. Y. Svensson, A. Linder, and K. Brolin, "A female head–neck model for rear impact simulations," *J. Biomech.*, vol. 51, pp. 49–56, 2017.

[58] M. V. Seeman, "Does Gender Influence Outcome in Schizophrenia?," *Psychiatr. Q.*, pp. 173–184, 2018.

[59] A. S. Mihailidou and A. W. Ashton, "Cardiac effects of aldosterone: Does gender matter?," *Steroids*, vol. 91, pp. 32–37, 2014.

[60] L. Schellen, M. G. L. C. Loomans, M. H. de Wit, B. W. Olesen, and W. D. va. M. Lichtenbelt, "The influence of local effects on thermal sensation under non-uniform environmental conditions - Gender differences in thermophysiology, thermal comfort and productivity during convective and radiant cooling," *Physiol. Behav.*, vol. 107, no. 2, pp. 252–261, 2012.

[61] B. Kingma and W. Van Marken Lichtenbelt, "Energy consumption in buildings and female thermal demand," *Nat. Clim. Chang.*, vol. 5, no. 12, pp. 1054–1056, 2015.

[62] J. K. Maykot, R. F. Rupp, and E. Ghisi, "A field study about gender and thermal comfort temperatures in office buildings," *Energy Build.*, vol. 178, pp. 254–264, 2018.

[63] R. Bleier, *Science and gender : a critique of biology and its theories on women*. New York: Peramon Press, 1984.

[64] S. V. Rosser, *Biology & Feminism: A Dynamic Interaction*. New York: Twayne Publishers, 1992.

[65] H. H. Kay and C. E. Spritzer, "Magnetic Resonance Imaging in Gynecology," in *The Global Library of Women's Medicine*, 2008.

[66] Y. C. Fung, *Biomechanics Mechanical Properties of Living Tissues,* 2nd ed. New York: Springer, 1993.

[67] D. C. Easley, S. D. Abramowitch, and P. A. Moalli, "Female pelvic floor biomechanics: Bridging the gap," *Curr. Opin. Urol.*, vol. 27, no. 3, 2017.

[68] D. Elad and S. Abramowitch, "Reproductive biomechanics: Innovations and challenges," *J. Biomech.*, vol. 48, no. 9, pp. 1509–1510, 2015.

[69] J. A. Ashton-Miller and J. O. L. DeLancey, "On the Biomechanics of Vaginal Birth and Common Sequelae," *Annu. Rev. Biomed. Eng.*, vol. 11, no. 1, pp. 163–176, 2009.

[70] Z. C. Jallah, "The Role of Vaginal Smooth Muscle in the Pathogenesis of Pelvic Organ Prolapse," University of Pittsburgh, 2014.

[71] T. M. Chandler, L. S. Machan, P. L. Cooperberg, A. C. Harris, and S. D. Chang, "Müllerian duct anomalies: From diagnosis to intervention," *Br. J. Radiol.*, vol. 82, no. 984, pp. 1034–1042, 2009.

[72] L. Wünsch and J. M. Schober, "Imaging and examination strategies of normal male and female sex development and anatomy," *Best Pract. Res. Clin. Endocrinol. Metab.*, vol. 21, no. 3, pp. 367–379, 2007.

[73] C. W. Colvin and H. Abdullatif, "Anatomy of Female Puberty : The Clinical Relevance of Developmental Changes in the Reproductive System," *Clin. Anat.*, vol. 129, no. 1, pp. 115–129, 2013.

[74] F. D. Cox and K. Demmitt, *Human Intimacy: Marriage, the Family, and Its Meaning*. Cengage Learning, 2013.

[75] A. Papadimitriou, "The Evolution of the Age at Menarche from Prehistorical to Modern Times," *J. Pediatr. Adolesc. Gynecol.*, vol. 29, no. 6, pp. 527–530, 2016.

[76] D. L. D. . N. E. D. . S. E. J. . I.-G. G. . C. G. P. . Cutler, "Variability in hormone concentrations and self-reported menstrual histories in young adolescents: Menarche as an integral part of a developmental process," *J. Youth Adolesc.*, vol. 28, no. 3, pp. 283–304, 1999.

[77] L. Steinberg, *Adolescence*, 8th ed. New York, NY: McGraw-Hill, 2008.

[78] *Women's Gynecologic Health*. Jones & Bartlett Publishers, 2011.

[79] B. B, "Adolescence in evolutionary perspective," *Acta Paediatr*, p. 406:29, 1994.

[80] S. M. Eickmeyer, "Anatomy and Physiology of the Pelvic Floor," *Phys. Med. Rehabil. Clin. N. Am.*, vol. 28, no. 3, pp. 455–460, 2017.

[81] M. Schimpf and P. Tulikangas, "Evolution of the female pelvis and relationships to pelvic organ prolapse," *Int. Urogynecol. J.*, vol. 16, no. 4, pp. 315–320, 2005.

[82] A. Schultz, “Birth, obstetrics and human evolution,” vol. 109, no. November, pp. 1199–1206, 2002.

[83] R. G. Rogers, *Female Pelvic Medicine and Reconstructive Surgery Clinical Practice & Surgical Atlas*, 1st ed. McGraw Hill Education Medical, 2013.

[84] M. Hoyte, Lennox; Damaser, Ed., *Bioemechanics of the Female Pelvic Floor*, 1st ed. Elsevier, 2016.

[85] H. O. Elftman, “THE EVOLUTION O F THE PELVIC FLOOR O F Man , standing habitually erect , would be in constant danger of derangements of the viscera lodged in the pelvis were it not for the presence of an adequate support of bone , muscle , and fascia . This pelvic floor ,” vol. 51, no. 2.

[86] B. Alicioglu, O. Kartal, H. Gurbuz, and N. Sut, “Symphysis pubis distance in adults: A retrospective computed tomography study,” *Surg. Radiol. Anat.*, vol. 30, no. 2, pp. 153–157, 2008.

[87] J. O. L. Chen, Luyun; Ashton-Miller, James A.; Hsu, Yvonne; DeLancey, “Interaction between Apical Supports and Levator Ani in Anterior Vaginal Support: Theoretical Analysis,” *Obs. Gynecol*, vol. 108, no. 2, pp. 324–332, 2009.

[88] C. A. Kent, “Preventing Maternal Injury During Childbirth.” pp. 1–8, 1989.

[89] L. Betti, “Human Variation in Pelvic Shape and the Effects of Climate and Past Population History,” *Anat. Rec.*, vol. 300, no. 4, pp. 687–697, 2017.

[90] K. M. Brown, V. L. Handa, K. J. MacUra, and V. B. Deleon, “Three-dimensional shape differences in the bony pelvis of women with pelvic floor disorders,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 24, no. 3, pp. 431–439, 2013.

[91] S. M. Eickmeyer, “A n a t o m y an d P h y s i o l o g y of the Pelvic Floor,” *Phys. Med. Rehabil. Clin. NA*, vol. 28, no. 3, pp. 455–460, 2018.

[92] S. Herschorn, “Female Pelvic Floor Anatomy: The Pelvic Floor, Supporting Structures, and Pelvic Organs Female Pelvic Floor Anatomy Bony Scaffolding,” *Rev. Urol. Rev. Urol. S3*, vol. 6, no. 5, pp. 2–10, 2004.

[93] P. Messelink, B. , Benson, T. , Berghmans, B. , Bø, K. , Corcos, J. , Fowler, C. , Laycock, J. , Lim, P. H., van Lunsen, R. , Lycklama á Nijeholt, G. , Pemberton, J. , Wang, A. , Watier, A. and Van Kerrebroeck, “Standardization of terminology of pelvic floor muscle function and dysfunction: Report from the pelvic floor clinical assessment group of the International Continence Society,” *Neurourol. Urodyn*, vol. 24, pp. 374–380, 2005.

[94] S. Abramowitch and D. Easley, *Biomechanical Characterization of Native Pelvic Floor Organs and Tissues*. 2016.

[95] R. Kearney, R. Sawhney, and J. O. L. DeLancey, “Levator ani muscle anatomy evaluated by origin-insertion pairs,” *Obstet. Gynecol.*, vol. 104, no. 1, pp. 168–173, 2004.

[96] F. (Federative C. on A. Terminology), “Terminologia Anatomica,” *Int. Anat. Terminol.*, 1998.

[97] K. T. Barnhart, E. S. Pretorius, and D. Malamud, “Lesson learned and dispelled myths: Three-dimensional imaging of the human vagina,” *Fertil. Steril.*, vol. 81, no. 5, pp. 1383–1384, 2004.

