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Predicting the mechanical behaviour of the vaginal wall and mesh implants in ball burst tests

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Abstract

The prolapse of pelvic organs (POP) is a condition that affects several women and is characterized by the displacement of one or more pelvic organs due to weakened support structures. The use of meshes in pelvic reconstruction surgeries aims to replace or strengthen these weakened tissues, complementing traditional surgical methods for improved clinical outcomes. However, the use of synthetic meshes can result in graft-related complications (GRCs), attributed to inadequate biocompatibility and improper mechanical qualities. The development of biodegradable meshes presents an innovative approach. Biodegradable meshes can provide support to the organs but also feature favorable characteristics such as flexibility and strength, contributing to enhanced reinforcement of the intervened region and reducing potential tissue injuries.

The main objective of this study is to enhance our understanding and provide valuable insights into the performance of vaginal tissue and mesh implants, which may contribute to the advancement of pelvic organ prolapse (POP) treatment methodologies.

To achieve this objective, various methodologies were addressed in this study: (1) printing of biodegradable meshes through melt electrowriting, (2) experimental analysis with the execution of uniaxial tests and ball burst tests on these meshes and on porcine vaginal tissue, (3) numerical simulation of the ball burst test which was validated based on experimental results.

Using the Melt Electrowriting technique, a specific type of 3D printing, meshes with different diameters and geometries were manufactured. This process enabled the controlled production of mesh structures essential for subsequent analyses.

The experimental tests were conducted with the aim of extracting mechanical properties of both tissues and meshes, essential for the accurate representation of materials within the ABAQUS simulation framework. The experimentally obtained results showed significant agreements with the literature. It can be concluded that the placement of biodegradable PCL meshes in sow's vaginal tissue increases the maximum force by 14 to 20 percent in ball burst tests. However, regarding the computational model, it is observed that the simulations created for the meshes and tissue were largely successful, with adjustments needed only for sample properties. Conversely, the simulation of tissue with mesh did not fare as well. In this case, it is necessary to review the model and identify the source of the error.

This multifaceted approach, combining simulation, material testing, and experimental validation, constitutes the cornerstone of comprehensive research on the mechanical behavior of vaginal tissue and mesh implants, substantially contributing to the field of research on POP treatment.

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Resumo

O prolapso de órgãos pélvicos (POP) é uma condição que afeta várias mulheres que é caracterizada pelo deslocamento de um ou mais órgãos pélvicos devido a estruturas de suporte enfraquecidas. O uso de malhas em cirurgias de reconstrução pélvica visa substituir ou fortalecer esses tecidos enfraquecidos, complementando os métodos cirúrgicos tradicionais para resultados clínicos aprimorados. No entanto, o uso de malhas sintéticas pode resultar em complicações relacionadas ao enxerto (GRCs), atribuídas à biocompatibilidade inadequada e qualidades mecânicas impróprias. O desenvolvimento de malhas biodegradáveis apresenta uma abordagem inovadora. As malhas biodegradáveis podem oferecer o suporte aos órgãos, mas também apresentam características favoráveis, como flexibilidade e resistência, contribuindo para o reforço aprimorado da região intervencionada e redução de possíveis lesões nos tecidos.

O objetivo principal deste estudo é aprimorar nossa compreensão e fornecer insights valiosos sobre o desempenho do tecido vaginal e implantes de malha que poderá contribuir para o avanço das metodologias de tratamento do prolapso de órgãos pélvicos (POP).

Para alcançar esse objetivo, neste estudo foram abordadas várias metodologias, (1) impressão de malhas biodegradáveis através de melt electrowriting, (2) análise experimental com a execução de testes uniaxiais e testes de explosão de bola nessas malhas e em tecido vaginal de suínos, (3) simulação numérica do teste de explosão de bola que foi validada com base nos resultados experimentais.

Utilizando a técnica Melt Electrowriting, um tipo específico de impressão 3D, foram fabricadas malhas com diferentes diâmetros e geometrias. Esse processo possibilitou a produção controlada de estruturas de malha essenciais para análises subsequentes.

Os testes experimentais foram executados com o objetivo de extrair propriedades mecânicas tanto dos tecidos como das malhas, essenciais para a representação precisa dos materiais dentro do framework de simulação do ABAQUS. Os resultados experimentalmente obtidos mostraram acordos significativos com a literatura. Pode-se concluir que o posicionamento de malhas biodegradáveis de PCL no tecido vaginal suíno aumenta a força máxima em 14 a 20 por cento nos testes de ball burst. No entanto, em relação ao modelo computacional, observa-se que as simulações criadas para as malhas e o tecido foram amplamente bem-sucedidas, com ajustes necessários apenas para propriedades das amostras. Por outro lado, a simulação do tecido com malha não teve um desempenho tão bom. Neste caso, é necessário revisar o modelo e identificar a origem do erro.

Esta abordagem multifacetada, combinando simulação, testes de materiais e validação experimental, constitui o pilar de uma investigação abrangente sobre o comportamento mecânico

do tecido vaginal e implantes de malha, contribuindo substancialmente para o campo da pesquisa sobre o tratamento do POP.

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Abbreviations, Acronyms and Symbols

- (A)- Area
- (AM)- Additive manufacturing
- (BMI)- Body mass index
- (CTS)- CriticalTangencial Speed
- (cm)- centimetres
- (D)- diameter
- (E)- Young Modulus
- (ES)- Eletrospinning
- (ESD)- Eletrostatic discharge
- (Er)- Extrusion rate
- (ϵ)- Strain
- (μm)- micrometres
- (FEM)- Finite Element Method
- (FEA)- Finite Element Analysis
- (FDM)- Fused Deposition Modeling
- (gh)- Genital hiatus
- (GRCs)- graft-related complications
- (ICS)- International Continence Society
- (INEGI)- Instituto de Ciência e Inovação em Engenharia Mecânica e Engenharia Industrial
- (LPDS)- Laboratório de Desenvolvimento de Produtos e Serviços
- (LA)- Levator ani
- (L)- length
- (MEW)- Melt eletrowriting
- (MPa)- Megapascals
- (N)- Newton
- (POP)- Pelvic organs prolapse
- (PFD)- Pelvic floor disfunction
- (POP-Q)- pelvic organ prolapse quantification system
- (pb)- perineal body

(PP)- polypropylene polyethylene terephthalate
(PET)- polyethylene terephthalate
(PTFE)- polytetrafluoroethylene
(PVDF)- polyvinylidene fluoride
(PCL)-Polycaprolactone
(RP)- Rapid prototyping
(tvL)- total vagina length
(USLs)- Ulterosacral ligaments
(X)- cross meshes

Chapter 1

Introduction

1.1 Motivation

Pelvic organs prolapse (POP) is a widespread condition characterized by the descent of pelvic structures into the vagina, often resulting from ligament or muscle weakening. This prevalent disorder significantly impacts the quality of life for millions of women globally [1].

Statistics reveal that 41% of women over the age of 60 experience POP, with one in four cases presenting symptoms. The prevalence of this condition ranges from 2.9% to 8% of the female population, and there is a 12.6% lifetime risk of women requiring surgery to address prolapse [2]. In Portugal, approximately 7 thousand women are affected annually, with an anticipated 40% increase in cases over the next 40 years due to the aging female population [3].

Researchers have been actively exploring treatment solutions for POP, introducing various biologic and synthetic graft materials to enhance reconstructive surgeries. However, these implants are still susceptible to complications [4]. To mitigate these issues, advanced manufacturing processes for medical devices, such as injection moulding, electrospinning, hot-melt extrusion, and 3D printing, have been introduced [5].

The combination of electrospinning technology with 3D printing has demonstrated significant advantages in addressing implant-related complications. This approach allows for the creation of complex, optimized structures through controlled and precise deposition of small-scale fibers. Melt electrowriting offers the ability to tailor material properties for personalized constructs, utilizing biodegradable polymers and their blends to enhance biocompatibility and production efficiency [6].

Another noteworthy development gaining popularity is the application of finite element method (FEM) analysis in the medical field. FEM proves attractive due to its rapid facilitation of early device performance testing before costly prototyping and bench testing. Integrating FEM

into product development has the potential to reduce costs by expediting the process and minimizing bench testing iterations [7].

1.2 Objectives

This dissertation aims to present the outcomes and findings obtained from a computational and experimental analysis of the ball burst test.

The primary objectives include:

- Designing and manufacturing 3D melt electrowriting meshes featuring varied geometries and configurations for pelvic organ prolapse (POP) repair.
- Conducting a uniaxial tensile test on sow's vaginal tissue and a PCL filament to determine their individual mechanical properties.
- Performing ball burst tests on meshes, sow's vaginal tissue, and combinations of meshes with tissue.
- Employing Abaqus® software, computational models are crafted to simulate the ball burst test. The objective is to attain simulation results that closely align with the findings from the corresponding experimental tests.

1.3 Dissertation Structure

The dissertation is structured as follows:

- Chapter 2: Describes a review of the female pelvic area and the POP. It also includes an overview of the computational modelling and rapid prototyping.
- Chapter 3: This chapter outlines the methodology employed during the development of the design and production of the biodegradable meshes, the experimental work and the computational models, detailing the instruments, tools and materials used.
- Chapter 4: This chapter presents the results of the ball burst tests performed and the results obtained on the simulations carried out.
- Chapter 5: The final chapter comprises the dissertation's conclusions and recommendations for future work.
- Appendix:

Chapter 2

State of the Art

The upcoming chapter will delve into the theoretical foundations essential for comprehending the subsequent studies in this thesis. Initially, a detailed overview of the female pelvic area will be provided, followed by an exploration of pelvic organ prolapse (POP) to elucidate its complexities. To facilitate understanding of the simulation methodologies employed, an exposition on the finite element method (FEM) and finite element analysis (FEA) will be presented, supplemented by pertinent examples. Additionally, a dedicated section on rapid prototyping, with a focus on melt electrowriting, will be included, featuring insightful applications in the medical field.

2.1 Female pelvis

To gain a comprehensive understanding of pelvic floor dysfunction (PFD), it is crucial to understand the underlying pathophysiological processes. This needs a profound comprehension of the pelvic anatomy and the functions associated with each structure. The structure of the female pelvic floor is an interrelated system of bony pelvis, muscles, fasciae, and ligaments with multiple functions. Mechanically, the pelvic organ support system is of two types: supporting system of the levator ani (LA) muscle and the suspension system of the endopelvic fascia [8]. At normal resting conditions, the soft and intact connective tissue holds the pelvic organs to store urine and stool which relaxes in demand to allow the organ mobility for excretion. On the other hand, the muscle system provides normal resting contraction and reflex contraction to maintain the urogenital hiatus[9].

2.1.1 Bony Pelvis

Pelvis (Figure 1), in human anatomy, is a basin-shaped complex of bones that connects the trunk and the legs, supports the trunk and contains the intestines, the urinary bladder and the internal sex organs. The ring made by the pelvis functions as the birth canal in females.[10] It is key to many functions of the body, as a transitional zone for neurovascular structures traversing between the abdomen and the lower limbs, a junctional point between the spine and lower limb forces during locomotion and a structure which lies crucial visceral structures such as the female reproductive organs, urinary bladder, and rectum.[11]

It is usually divided into two separate anatomic regions: the pelvic girdle and pelvic spine. The pelvic girdle, also known as the hip bone, is composed of three fused bones: the ilium, ischium and the pubic bone. The pelvic spine is the posterior portion of the pelvis below the lumbar spine, composed of the sacrum and coccyx. The two pelvic bones are connected anteriorly by the pubic symphysis, while posteriorly they articulate with the pelvic spine to form the sacroiliac joints. [12] [13]

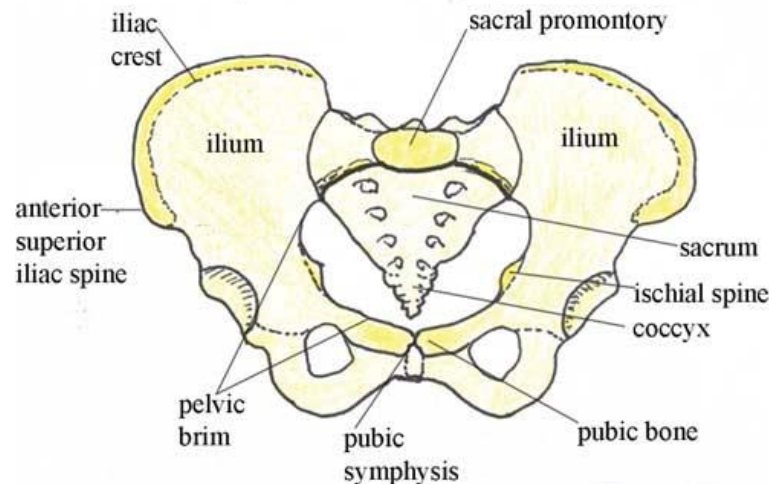


Figure 1 Representation of the women's pelvises (adapted from [13])

The ilium is the physically largest of the three pelvic bones. This structure is a blade-shaped bone found superior to the hip joint. It consists of the two main parts: the body and ala. The body of ilium is a smaller, inferior, part that contributes to the formation of the acetabulum. The superior part, called ala, is a large, flat portion of the bone that has four borders and three surfaces. [14]

The ischium is located posteroinferiorly to the hip joint and is shaped like an 'L'. It continues superiorly with the ilium and anteriorly with the pubic bone. The ischium has two parts - the body and ramus. The body of the ischium is rough and broad, featuring three bony surfaces: medial (pelvic), lateral (femoral), and posterior surfaces. [12]

The pubis constitutes the inferior portion of the hip bone and is composed of a superior ramus and inferior ramus. The superior ramus aids in forming the acetabulum and is marked by an upper pectineal line and lower obturator crest. The inferior ramus of the pubis fuses with the inferior ramus of the ischium, together forming the obturator foramen through which essential neurovascular structures pass. [15]

The sacrum, a triangular bone, results from the fusion of five sacral vertebrae. It presents anterior (pelvic) and posterior (gluteal) surfaces, a base, two alae, and an apex. The pelvic surface is smooth and concave, while the gluteal surface is rough and irregular, featuring a median sacral crest marked by numerous rudimentary spinous processes. [12]

The coccyx is a triangular bone formed by the fusion of four small pieces, articulating with the lowest part of the sacrum at the sacrococcygeal joint. This joint is reinforced anteriorly and posteriorly by corresponding sacrococcygeal ligaments. [16]

2.1.2 Muscles

The pelvic floor is comprised of a number of muscles (Figure 2), and they are organized into superficial and deep muscle layers. The LA muscle complex consists of the pubococcygeus, the puborectalis, and iliococcygeus muscles. These muscles are tonically contracted at rest and act to close the genital hiatus and provide a stable platform for the pelvic viscera. The LA muscles play an essential role in support of the pelvic organs and are innervated by the fourth sacral nerve.[17]

The pubococcygeus muscle arises from the posterior portion of the superior pubic ramus and attaches to the anococcygeal and the superior surface of the coccyx. The puborectalis muscle arises from the back of the pubis and form a U-shaped loop behind the rectum that slings the anorectal junction to the symphysis pubis. The iliococcygeus muscle arises from the ischial spine and inserts on the anococcygeal raphe and the coccyx. [17]

The levator plate is made by the fusion of the LA muscles and the sustained resting tone of the pelvic floor muscles supports pelvic organ, resists increase in abdominal pressure, and is essential in control of urinary and fecal continence. With loss of tone from pelvic floor muscles or nerve injury, there is relaxation in the urogenital hiatus, which diminishes the horizontal orientation of the levator plate. [18] [19]

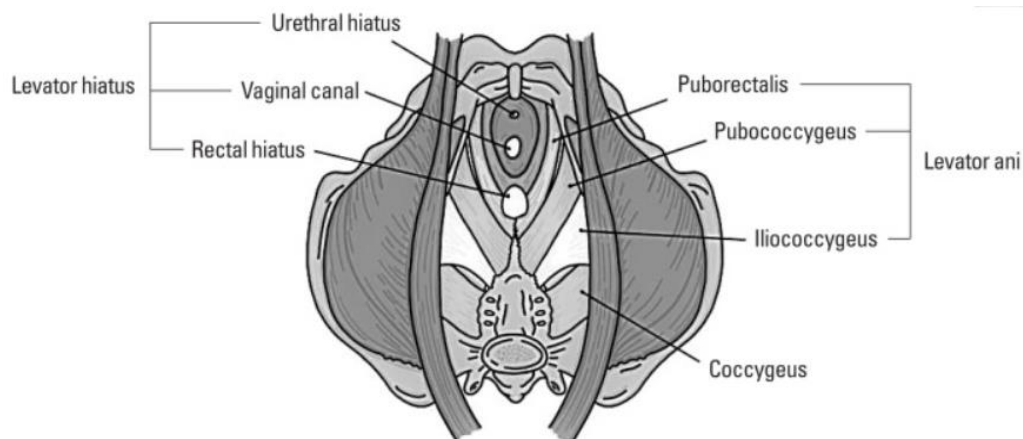


Figure 2 Pelvic floor muscles of female. (Adapted from [19])

2.1.3 Fascia

The pelvic floor fasciae are thought to contribute to urethral and pelvic organ support, thereby preventing incontinence and prolapse[20]. The structures that form the pelvic region are arranged as a series of muscles and fascia layers that are interwoven with vascular and nervous networks and connected to the various viscera. Structural and biomechanical alterations of the fasciae, such as thickening, reduced shear strain, and increased viscosity of hyaluronan, have also been suggested as pathophysiological mechanisms [21].

The bladder, urethra, the vagina and uterus are attached to the pelvic walls by a system of connective tissue that is called endopelvic fascia. The endopelvic fascia is the connective-tissue network that envelops all organs of the pelvis and connects them loosely to the supportive musculature and bones of the pelvis. This network allows the mobility of the viscera to permit storage of urine and stool, coitus, parturition, and defecation. Disruption or stretching of these connective-tissue attachments happens during vaginal delivery or hysterectomy, with chronic straining, or with normal ageing. [22] Evidence suggests that abnormalities of connective tissue

and connective-tissue repair might predispose some women to pelvic organ prolapse. Endopelvic fascia and ligaments are a mesh-like group of collagen fibers interlaced with elastin, smooth muscle cells, fibroblasts, and vascular structures. The structures that attach the uterus to the pelvic wall, the cardinal ligaments, derive strength from the supportive collagen forming the walls of arteries and veins. [23]

2.1.4 Ligaments

The pelvic ligaments (Figure 3) are not classic ligaments but are thickenings of retroperitoneal fascia and consist primarily of blood and lymphatic vessels, nerves and fatty connective tissue. [24] The key ligaments of the pelvis present in both sexes are the sacrotuberous, sacrospinous and iliolumbar ligaments. Thus, specific female pelvic ligaments are the broad ligament and the ligaments of the ovaries and uterus. The connective tissue is denser immediately adjacent to the lateral walls of the cervix and the vagina. The broad ligaments are a thin, mesenteric-like double reflection of peritoneum stretching from the lateral pelvic sidewalls to the uterus. [25]

The broad ligament is a sheet of pelvic peritoneum extending bilaterally from the lateral pelvic sidewalls to the uterus in the midline. The broad ligament folds over the fallopian tubes and ovaries and covers them anteriorly and posteriorly and is subdivided into the mesovarium, mesosalpinx, and mesometrium. [26]

Four ligaments are attached to the uterus: the round ligament, the cardinal ligament, the pubocervical ligament, and the uterosacral ligament. The round ligament of the uterus is attached to the cornu of the uterus. It travels through the inguinal canal and blends with labia majora and mons pubis. [27] The cardinal ligament, otherwise known as the transverse cervical ligament, is attached from the lateral aspect of the cervix to the respective pelvic wall. It forms the inferior border of the broad ligament and houses the uterine artery and uterine veins. The pubocervical ligament is attached to the cervix and extends to the posterior surface of the pubic symphysis. The uterosacral ligaments provide, along with the cardinal ligaments, the key support for the uterus within the pelvis and attach from the cervix below the peritoneum backward to the anterior aspect of the sacrum. [28] [29]

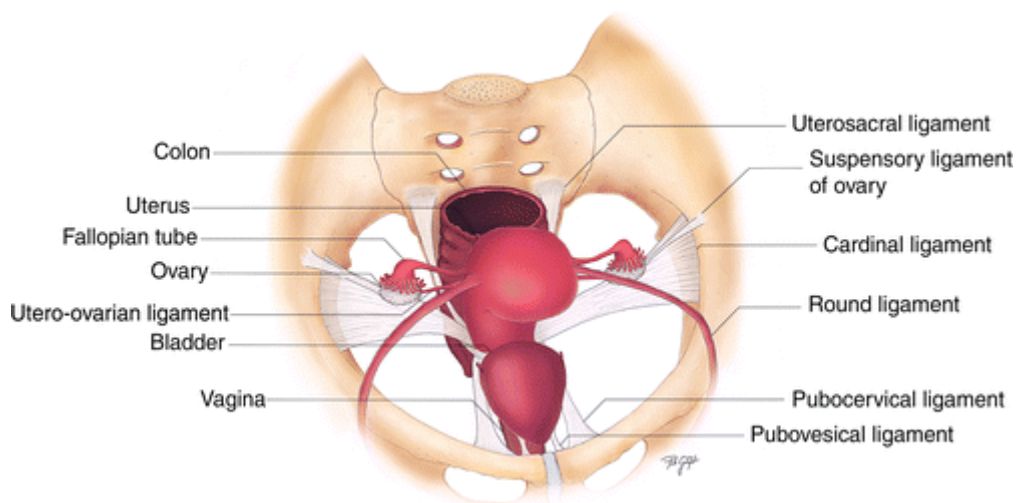


Figure 3 Suspensory ligaments of the female genital (adapted from [29])

2.2 Pelvic Organ Prolapse

Pelvic organs prolapse (POP) in females is the dysfunction under study and involves altering the normal anatomical position of one or more pelvic organs due to weakness and flaccidity of the pelvic floor support structures. The muscles, ligaments and fascia cannot maintain the organs in their correct positions, resulting in the protrusion of the vaginal walls and adjacent organs through the vaginal introitus. [30]

2.2.1 Types of POP

As we could see in the previous chapter, the anatomical support of pelvic viscera is mainly provided by the LA muscle complex, connective-tissue attachments of the pelvic organs (endopelvic fascia) and the ligaments that suspends the uterus. Disruption or dysfunction of one or both of these components can lead to loss of support and, eventually, pelvic organ prolapse. This condition has a negative impact on a woman's quality of life and can take many different forms. POP's include anterior and posterior vaginal prolapse, prolapse of the upper part of the vagina and uterine prolapse (Table 2). [31][32]

Table 1 Classification of the different types of pelvic organ prolapse. (adapted from [32])

Compartment	Anterior vaginal wall	Posterior vaginal wall	Apical
Types of Prolapse	Cystocele	Rectocele	Uterine
	Urethrocele	Enterocoele	Vaginal Vault prolapse

Anterior prolapse involves the descent of one or more anterior vaginal walls, leading to the protrusion of structures such as the bladder (cystocele) or the urethra (urethrocele). The anterior wall of the vagina relies on support structures like the pubovaginal ligament and surrounding connective tissue.[31]

Posterior prolapse encompasses the descent of one or more posterior vaginal walls, causing the protrusion of the rectum (rectocele) or the small intestine (enterocele). The support for the posterior vaginal wall involves connective tissue and pelvic floor muscles.[31]

Superior or apical prolapse refers to the descent of the upper part of the vagina. This condition is primarily associated with the loss of apical support provided by structures like the uterosacral ligaments and endopelvic fascia. [33]

Uterine prolapse occurs when the uterus displaces from its normal position in the pelvis, potentially protruding beyond the vaginal opening. This type of prolapse is closely tied to the uterosacral ligaments, round ligaments, and other uterine supports. [33]

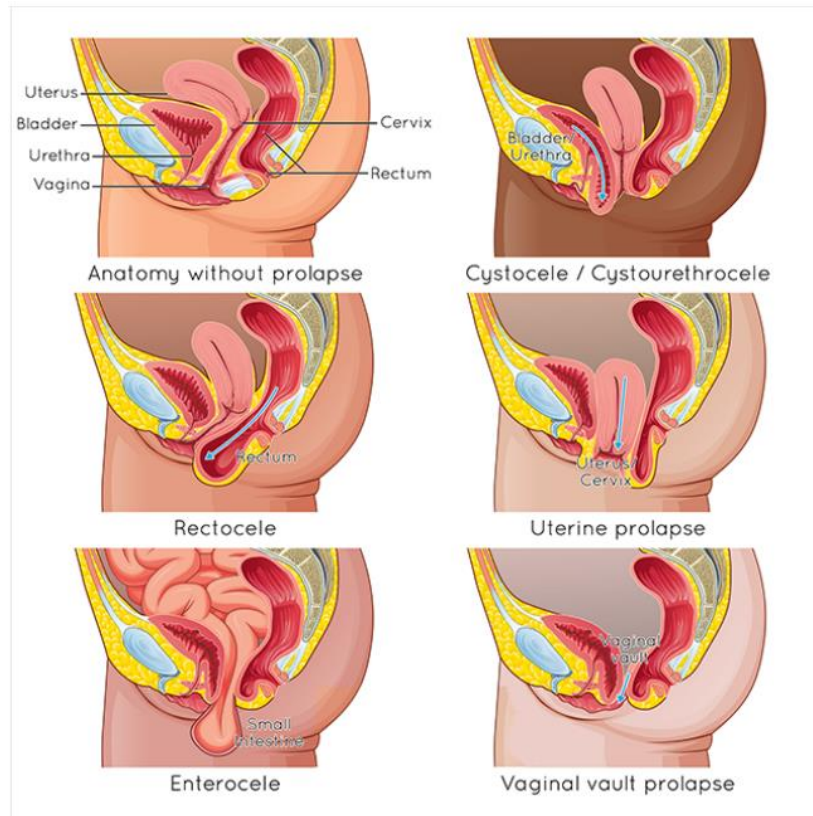


Figure 4 Types of pelvic organ (adapted from [31])