[98] K. T. Barnhart, A. Izquierdo, E. S. Pretorius, D. M. Shera, M. Shabbout, and A. Shaunik, “Baseline dimensions of the human vagina,” *Hum. Reprod.*, vol. 21, no. 6, pp. 1618–1622, 2006.

[99] J. Luo, C. Betschart, J. A. Ashton-Miller, and J. O. L. L. DeLancey, “Quantitative analyses of variability in normal vaginal shape and dimension on MR images,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 27, no. 7, pp. 1087–1095, 2016.

[100] R. N. Miftahof and H. G. Nam, *Biomechanics of the Gravid Human Uterus*. 2011.

[101] S. Daftary and S. Chakravarti, *Manual of Obstetrics*. India: Elsevier Reed, 2011.

[102] D. D. Lee, E. S. Siegelman, W. Y. Chua, L. A. Arya, and H. S. Harvie, “Comparison of Vaginal Axis in Women who Have Undergone Hysterectomy Versus Women With an Intact Uterus,” vol. 00, no. 00, pp. 1–5, 2018.

[103] P. A. Moalli *et al.*, “A rat model to study the structural properties of the vagina and its supportive tissues,” *Am. J. Obstet. Gynecol.*, vol. 192, no. 1, pp. 80–88, 2005.

[104] M. H. Kerkhof, L. Hendriks, and H. A. M. Brölmann, “Changes in connective tissue in patients with pelvic organ prolapse—a review of the current literature,” *Int. Urogynecol. J.*, vol. 20, no. 4, pp. 461–474, 2009.

[105] R. Ramanah, M. B. Berger, B. M. Parratte, and J. O. L. De Lancey, “Anatomy and histology of apical support: A literature review concerning cardinal and uterosacral ligaments,” *Int. Urogynecol. J.*, vol. 23, no. 11, pp. 1483–1494, 2012.

[106] N. Ozkaya and M. Nordin, *Fundamentals of Biomechanics Equilibrium, Motion, and Deformation*, 2nd ed. New York: Springer-Verlag, 1999.

[107] M. Marieswaran, I. Jain, B. Garg, V. Sharma, and D. Kalyanasundaram, “A review on biomechanics of anterior cruciate ligament and materials for reconstruction,” *Appl. Bionics Biomech.*, vol. 2018, 2018.

[108] V. L. Handa *et al.*, “Racial Differences in Pelvic Anatomy by Magnetic Resonance Imaging,” *OBs*, vol. 111, no. 4, pp. 914–920, 2008.

[109] P. A. Moalli, S. H. Shand, H. M. Zyczynski, S. C. Gordy, and L. A. Meyn, “Remodeling of vaginal connective tissue in patients with prolapse,” *Obstet. Gynecol.*, vol. 106, no. 5, pp. 953–96, 2006.

[110] Z. Krkeljas, “Changes in gait and posture as factors of dynamic stability during walking in pregnancy,” *Hum. Mov. Sci.*, vol. 58, no. October 2017, pp. 315–320, 2018.

[111] W. Congress, “Reproductive biomechanics : Innovations and challenges,” vol. 48, pp. 1509–1510, 2015.

[112] V. Lucente *et al.*, “Biomechanical paradigm and interpretation of female pelvic floor conditions before a treatment,” *Int. J. Womens. Health*, vol. 9, pp. 521–550, 2017.

[113] C. López-otín, M. A. Blasco, L. Partridge, and M. Serrano, “The Hallmarks of Aging (copy without figures, can’t seem to remove),” vol. 153, no. 6, pp. 1194–1217, 2013.

[114] B. Grubeck-Loebenstein, “What Is Aging?,” *Transfus. Med. Hemotherapy*, vol. 39, no. 5, pp. 299–300, 2012.

[115] D. A. J. M. Schoenaker, C. A. Jackson, J. V. Rowlands, and G. D. Mishra, “Socioeconomic position, lifestyle factors and age at natural menopause: A systematic review and meta-analyses of studies across six continents,” *Int. J. Epidemiol.*, vol. 43, no. 5, pp. 1542–1562, 2014.

[116] M. Alperin, M. Cook, L. J. Tuttle, M. C. Esparza, and R. L. Lieber, “Impact of vaginal parity and aging on the architectural design of pelvic floor muscles,” *Am. J. Obstet. Gynecol.*, vol. 215, no. 3, pp. 312.e1-312.e9, 2016.

[117] D. E. E. Rizk and M. A. Fahim, “Ageing of the female pelvic floor: Towards treatment a la carte of the ‘geripause,’” *Int. Urogynecol. J.*, vol. 19, no. 4, pp. 455–458, 2008.

[118] N. M.V. and M. C.N., “Adaptability of elderly human muscles and tendons to increased loading,” *J. Anat.*, vol. 208, no. 4, pp. 433–443, 2006.

[119] L. de Landsheere *et al.*, “Elastin density: Link between histological and biomechanical properties of vaginal tissue in women with pelvic organ prolapse?,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 27, no. 4, pp. 629–635, 2016.

[120] S. Cowin, *Tissue Mechanics*. Springer Science & Business Media, 2008.

[121] P. A. Moalli *et al.*, “Impact of menopause on collagen subtypes in the arcus tendineous fasciae pelvis,” *Am. J. Obstet. Gynecol.*, vol. 190, no. 3, pp. 620–627, 2004.

[122] I. Sridharan, Y. Ma, T. Kim, W. Kobak, J. Rotmensch, and R. Wang, “Structural and mechanical profiles of native collagen fibers in vaginal wall connective tissues,” *Biomaterials*, vol. 33, no. 5, pp. 1520–1527, 2012.

[123] P. A. Moalli, K. M. Debes, L. A. Meyn, N. S. Howden, and S. D. Abramowitch, "Hormones restore biomechanical properties of the vagina and supportive tissues after surgical menopause in young rats," *Am. J. Obstet. Gynecol.*, vol. 199, no. 2, 2008.

[124] A. L. Clark, O. D. Slayden, K. Hettrich, and R. M. Brenner, "Estrogen increases collagen I and III mRNA expression in the pelvic support tissues of the rhesus macaque," *Am. J. Obstet. Gynecol.*, vol. 192, no. 5 SPEC. ISS., pp. 1523–1529, 2005.

[125] S. S. Faubion *et al.*, "Data Registry on Experiences of Aging, Menopause, and Sexuality (DREAMS): A cohort profile," *Maturitas*, vol. 107, no. September 2017, pp. 44–49, 2018.

[126] J. L. J. Lowder, K. M. K. Debes, D. K. Moon, N. Howden, S. D. Abramowitch, and P. a Moalli, "Biomechanical adaptations of the rat vagina and supportive tissues in pregnancy to accommodate delivery," *Obstet. Gynecol.*, vol. 109, no. 1, pp. 136–43, 2007.

[127] C. E. Turner, J. M. Young, M. J. Solomon, J. Ludlow, and C. Benness, "Incidence and etiology of pelvic floor dysfunction and mode of delivery: An overview," *Dis. Colon Rectum*, vol. 52, no. 6, pp. 1186–1195, 2009.

[128] I. Nygaard, M. Barber, and K. Burgio, "Prevalence of symptomatic pelvic floor disorders in US women," *J. Am. Med. Assoc.*, vol. 300, no. 11, pp. 1311–1316, 2008.

[129] J. E. Jelovsek *et al.*, "Models for predicting recurrence, complications, and health status in women after pelvic organ prolapse surgery," *Obstet. Gynecol.*, vol. 132, no. 2, pp. 298–309, 2018.

[130] M. D. Barber *et al.*, "Comparison of 2 transvaginal surgical approaches and perioperative behavioral therapy for apical vaginal prolapse: The OPTIMAL randomized trial," *JAMA - J. Am. Med. Assoc.*, vol. 311, no. 10, pp. 1023–1034, 2014.

[131] S. Palacios, R. S. Borrego, and A. Forteza, "The importance of preventive health care in post-menopausal women," *Maturitas*, vol. 52, no. SUPPL. 1, 2005.

[132] K. M. Luber, S. Boero, and J. Y. Choe, "The demographics of pelvic floor disorders: Current observations and future projections," *Am. J. Obstet. Gynecol.*, vol. 184, no. 7, pp. 1496–1503, 2001.

[133] C. Rubod, M. Boukerrou, M. Brieu, P. Dubois, and M. Cosson, "Biomechanical Properties of Vaginal Tissue. Part 1: New Experimental Protocol," *J. Urol.*, vol. 178, no. 1, pp. 320–325, 2007.

[134] A. C. Richardson, J. B. Lyon, and N. L. Williams, "A new look at pelvic relaxation," *Am. J. Obstet. Gynecol.*, vol. 126, no. 5, pp. 568–573, Nov. 1976.

[135] L. L. Subak, L. E. Waetjen, S. van den Eeden, D. H. Thom, E. Vittinghoff, and J. S. Brown, "Cost of pelvic organ prolapse surgery in the United States," *Obstet. Gynecol.*, vol. 98, no. 4, pp. 646–51, 2001.

[136] B. M. Zeleke, T. A. Ayele, M. A. Woldetsadik, T. A. Bisetegn, and A. A. Adane, "Depression among women with obstetric fistula, and pelvic organ prolapse in northwest Ethiopia," *BMC Psychiatry*, vol. 13, no. 1, p. 236, 2013.

[137] S. E. Swift, "The distribution of pelvic organ support in a population of female subjects seen for routine gynecologic health care," *Am. J. Obstet. Gynecol.*, vol. 183, pp. 277–285, 2000.

[138] Bradley CS, Zimmerman MB, Qi Y, and N. IE, "Natural history of pelvic organ prolapse in postmenopausal women," *Obs. Gynecol*, vol. 109, no. 4, pp. 848–54, 2007.

[139] H. K. Pannu, J. C. Scatarige, and J. Eng, "MRI diagnosis of pelvic organ prolapse compared with clinical examination," *Acad. Radiol.*, vol. 18, no. 10, pp. 1245–1251, 2011.

[140] C. M. Durnea, A. S. Khashan, L. C. Kenny, U. A. Durnea, M. M. Smyth, and B. A. O'Reilly, "Prevalence, etiology and risk factors of pelvic organ prolapse in premenopausal primiparous women," *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 25, no. 11, pp. 1463–1470, 2014.

[141] A. L. O'Boyle, J. D. O'Boyle, B. Calhoun, and G. D. Davis, "Pelvic organ support in pregnancy and postpartum," *Int. Urogynecol. J.*, vol. 16, no. 1, pp. 69–72, 2005.

[142] J. Mant, R. Painter, and M. Vessey, "Epidemiology of genital prolapse: observations from the Oxford Family Planning Association study," *BJOG An Int. J. Obstet. Gynaecol.*, vol. 104, no. 5, pp. 579–585, 1997.

[143] C. Glazener *et al.*, "Childbirth and prolapse: Long-term associations with the symptoms and objective measurement of pelvic organ prolapse," *BJOG An Int. J. Obstet. Gynaecol.*, vol. 120, no. 2, pp. 161–168, 2013.

[144] T. Wilcox and A. Hirshkowitz, "Obesity and Cardiovascular Disease," *Circulation*, vol. 125, no. 9, pp. 1178–1182, 2012.

[145] L. Elizondo-Montemayor, C. Hernández-Escobar, E. Lara-Torre, B. Nieblas, and M. Gómez-Carmona, "Gynecologic and Obstetric Consequences of Obesity in Adolescent Girls," *J. Pediatr. Adolesc. Gynecol.*, 2016.

[146] et al Ogden C, Carroll M, Kit B, "Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010," *JAMA*, p. 307:483, 2012.

[147] M. Alperin, T. Kaddis, R. Pichika, M. C. Esparza, and R. L. Lieber, "Pregnancy-induced adaptations in intramuscular extracellular matrix of rat pelvic floor muscles," *Am. J. Obstet. Gynecol.*, vol. 215, no. 2, pp. 210.e1-210.e7, 2016.

[148] K. M. Knight, P. A. Moalli, A. Nolfi, S. Palcsey, W. R. Barone, and S. D. Abramowitch, "Impact of parity on ewe vaginal mechanical properties relative to the nonhuman primate and rodent," *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 27, no. 8, pp. 1255–1263, 2016.

[149] S. Swift *et al.*, “Pelvic Organ Support Study (POSST): The distribution, clinical definition, and epidemiologic condition of pelvic organ support defects,” *Am. J. Obstet. Gynecol.*, vol. 192, no. 3, pp. 795–806, 2005.

[150] C. Persu, C. R. Chapple, V. Cauni, S. Gutue, and P. Geavlete, “Pelvic Organ Prolapse Quantification System (POP-Q) - a new era in pelvic prolapse staging.,” *J. Med. Life*, vol. 4, no. 1, pp. 75–81, 2011.

[151] R. C. Bump *et al.*, “The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction.,” *Am. J. Obstet. Gynecol.*, vol. 175, no. 1, pp. 10–17, 1996.

[152] A. C. A. Silva and D. D. T. Maglinte, “Pelvic floor disorders: What’s the best test?,” *Abdom. Imaging*, vol. 38, no. 6, pp. 1391–1408, 2013.

[153] H. P. Dietz, “Pelvic floor ultrasound: a review,” *Am. J. Obstet. Gynecol.*, vol. 202, no. 4, pp. 321–334, 2010.

[154] D. R. Karp, T. V. Peterson, M. Jean-Michel, R. Lefevre, G. W. Davila, and V. C. Aguilar, “‘Eyeball’ POP-Q examination: Shortcut or valid assessment tool?,” *Int. Urogynecol. J.*, vol. 21, no. 8, pp. 1005–1009, 2010.

[155] M. D. Barber, A. R. Lambers, A. G. A. G. Visco, and R. C. Bump, “Effect of patient position on clinical evaluation of pelvic organ prolapse,” *Obstet. Gynecol.*, vol. 96, no. 1, pp. 18–22, 2000.

[156] A. L. O’Boyle, J. D. O’Boyle, R. E. Ricks, T. H. Patience, B. Calhoun, and G. Davis, “The natural history of pelvic organ support in pregnancy,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 14, no. 1, pp. 46–49, 2003.

[157] U. Due, S. Brostrøm, and G. Lose, “Lifestyle advice with or without pelvic floor muscle training for pelvic organ prolapse: a randomized controlled trial,” *Int. Urogynecol. J.*, vol. 27, no. 4, pp. 555–563, 2016.

[158] I. Kuncharapu, B. A. Majeroni, and D. W. Johnson, “Pelvic Organ Prolapse,” *Am. Fam. Physician*, vol. 81, no. 9, pp. 1111–1117, 2010.

[159] B. D. Smith, “Female Pelvic Floor Health: A Developmental Review,” *J WOCN*, vol. 31, no. 3, pp. 5159–61, 2004.

[160] C. Rubod *et al.*, “Biomechanical properties of human pelvic organs,” *Urology*, vol. 79, no. 4, pp. 968.e17-968.e22, 2012.

[161] M. D. Barber and C. Maher, “Epidemiology and outcome assessment of pelvic organ prolapse,” *Int. Urogynecol. J.*, vol. 24, no. 11, pp. 1783–1790, 2013.

[162] J. P. Shepherd, A. J. Feola, S. D. Abramowitch, and P. A. Moalli, “Uniaxial biomechanical properties of seven different vaginally implanted meshes for pelvic organ prolapse,” *Int. Urogynecol. J.*, vol. 23, no. 5, pp. 613–620, 2012.

[163] A. Feola, W. Barone, P. Moalli, and S. Abramowitch, "Characterizing the ex vivo textile and structural properties of synthetic prolapse mesh products," *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 24, no. 4, pp. 559–564, 2013.

[164] M. Boukerrou, L. Boulanger, C. Rubod, E. Lambaudie, P. Dubois, and M. Cosson, "Study of the biomechanical properties of synthetic mesh implanted in vivo," *Eur. J. Obstet. Gynecol. Reprod. Biol.*, vol. 134, no. 2, pp. 262–267, 2007.

[165] A. J. Feola, "Impact of Vaginal Synthetic Prolapse Meshes on the Mechanics of the Host Tissue Response," University of Pittsburgh, 2011.

[166] U. Lee and S. Raz, "Emerging concepts for pelvic organ prolapse surgery: What is cure?," *Curr. Urol. Rep.*, vol. 12, no. 1, pp. 62–67, 2011.

[167] S. Jha, A. Cutner, and P. Moran, "The UK National Prolapse Survey: 10 years on," *Int. Urogynecol. J.*, vol. 29, no. 6, pp. 795–801, 2018.

[168] M. L. A. Schofield, P. Higgs, and J. M. Hawnaur, "MRI findings following laparoscopic sacrocolpopexy," *Clin. Radiol.*, vol. 60, no. 3, pp. 333–339, 2005.

[169] J. . Clemns and E. Al, "Impact of the 2011 FDA transvaginal mesh safety update on AUGS members' use of synthetic mesh and biologic grafts in pelvic reconstructive surgery," *Female Pelvic Med. Reconstr. Surg.*, vol. 19, no. 4, pp. 191–198, 2013.