2.2.2 Epidemiology

While POP stands as one of the most common indications for gynecological surgery, there is a scarcity of epidemiological studies addressing the incidence and prevalence of this disorder. [34]

Loss of vaginal or uterine support in women presenting for routine gynecological care is seen in up to 43-76% of patients, with 3-6% having descent beyond the hymen.¹³ In the Women's Health Initiative, 41% of women age 50-79 years showed some amount of pelvic organ prolapse, including cystocele in 34%, rectocele in 19%, and uterine prolapse in 14%. [35]

The prevalence of pelvic floor dysfunction is higher in females, affecting half of all women after the age of 50, and throughout life it is believed that it can range from 30-50%, with the incidence doubling after the age of 80. Of the patients with pelvic floor dysfunction, only 10-20% complain of genital prolapse, with an intervention rate of 6.3% before and 20% after the age of 80, with 30% subsequent surgery. [36]

2.2.2 POP Stages

The initial efforts to classify pelvic organ prolapse were based on simplistic descriptions, categorizing prolapse as complete or incomplete. In attempts to classify the severity of pelvic organ prolapse, there has been disagreement over which pelvic landmarks to use. The widely adopted Baden-Walker system (Figure 5), developed and modified over time, employed the hymen as a reference point.[37] However, the definitions such as "normal" "halfway" or "maximum descent" are still open to interpretation by different examiners.[38] The limitations of these classification systems have impeded effective communication about findings in patients.

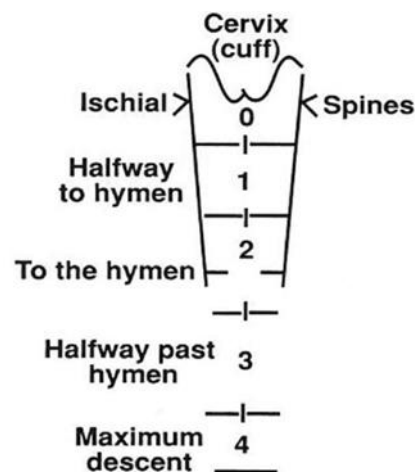


Figure 5 Baden-Walker Halfway Scoring System: grade 0 - no prolapse, grade 1 - descent halfway to the hymen, grade 2 - descent to the hymen, grade 3 - descent halfway past hymen, grade 4 - maximum descent (adapted from [39])

In recognition of the need for an objective and validated system to describe POP, the International Continence Society established an international, multidisciplinary committee to standardize prolapse terminology in 1993. The committee published a document describing the pelvic organ prolapse quantification system (POP-Q) which was revised and adopted by the members of the International Continence Society (ICS), the American Urogynecological Society and the Society of Gynecologic Surgeons in 1996. [40]

The Pelvic Organ Prolapse Quantification system is a standardized and objective approach used to describe, measure, and stage pelvic support in women. This system provides a consistent tool for documenting clinical findings with proven reliability among different observers and within the same observer. This quantification system has gained global recognition and approval from organizations such as the International Continence Society and the Society of Gynecologic Surgeons for characterizing female pelvic organ prolapse, becoming the preferred choice among gynecologists and urogynecologists. [20]

This method of quantifying prolapse involves using the hymen as a fixed reference point and six other defined points (Aa, Ba, C, D, Ap, and Bp), as well as considering the genital hiatus (gh), perineal body (pb), and total vaginal length (tvL). Measurements are recorded in centimetres (cm) in relation to the hymen, measurements above or proximal are negative numbers and measurements below or distal are positive numbers.[42] These measurements can be organized into a grid, as illustrated in Figure 6.

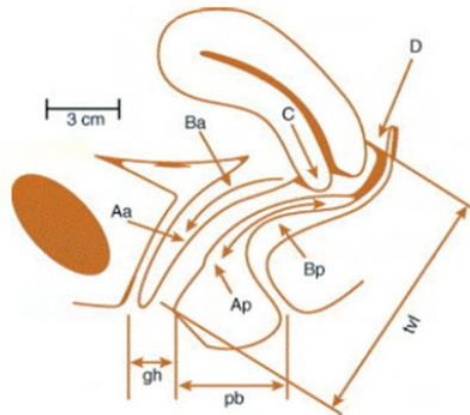


Figure 6 Points for PQP-Q system examination (adapted from [43])

According to the POP-Q, the prolapse can be classified into 5 stages [44]:

- Stage 0: no prolapse;
- Stage I: the prolapse is more than 1 cm above the hymen;
- Stage II: the prolapse is approximately 1 cm either above or below the level of the hymen;
- Stage III: the foremost part of the prolapse extends more than 1 cm below the hymen's level but does not bulge beyond 2 cm less than the entire vaginal length.
- Stage IV: vaginal eversion is fully extensive.

In a multicenter study of 1006 women age 18-83 years presenting for routine gynaecological care, 24% had normal support and 38% had stage I, 35% stage II, and 2% stage III pelvic organ prolapse. [45]

2.2.3 Causes

The cause of this disorder is likely to be multifactorial, attributable to a combination of risk factors, varying from patient to patient. Vaginal childbirth, advancing age and increasing body-mass index (BMI) are the most consistent risk factors with vaginal childbirth being the one most frequently associated with POP. Hysterectomy might heighten risk of subsequent pelvic organ prolapse; however, development of symptomatic prolapse typically happens many years after this procedure. Repetitive straining, such as that seen in patients with chronic constipation or workers whose jobs entail heavy lifting, has also been associated with pelvic organ prolapse. [46]

Variations in the orientation and shape of the bony pelvis contribute to prolapse development. Factors such as a loss of lumbar lordosis and a less vertically oriented pelvic inlet are more common in women with genital prolapse. A less vertical orientation of the pelvic inlet alters intra-abdominal vector forces, directing more pressure towards pelvic viscera and their supports. Women with a wide transverse pelvic inlet may be at increased risk due to a larger hiatus for abdominal pressure transmission, leading to the loss of pelvic visceral support. These variations also affect maternal soft-tissue damage and nerve injury during parturition. [47]

Heritable or genetic factors may play a role in pelvic organ prolapse. Data from the USA suggest ethnic differences, with Hispanic and Asian women having an increased risk of cystocele, and African-American women having a lower risk compared to white individuals. The reasons for these differences are unclear, but evidence indicates that African-American women may have smaller pelvic outlets than those of European descent. [48]

2.2.4 Symptoms

The pelvic floor has a variety of pathologies that can present non-specific and overlapping symptoms. Understanding the variation in pelvic organ support and how the degree of support relates to symptoms is essential to defining the disease state of pelvic organ prolapse.

Women with POP can be asymptomatic or have symptoms of vaginal discomfort, urination, bowel movements and difficulty with intercourse.

POP often coexists with urinary symptoms. Prevalence of any urinary incontinence rises with age, peaking in middle age. Stress urinary incontinence correlates with mild prolapse but decreases with advanced stages. [49] Urge urinary incontinence and POP don't share risk factors uniformly. Detrusor instability is more common in advanced anterior wall prolapse, with reported improvements post-surgery. [50]

Associations between bowel symptoms and POP are generally weak. Difficulty in rectum emptying, splinting and digestion is linked to posterior wall prolapse. About one-third of women with posterior wall prolapse may need digital assistance for faecal evacuation. Digital assistance prevalence is similar in stage II and stage III-IV POP-Q, indicating that advanced prolapse doesn't necessarily heighten symptoms. [51] Repairing a prolapse of the posterior wall, even if anatomically corrected, does not always solve the problem and can contribute to the functional problem, either by producing intestinal symptoms or by aggravating the disorders present. [52]

Women's sexuality and sexual function involve many dimensions, such as general physical and mental well-being, the quality of the partnership, age and the health of the partner. [53] Sexual dysfunction prevalence varies, particularly in middle-aged and elderly women with pelvic floor disorders. Recent studies suggest worse sexual function in women with symptomatic prolapse, especially those with anatomical prolapse (stage III-IV). [54]

2.2.5 Forms of Treatment

Management of POP is an important component of gynecological care. Options available for treatment include conservative management, mechanical devices and surgery. Treatment of prolapse depends on the severity of the prolapse, symptoms, the woman's general health and the surgeon's preference of approach.

Regarding physiotherapy exercises, Kegel exercises stand out as a prevalent choice during the initial stages, right from the detection of prolapse. Their primary objective is to strengthen pelvic muscles through a regimen of controlled contractions and relaxations. Patients are typically introduced to a range of these exercises during physiotherapy sessions and subsequently instructed to continue practicing them at home. [55]

Pessary devices are inserted into the vagina to reduce prolapse, to provide support to related pelvic structures and to relieve pressure on the bladder and bowel. These mechanical devices are made of silicone or plastic and have different forms and shapes. The most frequently used are the ring, ring with support, Gelhorn and donut pessaries (Figure 7). [56]



Figure 7 Various pessary types (Top left to right) Marland with support, Ring with support, Donut, Shaatz, Gelhorn and Smith-Hodge with support (adapted from [57]).

The patient should be asked to undertake various activities, including standing, walking, doing a Valsalva maneuver and bending, to ensure that the pessary is retained. It can be used for months, however, it needs to be removed at least once every three months to be cleaned as well as to assess the vagina for possible signs of erosion. [58]

The most typical side-effect of pessary use is vaginal discharge, vaginal irritation and odor. Serious complications reported with use of these devices include vesicovaginal and rectovaginal fistulas, fecal impaction, hydronephrosis, and urosepsis. [59]

All these solutions, although practically non-invasive, are only useful in the initial phase of the problem, and if the situation worsens, surgery is necessary. Surgical treatment for prolapse can be categorized into reconstructive and obliterative techniques.

Reconstructive surgery (Figure 8) for prolapse aims to correct the prolapsed vagina while maintaining (or improving) vaginal sexual function and relieving any associated pelvic symptoms. Surgery can be undertaken by either abdominal or vaginal route. [60]

The correction of apical prolapse can be achieved by abdominal sacral colpopexy, which suspends the upper vagina from the sacral promontory with synthetic mesh or by vaginal sacrospinous ligament suspension, which attaches either the upper vagina or cervix to the ligament between the ischial spine and the sacrum transvaginal. Other transvaginal apical suspension procedures include iliococcygeus ligament fixation and high uterosacral ligament suspension. [61]

For Anterior Vaginal Prolapse, a common technique is anterior colporrhaphy, involving plicating the fibromuscular layer of the anterior vaginal wall. Success rates vary (80-100% in case series, 40-60% in randomized trials). Another approach repairs paravaginal defects, reapproximating torn vaginal tissue to correct anterior prolapse (success rate: 67-100%). [62]

In addressing Posterior Vaginal-Wall Prolapse, posterior colporrhaphy, while effective, is associated with high dyspareunia rates. Alternatives include midline fascial plication or site-specific repairs with success rates of 80-100%. [63] As we could see, the wide variety of surgical treatments available for prolapse indicates the lack of consensus regarding the optimal surgical treatment.