[170] "FDA public health notification: serious complications associated with transvaginal placement ofsurgical mesh in repair of pelvic organ prolapse and stress urinary incontinence," 2008. [Online]. Available: http://www.fda.gov/medicaldevices/safety/alertsandnotices/publichealthnotific.

[171] "FDA safety communication: UPDATE on serious complications associated with transvaginal place- ment of surgical mesh for pelvic organ prolapse," 2011. .

[172] G. Rostaminia, J. D. Peck, L. H. Quiroz, and S. A. Shobeiri, "Characteristics associated with pelvic organ prolapse in women with significant levator ani muscle deficiency," *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 27, no. 2, pp. 261–267, 2016.

[173] M. Weemhoff, K. L. Shek, and H. P. Dietz, "Effects of age on levator function and morphometry of the levator hiatus in women with pelvic floor disorders," *Int. Urogynecol. J.*, vol. 21, no. 9, pp. 1137–1142, 2010.

[174] D. V Valsky and S. Yagel, "Three-dimensional transperineal ultrasonography of the pelvic floor: improving visualization for new clinical applications and better functional assessment.," *J. ultrasound Med. Off. J. Am. Inst. Ultrasound Med.*, vol. 26, pp. 1373–1387, 2007.

[175] H. P. Dietz, "Translabial ultrasound in the assessment of pelvic floor and anorectal function in women with defecatory disorders," *Tech. Coloproctol.*, vol. 18, no. 5, pp. 481–494, 2014.

[176] I. Becker, M. D. Stringer, R. Jeffery, and S. J. Woodley, “Sonographic anatomy of the pubic symphysis in healthy nulliparous women,” *Clin. Anat.*, vol. 27, no. 7, pp. 1058–1067, 2014.

[177] F. W. Lone, R. Thakar, A. H. Sultan, and A. Stankiewicz, “Accuracy of assessing Pelvic Organ Prolapse Quantification points using dynamic 2D transperineal ultrasound in women with pelvic organ prolapse,” *Int. Urogynecol. J.*, vol. 23, no. 11, pp. 1555–1560, 2012.

[178] H. P. Dietz, B. T. Haylen, and J. Broome, “Ultrasound in the quantification of female pelvic organ prolapse,” *Ultrasound Obstet. Gynecol.*, vol. 18, no. 5, pp. 511–514, 2001.

[179] J. Caudwell-hall, M. Hons, I. K. Atan, R. G. Rojas, S. Langer, and R. N. Rm, “Atraumatic normal vaginal delivery : how many women get what they want ?,” no. October, pp. 1–8, 2018.

[180] K. Svabík, A. Martan, J. Masata, R. El-Haddad, P. Hubka, and M. Pavlikova, “Ultrasound appearances after mesh implantation - Evidence of mesh contraction or folding?,” *Int. Urogynecol. J.*, vol. 22, no. 5, pp. 529–533, 2011.

[181] H. P. Dietz, C. Shek, and B. Clarke, “Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound,” *Ultrasound Obstet. Gynecol.*, vol. 25, no. 6, pp. 580–585, 2005.

[182] H. P. Dietz, “Ultrasound imaging of the pelvic floor. Part I: Two-dimensional aspects,” *Ultrasound Obstet. Gynecol.*, vol. 23, no. 1, pp. 80–92, 2004.

[183] C. D. Alt, K. a Brocker, F. Lenz, C. Sohn, H. U. Kauczor, and P. Hallscheidt, “MRI findings before and after prolapse surgery,” *Acta radiol.*, vol. 55, no. 4, pp. 495–504, 2014.

[184] K. Singh, M. Jakab, W. M. N. Reid, L. A. Berger, and L. Hoyte, “Three-dimensional magnetic resonance imaging assessment of levator ani morphologic features in different grades of prolapse,” *Am. J. Obstet. Gynecol.*, vol. 188, no. 4, pp. 910–915, 2003.

[185] Y. M. Law and J. R. Fielding, “MRI of pelvic floor dysfunction: Self-assessment module,” *Am. J. Roentgenol.*, vol. 191, no. 6 SUPPL., pp. S54–S59, 2008.

[186] R. Farouk El Sayed, “The urogynecological side of pelvic floor MRI: The clinician’s needs and the radiologist’s role,” *Abdom. Imaging*, vol. 38, no. 5, pp. 912–929, 2013.

[187] Y. M. Law and J. R. Fielding, “MRI of pelvic floor dysfunction: Review,” *Am. J. Roentgenol.*, vol. 191, no. 6 SUPPL., pp. S45–S53, 2008.

[188] S. A. Taylor, “Imaging pelvic floor dysfunction,” *Best Pract. Res. Clin. Gastroenterol.*, vol. 23, no. 4, pp. 487–503, 2009.

[189] Y. Peng, R. Khavari, N. A. Nakib, T. B. Boone, and Y. Zhang, “Assessment of urethral support using MRI-derived computational modeling of the female pelvis,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 27, no. 2, pp. 205–212, 2016.

[190] A. Bhattarai and M. Staat, "Modelling of Soft Connective Tissues to Investigate Female Pelvic Floor Dysfunctions," *Comput. Math. Methods Med.*, vol. 2018, 2018.

[191] L. Chen, J. A. Ashton-Miller, and J. O. L. DeLancey, "A 3D finite element model of anterior vaginal wall support to evaluate mechanisms underlying cystocele formation," *J. Biomech.*, vol. 42, no. 10, pp. 1371–1377, 2009.

[192] D. C. Easley, P. G. Menon, S. D. Abramowitch, and P. A. Moalli, "Inter-observer variability of vaginal wall segmentation from MRI: A statistical shape analysis approach," in *ASME International Mechanical Engineering Congress and Exposition, Proceedings (IMECE)*, 2015, vol. 3–2015.

[193] S. Ginath *et al.*, "MRI pelvic landmark angles in the assessment of apical pelvic organ prolapse," *Arch. Gynecol. Obstet.*, vol. 284, no. 2, pp. 365–370, 2011.

[194] A. Yousuf, L. Chen, K. Larson, J. A. Ashton-Miller, and J. O. L. DeLancey, "The length of anterior vaginal wall exposed to external pressure on maximal straining MRI: relationship to urogenital hiatus diameter, and apical and bladder location," *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 25, no. 10, pp. 1349–1356, 2014.

[195] C. Betschart, L. Chen, J. A. Ashton-Miller, and J. O. L. DeLancey, "On pelvic reference lines and the MR evaluation of genital prolapse: A proposal for standardization using the Pelvic inclination correction system," *Int. Urogynecol. J.*, vol. 24, no. 9, pp. 1421–1428, 2013.

[196] L. Chen, R. Ramanah, Y. Hsu, J. A. Ashton-Miller, and J. O. L. Delancey, "Cardinal and deep uterosacral ligament lines of action: MRI based 3D technique development and preliminary findings in normal women," *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 24, no. 1, pp. 37–45, 2013.

[197] J. L. Lowder, S. S. Oliphant, J. P. Shepherd, C. Ghetti, and G. Sutkin, "Genital hiatus size is associated with and predictive of apical vaginal support loss," *Am. J. Obstet. Gynecol.*, vol. 214, no. 6, pp. 718.e1-718.e8, 2016.

[198] M. I. FUNT, J. D. THOMPSON, and H. BIRCH, "Normal Vaginal Axis," *South. Med. J.*, vol. 71, no. 12, pp. 1534–1535, 1978.

[199] R. M. Otto, Lesley N.; Slayden, Ov D.; Clark, Amanda L.; Brenner, "The rhesus macaque as an animal model for pelvic organ prolapse," *Am. J. Obstet. Gynecol.*, vol. 186, no. 3, pp. 416–421, 2002.

[200] S. Parker, *A Short History of Medicine*. New York: Dorling Kindersley Ltd., 2019.

[201] A. Lienemann and T. Fischer, "Functional imaging of the pelvic floor," *Eur. J. Radiol.*, vol. 47, no. 2, pp. 117–122, 2003.

[202] H. K. Walker, "The Origins of the History and Phsyical Examination," 1990.

[203] N. C. Benda, M. L. Meadors, A. Z. Hettinger, and R. M. Ratwani, “Emergency Physician Task Switching Increases with the Introduction of a Commercial Electronic Health Record,” *Ann. Emerg. Med.*, vol. 67, no. 6, pp. 741–746, 2016.

[204] A. Mathioudakis, I. Rousalova, A. A. Gagnat, N. Saad, and G. Hardavella, “How to keep good clinical records,” *Breathe*, vol. 12, no. 4, pp. 371–375, 2016.

[205] Z. Wang, R. Zhu, S. Zhang, Y. Bian, D. Lu, and C. Li, “Differentiating between monozygotic twins through next-generation mitochondrial genome sequencing,” *Anal. Biochem.*, vol. 490, pp. 1–6, 2015.

[206] M. Sanz-Cortes *et al.*, “205: Application of different fetal head circumference normality ranges for the identification of abnormal head growth in Zika infected fetuses in a Colombian Cohort,” *Am. J. Obstet. Gynecol.*, vol. 216, no. 1, p. S131, 2017.

[207] D. A. Morris *et al.*, “Lower limit of normality and clinical relevance of left ventricular early diastolic strain rate for the detection of left ventricular diastolic dysfunction,” *Eur. Heart J. Cardiovasc. Imaging*, vol. 19, no. 8, pp. 905–915, 2018.

[208] G. D. Aquaro *et al.*, “Reference values of cardiac volumes, dimensions, and new functional parameters by MR: A multicenter, multivendor study,” *J. Magn. Reson. Imaging*, vol. 45, no. 4, pp. 1055–1067, 2017.

[209] K. L. Shek, H. G. Krause, V. Wong, J. Goh, and H. P. Dietz, “Is pelvic organ support different between young nulliparous African and Caucasian women?,” *Ultrasound Obstet. Gynecol.*, vol. 47, no. 6, pp. 774–778, 2016.

[210] A. Giri *et al.*, “Genetic determinants of pelvic organ prolapse among African American and Hispanic women in the Women’s Health Initiative,” *PLoS One*, vol. 10, no. 11, pp. 1–19, 2015.

[211] Z. Abdool, H. P. Dietz, and B. G. Lindeque, “Interethnic variation in pelvic floor morphology in women with symptomatic pelvic organ prolapse,” *Int. Urogynecol. J.*, vol. 29, no. 5, pp. 745–750, 2018.

[212] R. Wang, A. Munoz, J. L. Blomquist, and V. L. Handa, “Association of Race with Anal Incontinence in Parous Women,” *Female Pelvic Med. Reconstr. Surg.*, vol. 25, no. 5, 2019.

[213] J. F. Culhane and R. L. Goldenberg, “Racial Disparities in Preterm Birth,” *Semin. Perinatol.*, vol. 35, no. 4, pp. 234–239, 2011.

[214] C. O. F. P. S and G. E. Commission, “Pittsburgh ’ S Inequality Across,” 2019.

[215] Y. Peng, J. He, R. Khavari, T. B. Boone, and Y. Zhang, “Functional mapping of the pelvic floor and sphincter muscles from high-density surface EMG recordings,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 27, no. 11, pp. 1689–1696, 2016.

[216] G. Lamblin *et al.*, “Pathophysiological aspects of cystocele with a 3D finite elements model,” *Arch. Gynecol. Obstet.*, vol. 294, no. 5, pp. 983–989, 2016.

[217] M. S. Cook, L. Bou-Malham, M. C. Esparza, and M. Alperin, “Age-related alterations in female obturator internus muscle,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, 2016.

[218] B. N. Patel, A. Lucioni, and K. C. Kobashi, “Anterior pelvic organ prolapse repair using synthetic mesh,” *Curr. Urol. Rep.*, vol. 13, no. 3, pp. 211–215, 2012.

[219] R. N. Pauls, A. N. Fellner, and G. W. Davila, “Vaginal laxity: A poorly understood quality of life problem; A survey of physician members of the International Urogynecological Association (IUGA),” *Int. Urogynecol. J.*, vol. 23, no. 10, pp. 1435–1448, 2012.

[220] M. L. Kingsberg S., “Vaginal laxity after childbirth: Qualitative survey of women’s perceptions, effect on changes in self-image and sexual relationships,” *J. Sex. Med.*, vol. 7, pp. 127–128, 2010.

[221] S. M. Kari Bo, Bary Berghmans, “Clinical Assessment of Pelvic Organ Prolapse,” in *Evidence-based Physical Therapy for the Pelvic Floor: Bridging Science and Clinical Practice,* S. M. Kari Bø, Kari Bo, Bary Berghmans, Ed. Elsevier Health Sciences, 2007, pp. 109–11.

[222] T. W. Muir, K. J. Stepp, M. D. Barber, and R. Chesson, “Adoption of the pelvic organ prolapse quantification system in peer-reviewed literature,” *Am. J. Obstet. Gynecol.*, vol. 189, no. 6, pp. 1632–1636, 2003.

[223] A. F. Hall *et al.*, “Interobserver and intraobserver reliability of the proposed International Continence Society, Society of Gynecologic Surgeons, and American Urogynecologic Society pelvic organ prolapse classification system,” *Am. J. Obstet. Gynecol.*, vol. 175, no. 6, pp. 1467–1471, 1996.

[224] R. Nardos, A. S. Thurmond, T. R. Worstell, A. L. Clark, and W. T. Gregory, “Reference lines in dynamic magnetic resonance imaging of the pelvic floor,” *Female Pelvic Med. Reconstr. Surg.*, vol. 16, no. 4, pp. 242–5, 2010.

[225] S. R. Broekhuis, J. J. Fütterer, J. O. Barentsz, M. E. Vierhout, and K. B. Kluivers, “A systematic review of clinical studies on dynamic magnetic resonance imaging of pelvic organ prolapse: The use of reference lines and anatomical landmarks,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 20, no. 6, pp. 721–729, 2009.

[226] K. R. Fedorov A., Beichel R., Kalpathy-Cramer J., Finet J., Fillion-Robin J-C., Pujol S., Bauer C., Jennings D., Fennessy F., Sonka M., Buatti J., Aylward S.R., Miller J.V., Pieper S., “3D Slicer as an Image Computing Platform for the Quantitative Imaging Network,” *Magn. Reson. Imaging*, vol. 30, no. 9, pp. 1323–41, 2012.

[227] M. R. Routzong, P. A. Moalli, S. Maiti, R. De Vita, and S. D. Abramowitch, “Novel simulations to determine the impact of superficial perineal structures on vaginal delivery,” *Interface Focus*, vol. 9, no. 4, 2019.

[228] V. L. Handa, J. Roem, J. L. Blomquist, H. P. Dietz, and A. Muñoz, "Pelvic organ prolapse as a function of levator ani avulsion, hiatus size, and strength," *Am. J. Obstet. Gynecol.*, vol. 221, no. 1, pp. 41.e1-41.e7, 2019.

[229] B. Cameron, J. Sabourin, M. S. Sanaee, N. A. Koenig, T. Lee, and R. Geoffrion, "Pelvic floor hypertonicity in women with pelvic floor disorders: A case control and risk prediction study," *Neurourol. Urodyn.*, vol. 38, no. 2, pp. 696–702, 2019.

[230] J. L. Lowder *et al.*, "The role of apical vaginal support in the appearance of anterior and posterior vaginal prolapse," *Obstet. Gynecol.*, vol. 111, no. 1, pp. 152–157, 2008.

[231] O. Mayeur, J. F. Witz, P. Lecomte, M. Brieu, M. Cosson, and K. Miller, "Influence of Geometry and Mechanical Properties on the Accuracy of Patient-Specific Simulation of Women Pelvic Floor," *Ann. Biomed. Eng.*, vol. 44, no. 1, pp. 202–212, 2016.

[232] J. O. L. DeLancey, "Anatomy and Biomechanics of Genital Prolapse," *Clinical obstetrics and gynecology*, vol. 36, no. 4. pp. 897–909, 1993.

[233] P. Bendova, P. Ruzicka, V. Peterova, M. Fricova, and I. Springrova, "MRI-based registration of pelvic alignment affected by altered pelvic floor muscle characteristics," *Clin. Biomech.*, vol. 22, no. 9, pp. 980–987, 2007.

[234] V. Lucente, H. van Raalte, M. Murphy, and V. Egorov, "Biomechanical paradigm and interpretation of female pelvic floor conditions before a treatment," *Int. J. Womens. Health*, vol. 9, pp. 521–550, 2017.

[235] M. Cosson, C. Rubod, A. Vallet, J. F. Witz, P. Dubois, and M. Brieu, "Simulation of normal pelvic mobilities in building an MRI-validated biomechanical model," *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 24, no. 1, pp. 105–112, 2013.

[236] M. D. Agarwal, E. L. Resnick, J. N. Mhuircheartaigh, and K. J. Mortele, "MR Imaging of the Female Perineum: Clitoris, Labia, and Introitus," *Magn. Reson. Imaging Clin. N. Am.*, vol. 25, no. 3, pp. 435–455, 2017.

[237] S. Gupta, J. B. Sharma, S. Hari, S. Kumar, K. K. Roy, and N. Singh, "Study of dynamic magnetic resonance imaging in diagnosis of pelvic organ prolapse," *Arch. Gynecol. Obstet.*, vol. 286, no. 4, pp. 953–958, 2012.