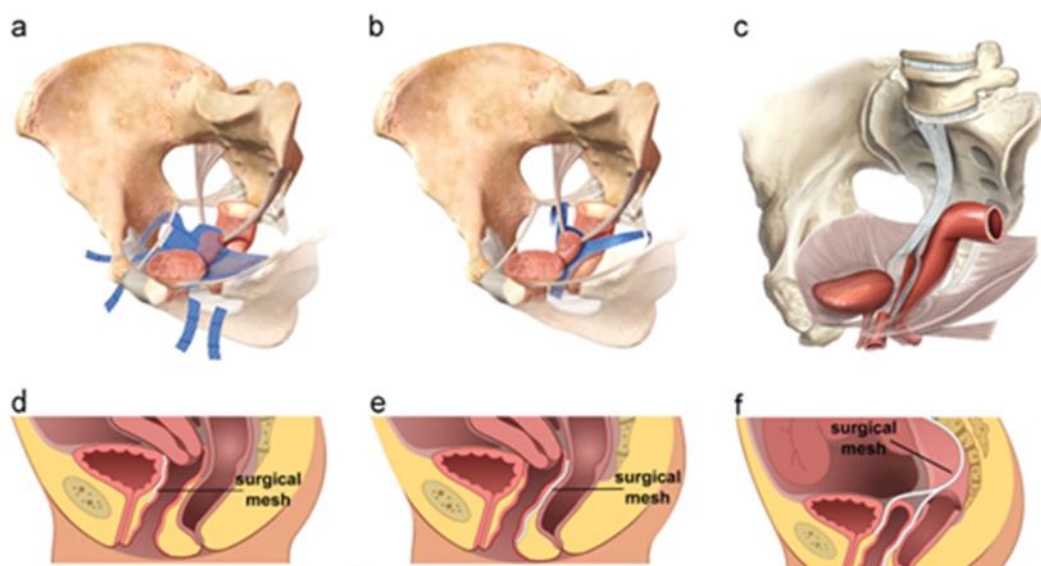


Figure 8 Surgical repair with synthetic meshes of (a,d) cystocele (bladder prolapse); (b,e) rectocele (rectum prolapse); (c,f) vaginal vault or uterine prolapse (adapted from [64])

Obliterative surgery, such as total colpocleisis or LeFort's partial colpocleisis, corrects pelvic organ prolapse by moving pelvic viscera back into the pelvis and closing of the vaginal canal either partly or totally. These procedures are usually reserved for women who are elderly, medically compromised and no longer sexually active. [65] The purported advantages of obliterative surgery in this population are shortened operative time, decreased perioperative morbidity and a very low prolapse recurrence risk. The obvious disadvantage is elimination of the potential for vaginal intercourse. Findings of a prospective study showed a substantial improvement in health-related quality of life without alteration in body image in a group of carefully selected women with stage III or IV pelvic organ prolapse who received obliterative vaginal surgery. [66]

2.3 Surgical Procedure with Synthetic Meshes

As mentioned earlier, reconstructive surgery is a treatment for POP that involves the repair with native tissue or the use of meshes. Regarding meshes, these can include biological graft meshes or synthetic meshes. [67]

Biological grafts can be classified into autografts, allografts and xenografts. Allografts are taken from human donors (usually cadavers), whereas xenografts are taken from other species (e.g. porcine dermis or porcine small intestine). [67] Allografts used in pelvic floor reconstruction usually consist of fascia. A concern with these grafts is that they are often donated by the elderly who have an age-related weakening in connective tissues. [68] Tissues are mainly from porcine and bovine that have been used in pelvic floor surgery. These materials undergo extensive processing after harvesting to decellularize them and render them non-immunogenic. Additionally, there are FDA regulations on animal source and vaccination status which must comply with. [69]

Synthetic meshes are currently manufactured from four main polymers: polypropylene (PP), polyethylene terephthalate (PET), polytetrafluoroethylene (PTFE), and polyvinylidene fluoride (PVDF). These meshes are readily available and do not require harvesting. They also lack on transmission of infectious diseases and ease of availability, as well as the sustainable tensile strength due to their nondegradable nature. [70] The material used in manufacturing the meshes can be absorbable or non-absorbable. The absorbable ones do not tend to trigger infections, but they quickly lose properties such as tensile strength, unlike the non-absorbable ones, which maintain mechanical properties and have stability for a longer period of time, but their greater stiffness can develop inflammatory problems. [71]

Surgical meshes can be designed as mono or multifilament (Figure 9). Meshes with monofilament yarns are stiffer while multifilament are softer and more flexible, however they have a higher contact surface area, and they form by definition very small pores between the individual fibers. [72]

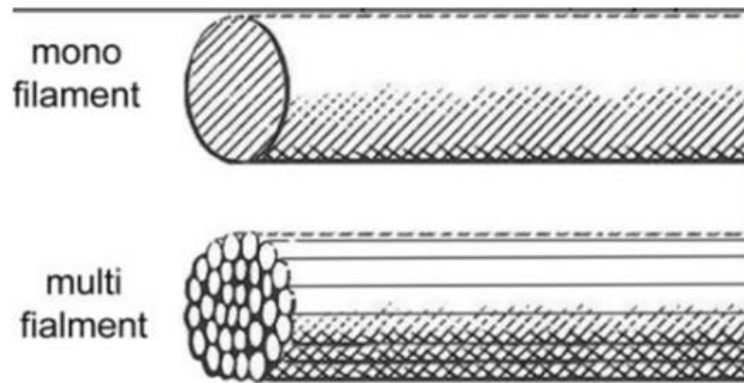


Figure 9 Fiber structure for meshes (adapted from [72])

When delving into the intricacies of mesh parameters, several pivotal factors come into play. Porosity holds paramount significance for permeability and is closely entwined with biocompatibility. The choice between monofilament and multifilament fiber filaments is equally essential. The diameter of the fiber significantly impacts cell behavior, especially in terms of adhesion and proliferation. Additionally, the weight of the mesh, categorized as lightweight, middleweight, or heavyweight, significantly influences not only mesh strength but also overall dynamics, including porosity and the potential for sensations of foreign presence and scar development.[73]

Transitioning to biodegradability, the efficacy of a mesh hinges on its ability to offer sustained support to pelvic floor tissues, ensuring long-term stability. Surgical meshes fall into two main categories: non-degradable and biodegradable. Non-degradable meshes maintain their integrity over an extended period within the body without degrading as the body metabolizes. However, the prolonged presence of non-degradable materials can lead to unavoidable complications in certain patients, such as mesh exposure and chronic pain. On the flip side, biodegradable polymers present favorable biocompatibility, fostering cell attachment and tissue remodeling. Nevertheless, biodegradable vaginal meshes encounter a challenge—early absorption into surrounding tissues can diminish their capacity to provide long-term support. Striking a balance between the advantages of non-degradable strength with potential complications and the benefit of biodegradable biocompatibility underscores the intricate decision-making process in mesh selection.[73]

The success of implants is heavily influenced by the manufacturing techniques employed. Electrospinning enables the production of ultrafine fibers, assembled as a non-woven matrix-like structure, which can physically mimic the structure of the natural extracellular matrix of most

connective tissues despite facing challenges in controlling the scaffold. [74] Knitted meshes excel in providing excellent porosity and mechanical properties, which can be fine-tuned through various knitting parameters. However, the limitation on fiber size may impact cell attachment. On the other hand, 3D printing offers precise control over mesh characteristics such as pore size and shape, but it encounters challenges like material limitations, high costs, and accuracy hurdles.[73]

In conclusion, the process of selecting materials and parameters for pelvic floor repair meshes is a nuanced task that demands a delicate equilibrium between mechanical attributes and biocompatibility. Researchers have leaned towards synthetic polymers, drawn to their robust mechanical properties and the heightened anatomical success observed in pelvic organ prolapse repair. Despite these advantages, complications and reoperation rates continue to be significant, often linked to the enlarged surface area of the mesh. Persistent issues include erosion of the vaginal mucosa, mesh retraction, infections, pain, fistulas, and complications such as persistent vaginal discharge and urinary tract disorders.

2.4 Computational Modelling

2.4.1 Finite Element Method

Invented during the mid-1950s, the Finite Element Method (FEM) provides a numerical approach to address intricate problems, particularly when traditional mathematical methods fall short due to problem complexity. Conceptually, FEM involves breaking down a substantial problem into a sequence of more manageable components, aptly named finite elements. This simplifies the investigation of complex issues and proves invaluable for engineers striving to design solutions that meet specific practical needs, even if absolute perfection is unattainable. [75]

The finite element discretization procedure involves dividing a continuum (solid, liquid, or gas) or a region of space into elements. The unknown field variable is expressed in terms of assumed approximating functions within each element. These functions, often called interpolation functions, are defined by values at specified points called nodes. Nodes are located on element boundaries, where adjacent elements connect, and may also be placed within the element. Nodal values and interpolation functions completely define the behavior of the field variable within the elements. The nature and accuracy of the solution depend on the size, number, and interpolation functions of the elements used. These functions are chosen to satisfy compatibility conditions, ensuring continuity across element boundaries. [76]

For the finite element representation of a problem, the nodal values associated with the field variable become the unknowns. After determining these variable values, the interpolation functions define how the field variable behaves across the entirety of the element assembly. The nature of the solution and the extent of approximation are influenced not solely by the quantity

and size of the elements employed but also by the specific interpolation functions chosen. These functions cannot be chosen arbitrarily, as they need to adhere to certain compatibility conditions, often selected to ensure the continuity of the field variable or its derivatives across the boundaries where elements connect. [76]

An important feature of the finite element method, setting it apart from other numerical methods, is its ability to formulate solutions for individual elements before combining them to represent the entire problem. Treating a problem in stress analysis, for instance, involves finding the force-displacement characteristics of each individual element and then assembling the elements to find the stiffness of the entire structure. Essentially, a complex problem reduces to a series of greatly simplified problems. Another advantage of the finite element method is the variety of ways in which one can formulate the properties of individual elements. [77]

The analyst's true ability lies in building a model that simulates reality without exceeding finesse in points of little structural interest, identifying constraints and loads reflecting the physics of the problem. A successful application of FEM necessitates a strong theoretical knowledge guiding the choice of elements based on the analysis to be conducted and a critical interpretation of results considering the method's limitations. Constant attention to experimental analyses is necessary for validating hypothesized approximations. Bioengineering and biomedical investigations, especially in prosthetics and dentistry, significantly contribute to FEM applications.[78]

The stages of realizing a finite element model are as follows:

- (i) Preparation of the geometric model
- (ii) Discretization of the entire volume into finite elements
- (iii) Assignment of the mechanical properties of the materials
- (iv) Identification of the boundary conditions
- (v) Choice of the type of solution (static or dynamic analysis, linear or nonlinear, etc.)
- (vi) Analysis of the results. [79]

2.4.2 Finite Element Analysis

The Finite Element Method is practically applied through a simulation known as Finite Element Analysis (FEA). This simulation is crucial for conducting structural evaluations to assess how specific products or designs respond to real-world stress conditions.

Finite element analysis is a technique that virtually reproduces, from a physical-mechanical point of view, a real condition for studying the interaction between different objects and predicting their mutual behavior under certain load conditions and stress. It is a technique that derives from engineering and is still applied to many fields of the mechanical and aeronautical industry and also in the biomedical sector. Normally, this type of analysis, given its difficulty, is limited to biomedical devices before their industrial production to verify their mechanical properties in relation to their shape. [80] There are various typologies of prosthesis: these are

examined by FEM before their production to verify their correspondence with the biomechanical criteria that they must face once implanted. However, the use of FEM has gradually expanded also in the medical sector for the study of mechanically active anatomical parts. [81]

FEA was initially developed in the early 1960s to solve structural problems in the aerospace industry but has since been extended to solve problems in heat transfer, fluid flow, mass transport, and electromagnetics. In 1976, Weinstein and his team were the first to use FEA in medicine, dentistry implant in this case. Atmaram and Mohamed analysed the stress distribution in a single-tooth implant to understand the effect of elastic parameters and geometry of the implant, implant length variation, and pseudo-periodontal ligament incorporation. Borchers and Reichart⁵ performed a 3-dimensional FEA of an implant at different stages of bone interface development. Cook et al⁶ applied FEA to porous rooted. [82]

FEA dissects the complete model into smaller elements within a mesh, allowing for the evaluation of distinct design components under simulated stress factors. This analysis can be performed on tangible objects or models emulating real-world scenarios. Utilizing models instead of real objects enables earlier analysis, even before physical prototypes are constructed. Models can take various forms, such as physical renditions (mock-ups, scaled-down models, or photoelastic models) or mathematical constructs. Simple mathematical models can be solved analytically, while more intricate models require numerical approaches, with FEA being a prominent technique. In engineering practice, the terms Finite Element Analysis and Finite Element Method are often used interchangeably. [80]

FEA has a historical foundation in studying structural phenomena related to the stiffness, strength, and elastic stability of bodies. Manufacturers across various industries, including biomedical, aviation, civil, and structural engineering, have harnessed this method for structural calculations. In the medical field, FEA can address emerging problems, such as the design and performance analysis of medical devices, offering opportunities for improvement and optimization. [79]

FEM and FEA permit engineers to enhance precision and improve the design of the product, which means, the amalgamation of FEM and FEA yields heightened precision in structural analysis by illuminating intricate interactions among the various components of a design. Furthermore, they afford engineers the opportunity to scrutinize both the internal and external aspects of a design with meticulousness. Another advantage is the possibility to accelerate testing in a cost-effective way, by enabling the craft of virtual simulations, diminishing the necessity for physical testing and the construction of prototypes. Moreover, FEM and FEA have many applications in various fields, such as civil and aerospace engineering, biomechanics, biomedical engineering, electromagnetics, and other disciplines. [77]