[238] C. A. Woodfield, S. Krishnamoorthy, B. S. Hampton, and J. M. Brody, "Imaging pelvic floor disorders: Trend toward comprehensive MRI," *Am. J. Roentgenol.*, vol. 194, no. 6, pp. 1640–1649, 2010.

[239] J. E. Jelovsek *et al.*, "Predicting risk of pelvic floor disorders 12 and 20 years after delivery," *Am. J. Obstet. Gynecol.*, vol. 218, no. 2, pp. 222.e1-222.e19, 2017.

[240] A. Arian *et al.*, "Agreement of Manual Exam (POP-Q) with Pelvic MRI in Assessment of Anterior Pelvic Organ Prolapse," *Iran. J. Radiol.*, vol. In press, no. In press, 2016.

[241] L. Hoyte *et al.*, "Measurements from image-based three dimensional pelvic floor reconstruction: A study of inter- and intraobserver reliability," *J. Magn. Reson. Imaging*, vol. 30, no. 2, pp. 344–350, 2009.

[242] G. L. Morren, A. G. Balasingam, J. E. Wells, A. M. Hunter, R. H. Coates, and R. E. Perry, "Triphasic MRI of pelvic organ descent: Sources of measurement error," *Eur. J. Radiol.*, vol. 54, no. 2, pp. 276–283, 2005.

[243] M. E. Lockhart *et al.*, "Reproducibility of Dynamic MR Imaging Pelvic Measurements: A Multi-institutional Study," *Radiology*, vol. 249, no. 2, 2008.

[244] L. Hoyte and P. Ratiu, "Linear measurements in 2-dimensional pelvic floor imaging: The impact of slice tilt angles on measurement reproducibility," *Am. J. Obstet. Gynecol.*, vol. 185, no. 3, pp. 537–544, 2001.

[245] K. Suzuki, A. Masukawa, S. Aoki, Y. Arai, and E. Ueno, "A new coordinates system for cranial organs using magnetic resonance imaging," *Acta Otolaryngol.*, vol. 130, no. 5, pp. 568–75, 2010.

[246] M. Kimura *et al.*, "Reliability of a coordinate system based on anatomical landmarks of the maxillofacial skeleton: An evaluation method for three-dimensional images obtained by cone-beam computed tomography," *Oral Radiol.*, vol. 25, no. 1, pp. 37–42, 2009.

[247] S. S. Brandt, G. Karemore, N. Karssemeijer, and M. Nielsen, "An anatomically oriented breast coordinate system for mammogram analysis," *IEEE Trans. Med. Imaging*, vol. 30, no. 10, pp. 1841–1851, 2011.

[248] E. S. Grood and W. J. Suntay, "A Joint Coordinate System for the Clinical Description of Three-Dimensional Motions: Application to the Knee," *Journal of Biomechanical Engineering*, vol. 105, no. 2. pp. 136–144, 1983.

[249] G. Wu *et al.*, "ISB recommendation on definitions of joint coordinate system of various joints for the reporting of human joint motion—part I: ankle, hip, and spine," *J. Biomech.*, vol. 35, no. 4, pp. 543–548, 2002.

[250] Y. Kang, K. Engelke, C. Fuchs, and W. A. Kalender, "An anatomic coordinate system of the femoral neck for highly reproducible BMD measurements using 3D QCT," *Comput. Med. Imaging Graph.*, vol. 29, no. 7, pp. 533–541, 2005.

[251] M. J. Rainbow *et al.*, "Automatic determination of an anatomical coordinate system for a three-dimensional model of the human patella," *J. Biomech.*, vol. 46, no. 12, pp. 2093–2096, 2013.

[252] Z. A. Englander, H. C. Cutcliffe, G. M. Utturkar, W. E. Garrett, C. E. Spritzer, and L. E. DeFrate, "A Comparison of Knee Abduction Angles Measured by a 3D Anatomic Coordinate System Versus Videographic Analysis: Implications for Anterior Cruciate Ligament Injury," *Orthop. J. Sport. Med.*, vol. 7, no. 1, pp. 1–7, 2019.

[253] S. Tashman and W. Anderst, “In-Vivo Measurement of Dynamic Joint Motion Using High Speed Biplane Radiography and CT: Application to Canine ACL Deficiency,” *J. Biomech. Eng.*, vol. 125, no. 2, pp. 238–245, 2003.

[254] T. A. Stein, G. Kaur, A. Summers, K. A. Larson, and J. O. L. DeLancey, “Comparison of bony dimensions at the level of the pelvic floor in women with and without pelvic organ prolapse,” *Am. J. Obstet. Gynecol.*, vol. 200, no. 3, pp. 241.e1-241.e5, 2009.

[255] S. Abramowitch, J. Spring, and P. Moalli, “A New Method to Determine Vaginal Axis and Spatial Position Using a 3-D Anatomical Coordinate System,” *J. Women’s Heal.*, vol. 20, pp. 1387–1387, 2011.

[256] D. Easley, W. Barone, P. Moalli, and S. Abramowitch, “SPR-16 A preliminary evaluation of vaginal alignment following a transvaginal procedure using MatriStem^{TM} pelvic floor matrix in the rhesus macaque,” *Transl. Androl. Urol.*, vol. 5, pp. AB289–AB289, 2016.

[257] A. Rosset, L. Spadola, and O. Ratib, “OsiriX: An open-source software for navigating in multidimensional DICOM images,” *J. Digit. Imaging*, vol. 17, no. 3, pp. 205–216, 2004.

[258] Y. J. Zhang, *Geometric Modeling and Mesh Generation from Scanned Images*. CRC Press, LLC, 2016.

[259] J. Grant, *An Atlas of Anatomy*, 2nd ed. Baltimore, MD: Williams & Wilkins, 1943.

[260] A. Eycleshymer and D. Schoemaker, *A Cross Section in Anatomy*. New York: Appleton-Century-Crofts, 1983.

[261] B. Hadra, *Lesions of the vagina and pelvic floor*. Philadelphia: Mc Mullin, 1888.

[262] H. E. O’Connell, N. Eizenberg, M. Rahman, and J. Cleeve, “The anatomy of the distal vagina: Towards unity,” *J. Sex. Med.*, vol. 5, no. 8, pp. 1883–1891, 2008.

[263] “CAPS Imaging Study: Anatomic Characterization of the External/Internal Anal Sphincter at Six Months Postpartum.” .

[264] V. L. Handa *et al.*, “Pelvic organ support among primiparous women in the first year after childbirth,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 20, no. 12, pp. 1407–1411, 2009.

[265] T. K. Koo and M. Y. Li, “A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research,” *J. Chiropr. Med.*, vol. 15, no. 2, pp. 155–163, 2016.

[266] L. B. Petryshyn, “Comparison of Vaginal Axis in Women who have Undergone,” *CriMiCo 2013 - 2013 23rd Int. Crime. Conf. Microw. Telecommun. Technol. Conf. Proc.*, vol. 21, no. 1, pp. 547–548, 2013.

[267] K. K. Milligan, “Morphometric Analysis of the Sacrum Using Statistical Shape Modeling,” University of Colorado, 2008.

[268] C. S. Reiner *et al.*, “The 3D Pelvic Inclination Correction System (PICS): A universally applicable coordinate system for isovolumetric imaging measurements, tested in women with pelvic organ prolapse (POP),” *Comput. Med. Imaging Graph.*, vol. 59, pp. 28–37, 2017.

[269] S. B. Sholts, L. Flores, P. L. Walker, and S. K. T. S. Wärmländer, “Comparison of coordinate measurement precision of different landmark types on human crania using a 3D laser scanner and a 3D digitiser: Implications for applications of digital morphometrics,” *Int. J. Osteoarchaeol.*, vol. 21, no. 5, pp. 535–543, 2011.

[270] Y. J. Zhang, “Challenges and Advances in Image-Based Geometric Modeling and Mesh Generation,” in *Image-Based Geometric Modeling and Mesh Generation*, Springer, 2013.

[271] L. Hoyte *et al.*, “Segmentations of MRI images of the female pelvic floor: A study of inter- and intra-reader reliability,” *J. Magn. Reson. Imaging*, vol. 33, no. 3, pp. 684–691, 2011.

[272] J. M. R. S. Ma, Zhen; Jorge, Renato Natal M.; Mascarenhas, T.; Tavares, “Segmentation of female pelvic cavity in axial T2-weighted MR iages towards the 3D reconstruction,” *Int. j. numer. method. biomed. eng.*, vol. 28, pp. 714–726, 2012.

[273] L. Edelstein, *The Hippocratic Oath: Text, Translation and Interpretation*. .

[274] C. E. Harris, M. S. Pritchard, and M. J. Rabins, *Engineering Ethics Concepts & Cases*, Fourth. Canada: Wadsworth, Cengage Learning, 2009.

[275] L. Nielsen-Bohlman, A. M. Panzer, and D. a Kindig, *Health Literacy: A Prescription to End Confusion*. 2004.

[276] Unesco, “Understandings of literacy,” *Educ. All Glob. Monit. Rep.*, pp. 147–159, 2006.

[277] S. Ratzan and R. Parker, “Introduction,” in *National Library of Medicine Current Bibliographies in Medicine: Health Literacy*, NLM Pub. N., C. Selden, M. Zorn, S. Ratzan, and R. Parker, Eds. Bethesda, MD: National Institutes of Health, U.S. Department of Health and Human Services, 2000.

[278] D. J. Humes and J. Simpson, “Clinical review Acute appendicitis,” *Bmj*, vol. 333, no. September, pp. 530–534, 2006.

[279] C. S. Graffeo and F. L. Counselman, “Appendicitis,” *Emerg. Med. Clin. North Am.*, vol. 14, no. 4, pp. 653–71, 1996.

[280] K. E. Hobler, “Acute and Suppurative Appendicitis :,” *Perm. J.*, vol. 2, no. 2, pp. 5–8, 1998.

[281] P. G. Blomqvist, R. E. B. Andersson, F. Granath, M. P. Lambe, and A. R. Ekbom, “Mortality after appendectomy in Sweden, 1987-1996,” *Ann. Surg.*, vol. 233, no. 4, pp. 455–460, 2001.

[282] P. H. Literacy, “Promoting Health Literacy,” *J. Am. Med. Informatics Assoc.*, no. October, pp. 152–164, 2003.

[283] I. S. Kirsch, A. Jungeblut, L. Jenkins, and A. Kolstad, “Adult literacy in America,” *Educ. Res.*, pp. 1–176, 2002.

[284] L. J. Cornelius, P. L. Smith, and G. M. Simpson, “What factors hinder women of color from obtaining preventive health care?,” *Am. J. Public Health*, vol. 92, no. 4, pp. 535–539, 2002.

[285] J. DeGruy, *Post Traumatic Slave Syndrome: America’s Legacy of Enduring Injury and Healing*. Portland, OR: Joy DeGruy Publications Inc., 2005.

[286] C. Ghetti, L. C. Skoczylas, S. S. Oliphant, C. Nikolajski, and J. L. Lowder, “The Emotional Burden of Pelvic Organ Prolapse in Women Seeking Treatment: A Qualitative Study,” *Female Pelvic Med. Reconstr. Surg.*, vol. 21, no. 6, pp. 332–338, 2015.

[287] K. Castania, “The Evolving Language of Diversity,” *Cornell Coop. Ext.*, pp. 1–6, 2003.

[288] C. M. Labuski, “A black and white issue ? Learning to see the intersectional and racialized dimensions of gynecological pain,” *Soc. Theory Heal.*, vol. 15, no. 2, pp. 160–181.

[289] F. R. Hauck, K. O. Tanabe, and R. Y. Moon, “Racial and Ethnic Disparities in Infant Mortality,” *Semin. Perinatol.*, vol. 35, no. 4, pp. 209–220, 2011.

[290] L. Rosenthal and M. Lobel, “Explaining racial disparities in adverse birth outcomes: Unique sources of stress for Black American women,” *Soc. Sci. Med.*, vol. 72, no. 6, pp. 977–983, 2011.

[291] H. Shellae Versey, C. C. Cogburn, C. L. Wilkins, and N. Joseph, “Appropriated racial oppression: Implications for mental health in Whites and Blacks,” *Soc. Sci. Med.*, vol. 230, no. February, pp. 295–302, 2019.

[292] I. Wangi, A. Dilmohamed, and Y. Pierre, “Difference In The Trend of Preeclampsia Between Black Women and White Women Living In The Uk . J anine,” vol. 6, no. Oct, pp. 62–73, 2016.

[293] W. W. Dressler, K. S. Oths, and C. C. Gravlee, “RACE AND ETHNICITY IN PUBLIC HEALTH RESEARCH: Models to Explain Health Disparities,” *Annu. Rev. Anthropol.*, vol. 34, no. 1, pp. 231–252, 2005.

[294] A. S. Bryant, A. Worjoloh, A. B. Caughey, and A. E. Washington, “Racial/ethnic disparities in obstetric outcomes and care: prevalence and determinants,” *Am. J. Obstet. Gynecol.*, vol. 202, no. 4, pp. 335–343, 2010.

[295] C. L. Kothari *et al.*, “The interplay of race, socioeconomic status and neighborhood residence upon birth outcomes in a high black infant mortality community,” *SSM - Popul. Heal.*, vol. 2, no. April, pp. 859–867, 2016.

[296] J. Bröder *et al.*, “Health literacy in childhood and youth : a systematic review of definitions and models,” pp. 1–25, 2017.

[297] R. K. Britt, W. B. Collins, K. Wilson, G. Linnemeier, and A. M. Englebert, “EHealth literacy and health behaviors affecting modern college students:a pilot study of issues identified by the American college health association,” *J. Med. Internet Res.*, vol. 19, no. 12, 2017.

[298] J. A. Reid, C. L. Templeman, D. A. Groneberg, D. Brueggmann, and J. M. Jaque, “Patients’ Knowledge of Female Pelvic Health and Related Educational Preferences,” *J. Community Health*, vol. 42, no. 1, pp. 147–154, 2017.

[299] W. Volck, Z. A. Ventress, D. Herbenick, P. J. Adams Hillard, and J. S. Huppert, “Gynecologic Knowledge Is Low in College Men and Women,” *J. Pediatr. Adolesc. Gynecol.*, vol. 26, no. 3, pp. 161–166, 2013.

[300] W. Volck, Z. A. Ventress, D. Herbenick, P. J. Adams Hillard, and J. S. Huppert, “Gynecologic Knowledge Is Low in College Men and Women,” *J. Pediatr. Adolesc. Gynecol.*, vol. 26, no. 3, pp. 161–166, 2013.

[301] K. Kuo, T. Y. Zhu, S. Raidoo, L. X. Zhao, A. Sammarco, and K. Ashby, “Partnering with public schools: A resident-driven reproductive health education initiative,” *J. Pediatr. Adolesc. Gynecol.*, vol. 27, no. 1, pp. 20–24, 2014.

[302] P. K. Xaverius, L. E. Tenkku, and J. Salas, “Differences Between Women at Higher and Lower Risk for an Unintended Pregnancy,” *Women’s Heal. Issues*, vol. 19, no. 5, pp. 306–312, 2009.

[303] C. Principles, “Guidance Document Appropriate Practices in School-Based Health Education,” pp. 1–22.

[304] K. Kuo, T. Y. Zhu, S. Raidoo, L. X. Zhao, A. Sammarco, and K. Ashby, “Partnering with public schools: A resident-driven reproductive health education initiative,” *J. Pediatr. Adolesc. Gynecol.*, vol. 27, no. 1, pp. 20–24, 2014.

[305] J. S. Santelli, V. Sharma, and R. Viner, “3. Inequality, National Wealth, Economic Development and Global Trends in Teenage Birth Rates, 1990-2010,” *J. Adolesc. Heal.*, vol. 52, no. 2, pp. S4–S5, 2013.

[306] J. M. Hebert-Beirne, R. O’Conor, J. D. Ihm, M. K. Parlier, M. D. Lavender, and L. Brubaker, “A Pelvic Health Curriculum in School Settings: The Effect on Adolescent Females’ Knowledge.,” *J. Pediatr. Adolesc. Gynecol.*, 2015.

[307] K. Yammine and C. Violato, “The effectiveness of physical models in teaching anatomy: a meta-analysis of comparative studies,” *Adv. Heal. Sci. Educ.*, vol. 21, no. 4, pp. 883–895, 2016.

[308] S. Ford and T. Minshall, "3D printing in teaching and education: A review of where and how it is used," *Submitt. to "Additive Manuf. J.*, no. October, 2017.

[309] X. Amit, "How medical students learn spatial anatomy," 2001.

[310] D. L. Begoray, J. Wharf-Higgins, and M. MacDonald, "High school health curriculum and health literacy: Canadian student voices," *Glob. Health Promot.*, vol. 16, no. 4, pp. 35–42, 2009.

[311] A. J. Notebaert, "Student perceptions about learning anatomy," 2009.