2.4.3 Medical Applications of Finite Element Method

FEM proves to be an invaluable asset in the medical device arena, particularly in early device performance testing and reducing bench testing iterations. However, challenges exist, primarily requiring high expertise to navigate computational platforms and the revision of established product development strategies to integrate FEM into the early design phase, posing a significant effort for companies. Despite this, FEM has become a vital tool in medical equipment design processes.[83]

One notable application of FEA in the field of medicine revolves around the study of mesh anchoring techniques in uterine prolapse repair surgery, conducted by Silva et al. in 2021. The goal of the study was to evaluate the behavior of synthetic implants during the Valsalva maneuver, a diagnostic test used to assess pelvic floor function. Specifically, the study aimed to assess implants used to replace damaged uterosacral ligaments (USLs), simulating sacrocolpopexy repair. The researchers conducted uniaxial tests on two types of synthetic implants (A and B) to determine their mechanical properties, which were then incorporated into computational models. These models were integrated into a female pelvic cavity model to simulate the effects of total rupture or impairment of the USLs on pelvic floor displacement. The study analyzed variations in vaginal displacement (Figure 10) under different conditions, including total rupture and impairments of the USLs, as well as the impact of implantation on reducing these displacements.[84]

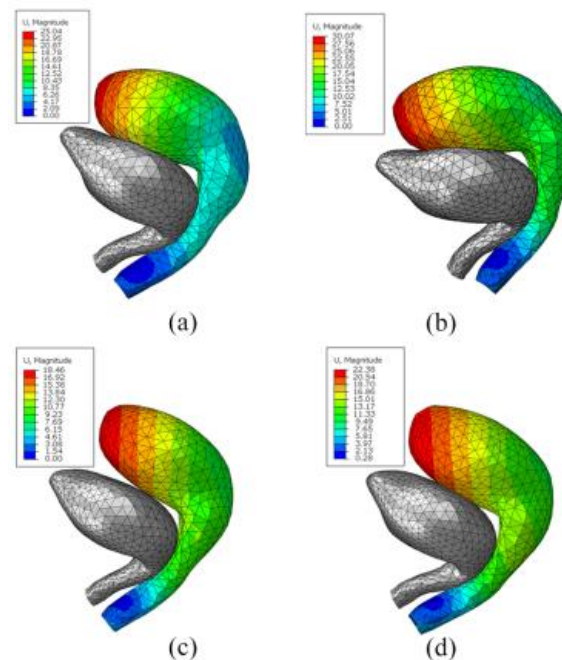


Figure 10 Displacement magnitude (mm) of the uterus: (a) asymptomatic case, (b) when a total rupture of the uterosacral ligament occurs, (c) insertion of the mesh implants A to correct a total rupture of the uterosacral ligament, and (d) insertion of the mesh B. (adapted from [84])

Finite Element Analysis plays a crucial role in dentistry by predicting stress and strain distribution on teeth, implants, and surrounding bones, addressing challenges not easily resolved in vivo. This method aids in studying the optimization of various dental components such as fillings, crowns, implants, dentures, and bridges. Additionally, FEA enables the examination of interactions among supporting structures of the stomatognathic system, the assessment of residual stresses resulting from mechanical and thermal expansion in dental materials, and the investigation of physiological and biochemical effects of chewing forces and occlusal forces on teeth, along with stress concentration phenomena.[83]

Furthermore, the Finite Element Method extends its applications to various medical fields, including orthopedics and cardiovascular surgery. In orthopedics, Finite Element Analysis aids in understanding joint behavior and complex articular biomechanics, contributing to advancements in treatment and surgical techniques.[83]

The application of Finite Element Analysis for Medical Device Design enables designers and engineers to efficiently upgrade designs. FEA, in combination with CAD software, proves to be a cost-effective and time-saving tool for quick redesigns, mitigating the risk of potential accidents. With advances in computer equipment and software packages, FEA plays a crucial role in managing the risks of medical equipment design processes, significantly accelerating the time required for the concept to reach the production stage. Improved initial prototypes reduce the time and number of cycles required for testing and development.[83]

The advantages of FEM in the medical device arena are numerous, notably in enabling early device performance testing, reducing bench testing iterations, and potentially performing bench testing via FEM or in silico instead of on the bench side or ex vivo. However, challenges persist, primarily related to the high expertise required to navigate computational platforms and the need to revise established product development strategies for successful FEM integration into the early design phase, which requires considerable effort for companies. Thus, FEM is gradually shifting its perception from being solely a research tool to becoming an indispensable development asset.[83]

2.5 Rapid Prototyping

The advent of rapid prototyping (RP) processes in the late 1980s has introduced transformative possibilities for cost-effective and swift production of functional prototypes. This promising technology has the potential to revolutionize various aspects of the dynamic and challenging field of medical science. RP involves the construction of prototypes or working models in a relatively short time, facilitating the exploration and testing of different design features, ideas, concepts, and functionalities, ultimately influencing outcomes and performance. The technology is known by various names, such as digital fabrication, 3D printing, layer-based manufacturing, laser prototyping, and additive manufacturing.[85]

2.5.1 Medical Applications of Rapid Prototyping

In the realm of medical applications, 3D printing technology has become ubiquitous, encompassing dentistry, anatomical models, medical devices, tissue engineering scaffolds, tissue models, and drug formulation.[86]

Dentistry stands out as a leading field in integrating 3D printing for producing end-use products such as restorations, dental models, and surgical guides. Following closely, medical devices have witnessed substantial growth, with over 85 3D-printed medical device products currently available in the market, ranging from implantable items like bone tether plates and hip cups to non-implantable products like spinal cages, knee implants, denture bases, craniofacial implants, and surgical instruments (Figure 11). Notably, approximately 99% of hearing aid shells are custom-built using 3D printing technology.[87]

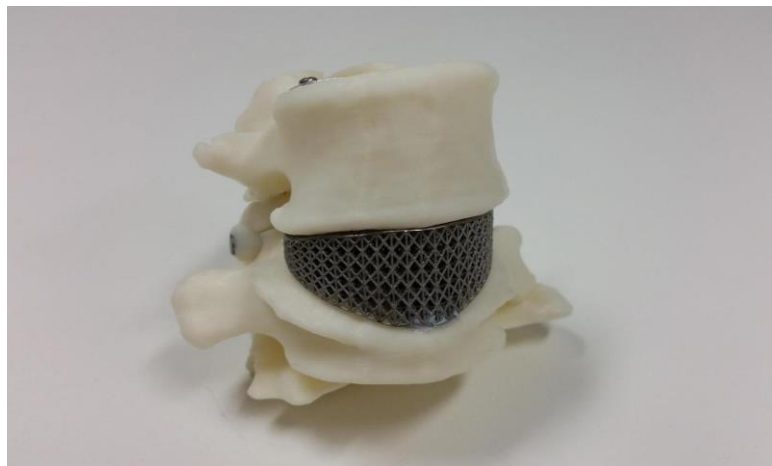


Figure 11 Spinal implant cage (adapted from [88])

In the cardiovascular field, 3D printing facilitates the rapid adaptation of medical systems for treating diseases of the circulatory system. Complex models of the cardiovascular system can be illustrated through printed models, allowing better planning for upcoming surgical interventions and enhancing the medical learning process. The technology also expands technical possibilities in medical teaching, complementing cadaveric dissection. Improved visualization of surgical

procedures through 3D models not only aids medical professionals, especially surgeons, but also enhances patient understanding, resulting in increased satisfaction. [89]

Engineered human tissue models have a particular focus on cancer, liver and skin. In liver models, for example, the aim is to replicate the complexity of liver architecture for drug testing and high-throughput drug screening. AM techniques such as Digital Light Processing 3D printing, extrusion-based direct cell writing and inkjet printing enable the precise organization of cells, allowing the creation of liver tissue models with hexagonal patterns and microfluidic chambers for drug metabolism studies. [90]

Conventional fabrication methods such as freeze-drying, molding, and electrospinning are utilized to produce tissue engineering scaffolds. In the context of functional tissues and organs, these scaffolds play a vital role by providing structural support for cell attachment, migration, proliferation, and extracellular matrix production. The ideal scaffolds should possess characteristics like biocompatibility, bioactivity, mechanical strength, porosity, and biodegradability, with tunable degradation rates. [91]

2.5.2 MEW

The integration of electrospinning methods, particularly in regenerative medicine, has ushered in transformative possibilities. The creation of constant, fine fibers has become pivotal, especially in intricate constructions. The convergence of electrospinning and Additive Manufacturing (AM) systems, notably in the form of melt electrowriting (MEW), has led to a symbiotic relationship between the two domains. [92]

In the context of this thesis, 3D printing applications based on melt electrowriting process will be discussed. Here we inevitably come across Electrospinning (ES), which is similar to MEW in its operation principles, but the structures produced are different (Figure 12). While ES produces loosely oriented fibres in the lower μm range that are laid on top of each other without a fixed orientation, in MEW we aim at a defined laying of fibres with a constant diameter in the range 50 to 350 μm , whereby we precisely specify the underlying geometry.

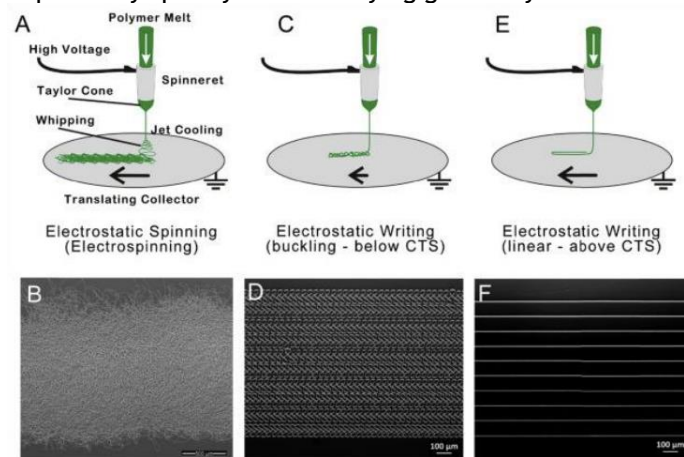


Figure 12 Principle of electrospinning and melt electrowriting with fibre patterns below and above critical translation speed (adapted from [93])

In the industrial sector, ES is already being used in filter technology to produce highly porous filters made of nonwovens nano fibres. Other areas of application are carrier materials for catalysts or tissue cultivation. The advantage of ES is the easily controllable structural parameters, which include the fibre diameter in the μm or nm range, the nonwoven architecture, and the porosity. [94] While ES deposits the fibres on a non-moving print bed, MEW uses a moving print bed, which enables targeted and directionally controlled deposition of polymer fibres. [95]

While ES uses polymer solutions, melt electrowriting uses polymer melts. The use of polymer solutions in ES has the disadvantage that medical application becomes less attractive due to toxic solvents and post manufacturing. By adding a movable print bed for MEW, we obtain a printing process that enables a wide variety of creating 3-dimensional structures made of fibres in the μm range. MEW is usually used to create scaffolds from biocompatible polymers. [95]

MEW has emerged as a crucial technology in additive biomanufacturing, particularly in creating meshes and scaffolds for biomedical devices. Traditional concepts involving 3D printing and electrospinning have evolved into bi-modal scaffolds with an external structure from Fused Deposition Modeling (FDM) and an inner section comprising electrospun fibers to induce cell adherence. [96]

The mobility of MEW is achieved by displacing the collecting plate relative to the spinneret, with designs generated through computer commands, similar to 3D printing. Overlapping is possible, allowing for the development of thicker sections. The versatility extends to the collector, where a rotating mandrel can be used to generate tube-like constructs. [96]

The parameters influencing fiber production in MEW can be categorized into material parameters, process parameters, and ambient parameters. A detailed analysis of these parameters reveals their significant impact on the shape and diameter of the produced fibers.

Material Parameters:

Viscosity/Molecular Weight: Viscosity plays a crucial role, and the viscosity of the polymer is particularly important in MEW as no solvent is involved. Molecular weight affects viscosity through chain entanglements, with reduced molecular weight leading to higher melt flow rates.

Electrical Conductivity: Electrical conductivity is essential for electrohydrodynamic processes, and in MEW, a suitable range of conductivity is required for fabricating continuous fibers. [92]

Process Parameters:

Nozzle Temperature: Elevated temperatures are necessary for efficient spinning, and spinneret temperature affects the viscosity of the polymer.

Applied Voltage: High voltage in MEW results in the production of continuous fibers. Voltage needs to be carefully controlled to avoid instabilities that may lead to bead formation.

Nozzle to Collector Distance: The distance between the spinneret and collector affects the electrical field intensity and restricts the altitude of the jet. Choosing a midway value is ideal for optimizing thinning effects.

Collector Speed: Collector velocity significantly impacts MEW deposition precision, with a critical translation speed determining the creation of straight fibers.

Collector: The collector's role is more critical in MEW, influencing residual charge elimination and kinematic accuracy on moving collectors. The choice of a conductive or insulating collector affects fiber buildup.

Extrusion Rate: Flow rate is considered the most essential factor influencing fiber diameter. Increased flow rate results in denser fibers.

Ambient Parameters:

Temperature: Increased ambient temperature inhibits heat transmission at the jet, delaying fiber solidification and allowing for greater thinning.

Humidity: Moisture in the environment affects polymers differently based on their hydrophobic or hydrophilic nature.

Chapter 3

Materials and Methods

This chapter addresses the materials and the methodology adopted to perform simulations on the computational models developed, as well as the mechanical tests done on a medical-grade PCL (polycaprolactone) mesh, and on the sow's vaginal tissue.

3.1 Materials

3.1.1 Technical PCL

Polycaprolactone (PCL), an FDA-approved polymer, has garnered significant attention for its application in 3D printing processes, particularly in Melt Electrowriting spinning. This popularity is attributed to its favourable characteristics, such as a low melting temperature and rapid solidification, making it an ideal choice for MEW. [97] Falling under the poly- α -hydroxy acid group, akin to polylactic and polyglycolic acids, PCL is a biocompatible, biodegradable, and bioresorbable polymer with a rich history dating back to its synthesis in the early 1930s through ring-opening polymerization of ϵ -caprolactone monomers. [98]

This hydrophobic, semi-crystalline polymer exhibits distinctive features, including a glass transition temperature of -60°C and a low melting point ranging from 59° to 64°C . Notably, PCL boasts superior viscoelastic properties compared to other biodegradable polymers, facilitating ease of manufacturing and manipulation, allowing for a diverse array of structures. [97]

In contemporary biomedical applications, PCL has established itself as a material of choice, finding utility in resorbable sutures, drug delivery systems, and tissue engineering scaffolds. Its prolonged hydrolytic degradation rate positions PCL favorably for long-term applications. Additionally, PCL has demonstrated its ability to support cell attachment and proliferation, further enhancing its standing in the biomedical field. [99]

The biodegradable meshes were printed using the technical PCL from Filament-PM. It is important to mention that during the printing process, the temperature and humidity were controlled.

3.1.2 Sow's Tissue

Although animals have been used in biomechanical investigations since the times of the ancient Greeks, their use in scientific research in injury biomechanics did not develop until the mid-20th century. Given the ethical and practical limitations on subjecting human volunteers to subinjury threshold testing, animals emerge as the most viable surrogates for studying the pathophysiological responses to impact injuries and comprehending the aftermath of such incidents. [100]

In the last decade, a few papers have shed light on the potential of pigs as ideal experimental animals for medical research, highlighting that pigs exhibit remarkable similarities to humans. While physical appearances distinguish pigs from humans, the biological analogies between the two are extensive, establishing pigs as physiologically the nearest animals to humans, with very few exceptions. [101]

For this study, DGAV - Direção-Geral da Alimentação e Veterinária, Porto, Portugal (protocol: N19128UDER) gave full approval to collected sow's vaginal tissues (Figure 13) at the slaughterhouse (Euroabate - Matadouro Industrial, Lda, NCV D 42, in Marco de Canavezes, Portugal). These procedures adhered to the regulations outlined in Regulation (EC) No. 1069/2009 dated 21 October.

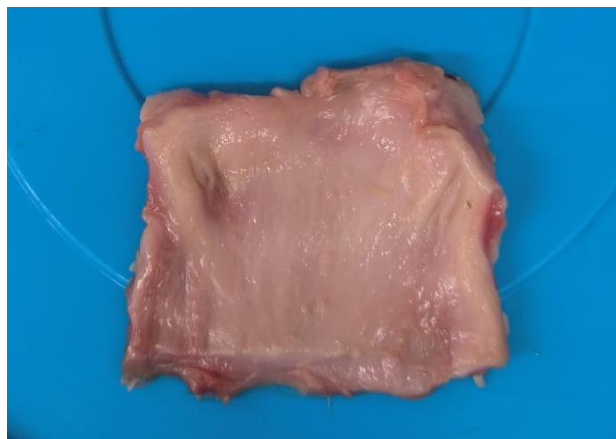


Figure 13 Sample of the vaginal tissue.

3.2 Instruments and Tools

Various instruments played a crucial role in both the experimental procedures and the construction of computational models for our biodegradable meshes. The Laboratório de Desenvolvimento de Produtos e Serviços (LDPS) at FEUP generously provided all the necessary instruments, with the exception of the "Mecmesin Multitest 10-í" machine used for the uniaxial tensile test and for the ball burst test of vaginal tissue (Figure 3.5) and the meshes, which was accessible at INEGI's laboratory.

Let's explore these essential instruments in detail:

- **NCViewer Software:**

This is a G-code simulator that interprets G-code and allows its edition.

- **Melt Electrowriting Device:**

This device was employed to print meshes and filaments (Figure 14). Recently, the device underwent adaptation with a pellets' extruder, aiming to print meshes with technical PCL, only available in pellets. The printer, constructed from aluminum, comprises a collector plate with X-Y movement for material deposition. It also features a Z-movable print head from where the material passes through, due to a heating mechanism that melts the material in a spinneret. With one electrode connected to the collection plate and the other to the nozzle, the high voltage supply is separated from the equipment. To prevent electrical disturbance and device failure, the equipment design incorporates electrostatic discharge (ESD) measures, with all regions isolated from the charged electrode being grounded. [102] These components are linked to an external high-voltage power supply via electrodes. Instructions are established through a computer and a translation system to define the intended direct writing patterns. [103]

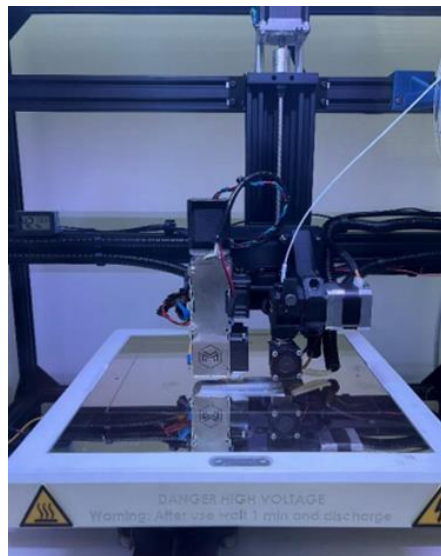


Figure 14 Melt electrowriting device.

The controller board stands out as a pivotal module in the MEW device, as it orchestrates the device's actions by interpreting inputs (such as G codes and equipment status) and generating corresponding outputs (commands for the movement of the collection plate, printing head, nozzle temperature, and location). The Duet 3D 2.0 Ethernet controller has been implemented in this machine, chosen from a variety of controller units available in the market. [102]

Facilitating the electrospinning process, the high-voltage source is a 60kV - 150W positive high voltage generator. This source interacts with the operator through a touchscreen LCD or a web interface, providing a user-friendly interface for control. Additionally, it boasts a minimum output current of 0.01mA, ensuring precision in the electrospinning process. [102]

- Temperature and Humidity Control:

Stability in temperature and humidity during electrowriting device trials was crucial. We utilized a digital thermometer and hygrometer for this purpose (Figure 15).



Figure 15 Temperature and Humidity control.

- Optical Microscope:

High magnification pictures of the fibers produced by the melt electrowriting device were collected using a binocular optical "Zeiss Axiophot Microscope" (Figure 16).



Figure 16 Binocular optical microscope.

- Fibre Measurement Software:

Olympus Stream software provided intelligent step-by-step work processes to acquire crisp, defined images ready for quantitative measurement and professional dissemination. It was used to make measurements in microscopic images of the meshes.

- Mechanical Tests Machines and Software:

For the uniaxial tensile test on the printed filaments, we utilized the “Mecmesin Multitest 2.5-dv” machine equipped with a 100 N load cell setup and a constant elongation rate of 10 mm/min (Figure 17). Data acquisition during these tests was efficiently managed through the "VectorPro Lite" software.



Figure 17 Uniaxial tensile test machine used to perform uniaxial tensile tests.

In addition to uniaxial tensile tests, we conducted both uniaxial and ball burst tests on the vaginal tissue and the meshes using the “Mecmesin Multitest 10-í” machine (Figure 18). For the uniaxial test, a 100 N load was applied, and a constant elongation rate of 10 mm/min was maintained. For the ball burst test a compression of 10 mm/min was used. These tests provided valuable insights into the mechanical properties and performance characteristics of both the vaginal tissue and the meshes under specific loading conditions.



Figure 18 Ball burst and uniaxial tensile test machine.

- Abaqus® Software:

For the development of computational models, we relied on Abaqus software v.2021 (Dassault Systemes Simulia Corp., Providence, RI, USA).

3.3 Mesh Prototyping

In this chapter, we delve into the comprehensive procedures employed in the fabrication of meshes, a crucial component in addressing pelvic organ prolapse. To gain a profound understanding of the desirable characteristics for these meshes, an exploration of existing ones and those historically employed for diverse cases of pelvic organ prolapse becomes imperative. Ideally, the mesh thickness should range between 0.08 mm, 0.16 mm, and 0.24 mm, aligning with dimensions documented in relevant literature. Additionally, the mesh pores, with an approximate size of 2.00 mm, are strategically designed to promote optimal cell growth, thereby correcting the prolapse condition. [104]

It's worth noting that meshes featuring smaller pores, specifically less than 1.00 mm, and low porosity may induce heightened inflammation and foster the development of connective tissue, leading to patient discomfort. This concern doesn't apply to meshes with pore sizes exceeding 1.00 mm, considered as having large pores and high porosity. Conversely, mesh contraction, indicated by pore collapse, is associated with vaginal pain. Usually, problematic areas for patients with pain are where the mesh pores collapse following tension forces. This collapse not only increases discomfort but also hampers cell growth during the initial phase until the mesh undergoes degradation. Therefore, the ability to control and predict pore behavior under exerted

forces is crucial for achieving optimal compatibility between the mesh and the patient's tissues. [105]

In the context of this thesis, my exploration extends to meshes featuring a pore size of 1.5 mm, coupled with varying thicknesses of 0.08 mm, 0.16 mm, and 0.24 mm. Additionally, these meshes will exhibit distinct shapes, including both quadratic and cross configurations (Figure 19). This investigation aims to contribute valuable insights into the development of meshes, aligning with the specified dimensions, and their potential applications in addressing pelvic organ prolapse.

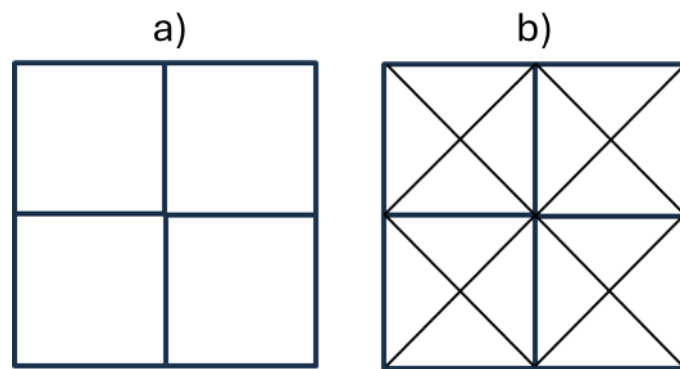


Figure 19 Meshes pore geometries. a) quadratic and b) cross.

3.3.1 Geometry Conception

The design process involves translating a concept into a code readable by a printing device. In the realm of surgical meshes, the design possibilities offered by Additive Manufacturing (AM) present significant advantages compared to traditional manufacturing methods. AM allows meshes to be built in multiple layers, with fibers firmly interconnected at overlapping points. This enables the connection of numerous layers with diverse functionalities, simulating three-dimensional biological structures. In contrast to traditional meshes, where the thickness is determined by the fibers and the manufacturing process, AM allows for customizable thicknesses or heights.

A specific G-code for the Melt Electrowriting device was necessary to design meshe's geometries. G-code is a set of instructions that outlines how an object should be printed, providing a blueprint for the printing device's movements and control of its actuators. The developed G-code was continuously written in NCVIEWER, facilitating real-time visualization of the generated geometries and enabling easy corrections to the designs (Figure 20). To help write the G-code, the open-source FullControl software was utilized.