[312] V. Singh and P. Kharb, "A paradigm shift from teaching to learning gross anatomy: Meta-analysis of implications for instructional methods," *Journal of the Anatomical Society of India*, vol. 62, no. 1. pp. 84–89, 2013.

[313] K. H. C. Li *et al.*, "The role of 3D printing in anatomy education and surgical training: A narrative review," *MedEdPublish*, vol. 6, no. 2, pp. 1–22, 2017.

[314] S. Chen *et al.*, "The role of three-dimensional printed models of skull in anatomy education: A randomized controlled trail," *Sci. Rep.*, vol. 7, no. 1, pp. 1–11, 2017.

[315] K. Hou *et al.*, "The role of 3D printing in anatomy education and surgical training: A narrative review," *MedEdPublish*, vol. 6, no. 2, pp. 1–22, 2017.

[316] B. L. Gleason *et al.*, "An Active Learning Strategies Primer for Achieving Ability Based Educational Outcomes," *Am. J. Pharm. Educ.*, vol. 75, no. 9, 2011.

[317] S. Freeman *et al.*, "Active learning increases student performance in science, engineering, and mathematics," *Proc. Natl. Acad. Sci.*, vol. 111, no. 23, pp. 8410–8415, 2014.

[318] "The Impacts of Active Learning on Learning Disabled Students," 2017.

[319] W. S. Colleges, "Chalkboard vs . Paper : Technique for Improving Collaboration in Active Learning Activities," 2013.

[320] G. A. Smith, "The National Teaching & Learning Cognitive Assemblies : An Learner-Centered Classroom " D," *Natl. Teach. Learn. forum*, vol. 17, no. 5, pp. 1–4, 2008.

[321] N. Kim and U. Program, "Impact of Classroom Demonstrations and Surveys on Higher-level Learning Impact of Classroom Demonstrations and Surveys on Higher-level Learning," 2017.

[322] N. Cowan, "What are the differences between long-term, short-term, and working memory? Nelson," *NIH Public Access*, vol. 6123, no. 07, pp. 323–338, 2009.

[323] M. M. McClelland, A. C. Acock, A. Piccinin, S. A. Rhea, and M. C. Stallings, "Relations between preschool attention span-persistence and age 25 educational outcomes," *Early Child. Res. Q.*, vol. 28, no. 2, pp. 314–324, 2013.

[324] C. Galloway, "Blink and they're gone: PR and the battle for attention," *Public Relat. Rev.*, vol. 43, no. 5, pp. 969–977, 2017.

[325] J. Handelsman, S. Miller, and C. Pfund, *Scientific Teaching*. New York: W.H. Freeman and Company, 2007.

[326] E. Education, "Pre-Adolescent Learners," vol. 101, no. 4, pp. 698–716, 2012.

[327] National Library of Medicine (US) Board of Regents, "Electronic Imaging: Report of the Board of Regents," Bethesda, MD, 1990.

[328] L. A. Romero, L. Asensio Romero, M. Asensio Gómez, A. Prats-Galino, and J. A. Juanes Méndez, "3D Models of Female Pelvis Structures Reconstructed and Represented in Combination with Anatomical and Radiological Sections," *J. Med. Syst.*, vol. 42, no. 3, pp. 1–8, 2018.

[329] W. R. Barone and W. R. Barone, "MECHANICAL CHARACTERIZATION OF SYNTHETIC MESH FOR PELVIC by," 2015.

[330] C. Linder, J. C. Harris, E. L. Allen, and B. Hubain, "Building Inclusive Pedagogy: Recommendations From a National Study of Students of Color in Higher Education and Student Affairs Graduate Programs," *Equity Excell. Educ.*, vol. 48, no. 2, pp. 178–194, 2015.

[331] N. Kober, *Reaching Students: What Research Says About Effective Instruction in Undergraduate Science and Engineering*. 2014.

[332] *Science and Engineering for Grades 6-12*. 2018.

[333] E. A. Gunderson, G. Ramirez, S. L. Beilock, and S. C. Levine, "Teachers' spatial anxiety relates to 1st- and 2nd-graders' spatial learning," *Mind, Brain, Educ.*, vol. 7, no. 3, pp. 196–199, 2013.

[334] J. R. Power, "Preparing Students for Engineering Success through Improving 3-D Spatial Skills Preparing Students for Engineering Success through Improving 3-D Spatial Skills Abstract," 2017.

[335] A. K. Dean, "Applied Spatial Visualization for Engineers Applied Spatial Visualization for Engineers," 2017.

[336] A. Sheharyar, E. Masad, and A. Srinivasa, "Enhancing 3D spatial skills of engineering students using augmented reality," *ASEE Annu. Conf. Expo. Conf. Proc.*, vol. 2020-June, 2020.

[337] CDC, "Erratum: Youth risk behavior surveillance United States, (Morbidity and Mortality Weekly Report," 2016.

[338] M. Smith, F. Jones, S. Gilbert, and C. Wieman, “The Classroom Observation Protocol for Undergraduate STEM (COPUS): A New Instrument to Characterize University STEM Classroom Practices,” *CBE Life Sci. Educ.*, vol. 12, no. 4, pp. 618–627, 2013.

[339] A. Kappas, E. Krumhuber, and D. Kuster, “Modalities of Nonverbal Communication,” *Nonverbal Commun.*, pp. 133–134, 2013.

[340] K. Bousmalis, M. Mehu, and M. Pantic, “Spotting agreement and disagreement: A survey of nonverbal audiovisual cues and tools,” *Proc. - 2009 3rd Int. Conf. Affect. Comput. Intell. Interact. Work. ACII 2009*, pp. 1–9, 2009.

[341] J. M. Webb, P. Luft, E. W. Brooks, E. L. Brennan, and E. M. Diana, “Influence of pedagogical expertise and feedback on assessing student comprehension from nonverbal behavior,” *J. Educ. Res.*, vol. 91, no. 2, pp. 89–97, 1997.

[342] L. M. Hunt, N. D. Truesdell, and M. J. Kreiner, “Genes, race, and culture in clinical care: Racial profiling in the management of chronic illness,” *Med. Anthropol. Q.*, vol. 27, no. 2, pp. 253–271, 2013.

[343] D. Gillborn, “Intersectionality, Critical Race Theory, and the Primacy of Racism: Race, Class, Gender, and Disability in Education,” *Qual. Inq.*, vol. 21, no. 3, pp. 277–287, 2015.

[344] Bigham and Non, “The Genetic Anthropologist’s Contribution to Understanding Race and Racial Health Disparities,” *Hum. Biol.*, vol. 87, no. 4, p. 291, 2016.

[345] O. K. Obasogie, I. Headen, and M. S. Mujahid, “Race, Law, and Health Disparities: Toward a Critical Race Intervention,” *Annu. Rev. Law Soc. Sci.*, vol. 13, no. 1, pp. 313–329, 2017.

[346] K. M. Bridges, “The Dangerous Law of Biological Race,” *Fordham Law Rev.*, vol. 66, no. 1997, pp. 37–39, 2013.

[347] L. I. A. Betti, “Human Variation in Pelvic Shape and the Effects of Climate and Past Population History,” vol. 697, no. August 2016, pp. 687–697, 2017.

[348] P. A. Norton, K. Allen-Brady, and L. A. Cannon-Albright, “The familiality of pelvic organ prolapse in the Utah Population Database,” *Int. Urogynecol. J. Pelvic Floor Dysfunct.*, vol. 24, no. 3, pp. 413–418, 2013.

[349] K. Sharma, “Genetic basis of human female pelvic morphology: A twin study,” *Am. J. Phys. Anthropol.*, vol. 117, no. 4, pp. 327–333, 2002.

[350] C. A. Ball *et al.*, “Ethnicity Estimate White Paper,” *AncestryDNA*, 2013.

[351] Bolnick, “Combating Racial Health Disparities through Medical Education: The Need for Anthropological and Genetic Perspectives in Medical Training,” *Hum. Biol.*, vol. 87, no. 4, p. 361, 2016.

[352] A. Thomson, *Women and health research, ethical and legal issues of including women in clinical studies*, vol. 11, no. 1. 1995.

[353] N. Black, M. Barker, and M. Payne, “Cross sectional survey of multicentre clinical databases in the United Kingdom,” *Br. Med. J.*, vol. 328, no. 7454, pp. 1478–1481, 2004.

[354] W. Y. Mbbs and M. He, “Predictive Medicine in Ophthalmology,” *Ophthalmology*, vol. 124, no. 4, pp. 420–421, 2017.

[355] A. Kaushik, R. D. Jayant, and M. Nair, *Advances in personalized nanotherapeutics*. 2017.

[356] M. Ridley, *The Evolution of Everything: How New Ideas Emerge*. New York: Harper Perennial, 2016.