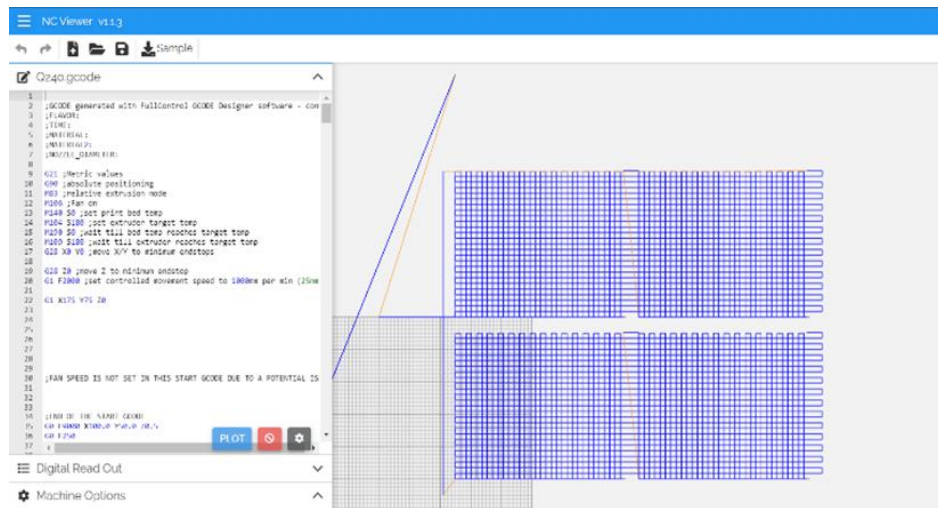


Figure 20 NC Viewer software used to develop the G-code

With FullControl, function-controlled print paths can be created that would be almost impossible to realize with manual creation of the G-code or would at least require complex spreadsheet calculations of individual printing points (Figure 21). The print path can be created by a different number of partial segments, influencing the accuracy of the geometry. Another, advantage of G-codes created by FullControl is the automatic determination of the corresponding amount of filament used for each sub-segment.

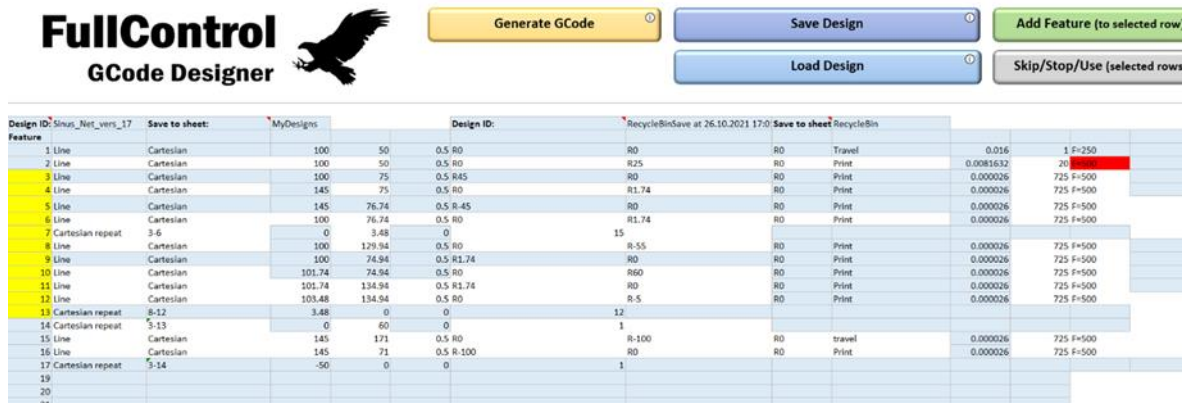


Figure 21 FullControl software used to assist in creating the G-code

3.3.2 Mesh Manufacturing

The print parameters are constant values that don't vary while printing and are determined before the print. Figure 22 shows the schematic structure of MEW and supplies an overview of the print parameters.

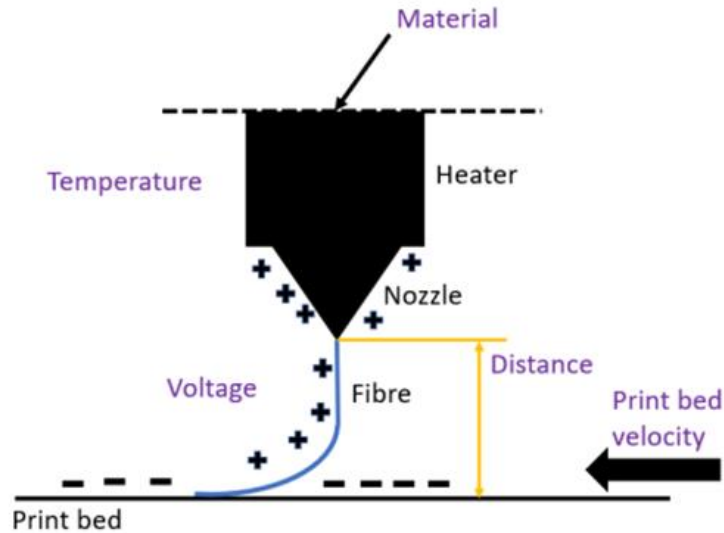


Figure 22 Melt eletrowriting principle with print parameters.

The temperature is closely related to the choice of material and approximately defines the temperature of the polymer in the nozzle. For PCL, as already mentioned, the melting point is around 60 °C. In the literature and in the data sheets of PCL filament manufacturers, different printing temperatures of 70 °C to 180 °C can be found. Rheological investigations on PCL show a simultaneous decrease in viscosity with an increase in temperature. This reduction in viscosity can have a positive effect on the printability of the polymer, as the flow behaviour within the nozzle can be improved by the reduction in viscosity. [106] In this work, a temperature of 180 °C will be used.

The voltage between the nozzle and the printing bed creates an electric field that charges the polymer flow and pull it towards the printing bed. The lower limit of this parameter is a minimum voltage value at which the polymer is attracted to the print bed. This lower voltage value is set at 3.25 kV to detect any noticeable influence of the voltage on the polymer flow. The upper limit of the parameter depends on the distance between the nozzle and the print bed. If the voltage reaches the maximum value for a defined distance between the nozzle and the print bed, lightning strikes occur, and the print is stopped automatically. The two parameters distance and voltage must therefore be precisely matched to each other. [107].

Another limiting factor for the voltage is the fibre diameter. A small fibre diameter at high voltages leads to a spinning effect on the polymer jet, which we must avoid since our desired geometry can no longer be replicated.

If we look at the distance between the nozzle and the print bed 0.17 mm to 300 mm are recommended depending on application. As already mentioned, the upper and lower limits of the voltage depend on the selected distance. [107] If the distance is too high it can also lead to increasing jet lag. Preliminary tests have already shown that increasing the distance between the nozzle and the print bed drastically worsens the print result and the geometric accuracy. A distance that is too small also leads to poorer results, as the polymer jet cannot form completely and does not transfer the corresponding movement of the print head clean to the polymer jet. For a distance of 3 mm between the nozzle and bed, lightning strikes occur at around 3.40 kV.

Print bed velocity is particularly important for reproducing desired geometries. The speed should be above the Critical Tangential Speed (CTS) to avoid patterns induced by independent swinging of the polymer jet. In the MEW, patterns represent oscillations of the polymer flow that lead to wavy, circular, or curly geometries, impairing the actual print path. Since the goal is to create desired geometries through the print path, the lower limit for travel speed is above the CTS. If the translation speed is too high, it also leads to an impairment of the print path, as the desired geometry is usually no longer reproduced, and the polymer stream is dragged across the print bed. [107] In this case, a bed velocity of 1500 mm/s will be employed.

The collection surface, critical for the process, is a 3 mm thick square-shaped aluminum plate with a surface area of 270x270 mm. Given its role as an electrode, maintaining electrical field uniformity across the entire collection region is paramount. Aluminum, known for its high electrical conductivity, was a judicious choice for this purpose.

Before transitioning to mesh production, another parameter, polymer flow rate (Extrusion rate), must be considered. The fiber diameter is determined by the extrusion rate, which is the amount of polymer extruded from the print head in relation to the travel distance of the print bed. Exact knowledge of the fiber diameter is necessary for precise stress calculation. The amount of filament required to print a fiber with a specific diameter is determined by the extrusion rate (Er) and can be calculated according to equation (1), assuming a constant volume between filament and printed fiber.

$$Er = \frac{D_{Fiber}^2 l_{Fiber}}{D_{Filament}^2} \quad (1)$$

With l_{Fiber} for the total length of a printed fibre.

While the Extrusion Rate (Table 2) can be determined using the provided equation, it's essential to note that the calculation method in FullControl differs (Figure 23). In this software, the user specifies the amount of material to be extruded by defining the cross-sectional area of the extrusion through the width and height parameters, equation (2). For simplicity, a rectangular cross-section is assumed. To accurately derive the extrusion rate value in G-code,

the Er was calculated initially, and subsequent adjustments were made to the extrusion width and height until the desired values were achieved. This process involved a trial-and-error method in order to fine-tune the parameters for optimal results.

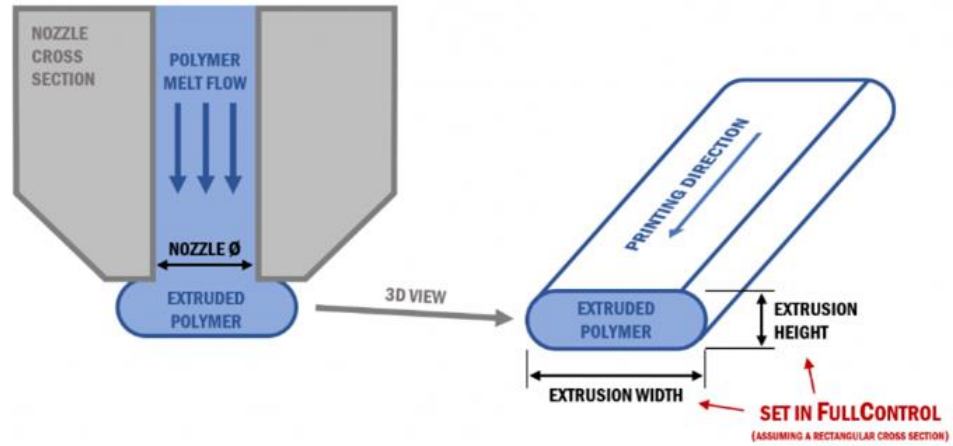


Figure 23 Extrusion rate calculation method in FullControl software.
(adapted from [84])

$$Er = Extrusion\ width * Extrusion\ height \quad (2)$$

Process Parameters:

- Nozzle Temperature: 180 °C
- Nozzle and Bed distance: 3mm
- Applied Voltage: 3.40 kV.
- Collector Velocity. 1500 mm/s
- Ambient Temperature: 21.5°C
- Humidity: 49%
- Collector: Allumnium

Table 2 Extrusion rate of each mesh

Geometry	Diameter Fiber(μ m)	Length(mm)	Extrusion Rate
Quadratic	80.00	50.00	0.10
	160.00	50.00	0.42
	240.00	50.00	0.94
Cross	80.00	70.00	0.15
	160.00	70.00	0.59
	240.00	70.00	1.32

3.3.3 Printing Production

Upon finalizing the printing parameters and generating the requisite G-code, the production of meshes with dimensions of 80, 160, and 240 micrometers, featuring both with square and cross configurations, becomes achievable (Figure 24).

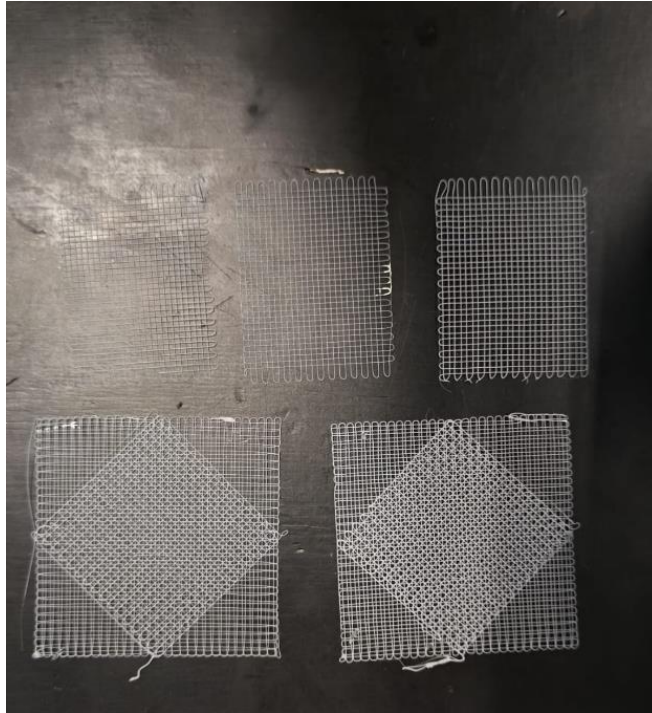


Figure 24 Printed meshes (top left to bottom right: 80 μ m, 160 μ m, 240 μ m, 160 μ m and 240 μ m)

Considering the delicate nature of meshes with 80-micrometer fibers, it was collectively agreed that these ultra-thin and fragile meshes would not undergo testing. Consequently, these meshes will not be further discussed or subjected to subsequent testing procedures.

The meticulous inspection of both fiber diameters and pore sizes is essential to ensure they match the planned specifications (Figure 25). For that, the utilization of the Zeiss Axiophot Microscope proves essential in this quality control process, enabling a thorough examination of mesh structure. This examination not only validates the accuracy of the 3D printing process but also ensures that the obtained dimensions faithfully match the intended design.

With the meshes produced and verified, we can now proceed to the next phase of this work, which involves obtaining the mechanical properties of both the fibers and the sow's vaginal tissue.

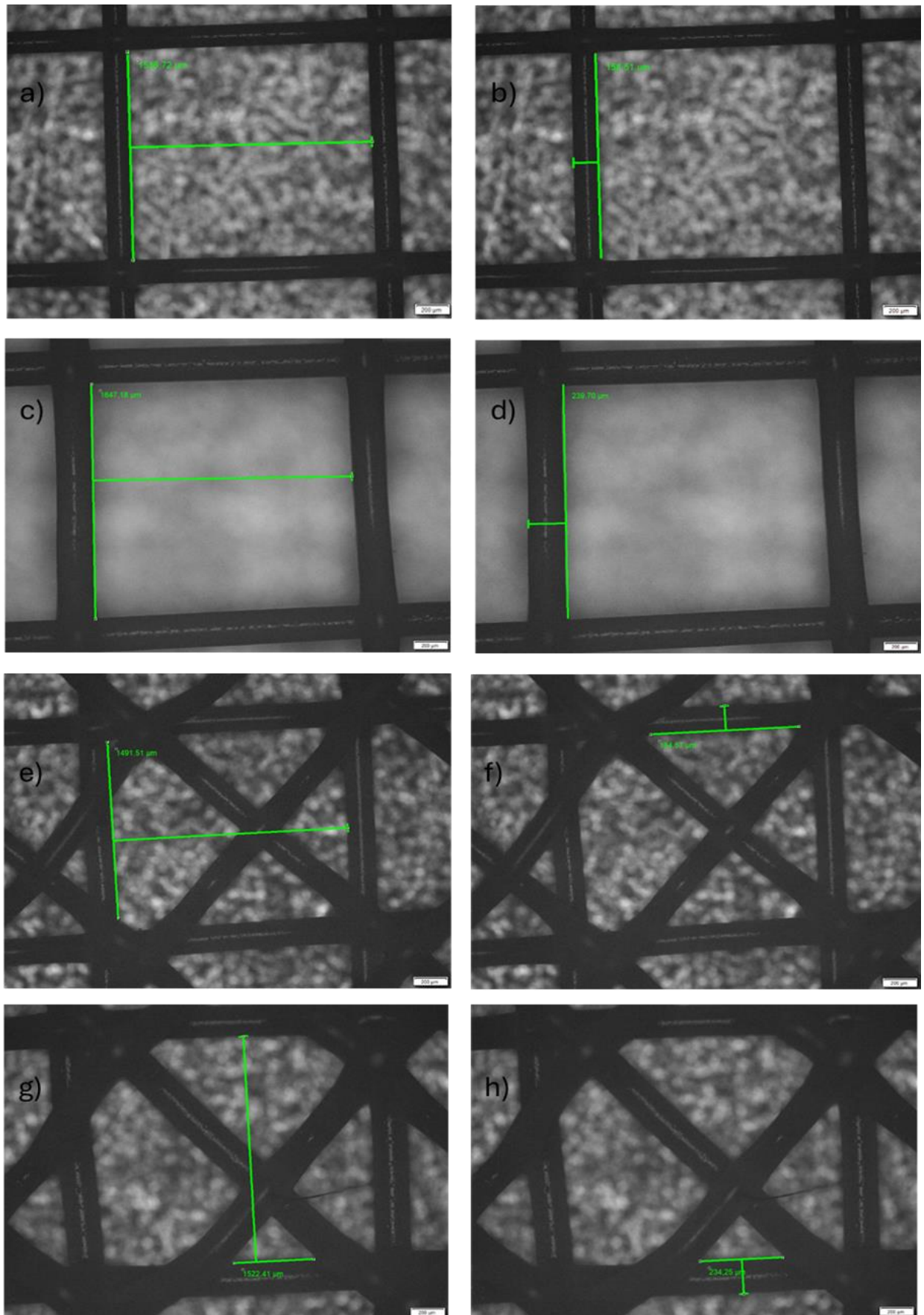


Figure 25 Meshes pore size and fiber diameter. a) b) 160 μm quadratic, c) d) 240 μm quadratic, e) f) 160 μm cross and g) h) 240 μm cross.

3.4 Mechanical Tests

3.4.1 Tensile Test

Uniaxial test is a fundamental method employed in materials testing, providing valuable insights into the mechanical properties of a specimen. In this process, the specimen is subjected to a force along a single axis, either in tension or compression, until it reaches the point of failure. The continuous monitoring of the force applied and the resulting displacement between the grips of the testing machine allows for the observation of critical properties.

Through uniaxial testing, researchers and engineers can directly evaluate parameters such as the ultimate tensile or compressive strength, as well as changes in the specimen's length and cross-sectional area. These measurements serve as the foundation for calculating essential mechanical properties, including stress, strain, and Young's Modulus. Stress reflects the force applied per unit area, strain represents the deformation of the material, and Young's Modulus quantifies the material's elasticity or stiffness.

In the context of this study, uniaxial tests were conducted on both sow's vaginal tissue and a PCL fiber, respectively (Figure 26).

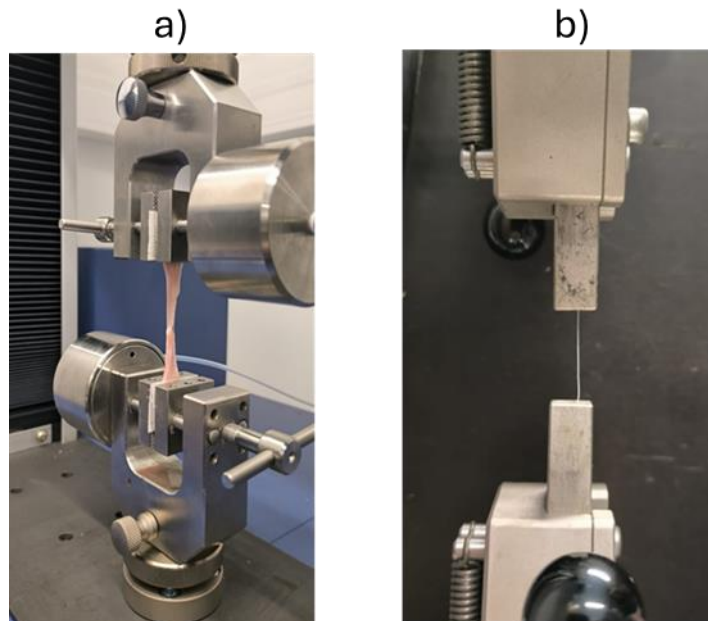


Figure 26 Uniaxial tensile tests. a) tissue and b) fiber

The dimensions of the vaginal tissue samples are visually depicted in Figure 27, featuring a width of 10 mm and a thickness of 4 mm. The PCL fiber had a diameter of 240 μm with a length of 50 mm.

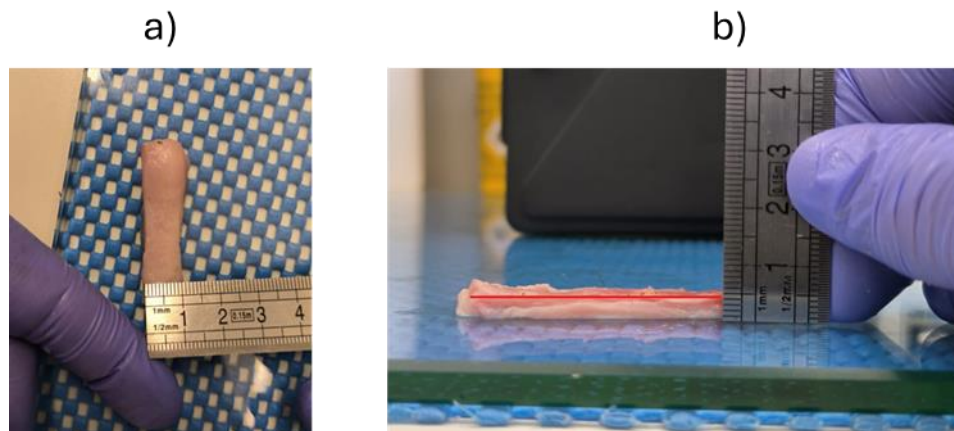


Figure 27 Sow's vaginal tissue samples for uniaxial test a) sample width and b) sample thickness.

Stress-strain curves are a result of the mean value of triplicate tests performed in each fiber and tissue. The evaluations were conducted using the "Mecmesin Multitest 2.5-dv" for fiber testing and the "Mecmesin Multitest 10-í" for tissue testing, with both applying a 100 N load and a constant elongation rate of 10 mm/min.

3.4.2 Ball Burst Test

Ball burst testing, also referred to as burst strength or burst pressure testing, is a crucial evaluation technique applied across industries to determine a material's ability to withstand internal pressure before rupturing or bursting. Conducted under controlled conditions, this test ensures accurate and repeatable results, offering valuable insights into the structural integrity and reliability of materials for real-world applications. [108]

Ball burst tests are conducted under controlled conditions to ensure accurate and repeatable results. The data obtained from these tests is essential for quality control, product development, and regulatory compliance across a wide range of industries, including manufacturing, packaging, automotive, aerospace, and more. [108]

In contrast to the tensile test, where the load or deformation is applied in-plane to the specimen, in the ball burst test an orthogonal load is applied to the central portion of the tissue specimen (Figure 28). Therefore, while the tensile test provides valuable data about the directional mechanical properties of the tested tissue, the ball burst test can provide data about the multiaxial mechanical properties of the whole tissue structure. [84]

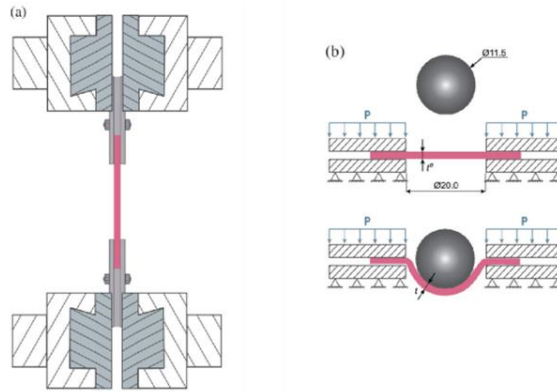


Figure 28 Experimental setup (a) Tensile test and (b) Ball burst test. (adapted from [84])

The materials subjected to testing included meshes with diameters of 160 μm and 240 μm , configured in both quadratic and cross patterns, as well as vaginal tissue with approximately 50 mm width, 50 mm length and 4 mm thickness (Figure 29).

Additionally, combined tests involving vaginal tissue and meshes were conducted, with the mesh positioned inferior to the vaginal tissue, corresponding to the distal part of the vaginal wall. It is worth noting that at least three trials were conducted for each test, with mesh and tissue tests solely performed using meshes of 0.24 mm.

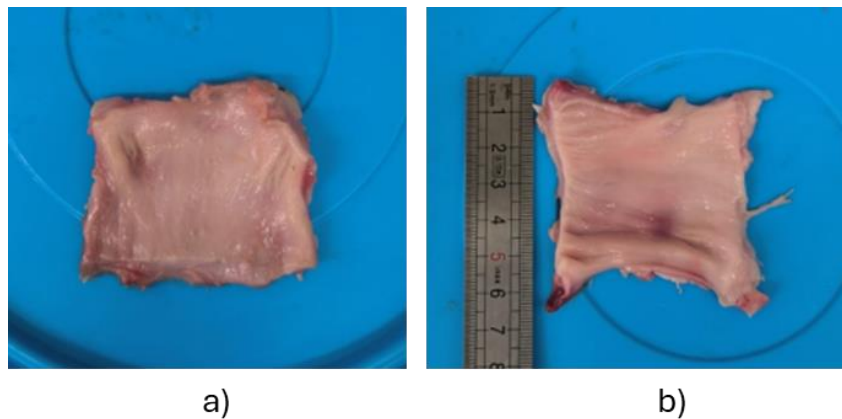


Figure 29 Sow's vaginal tissue sample for ball burst test. a) sample width and b) sample length

As there were no equipment available in the laboratory to perform the ball burst test, custom pieces were fabricated to fulfill this purpose (refer to Figure 31). The ball was represented by a column measuring 55 mm in length and with a diameter of 11.5 mm (despicted in Figure 30 a). Additionally, a base was utilized to ensure stability during the test, maintaining contact with the Mecmesin Multitest 10-i machine (illustrated in Figure 30 d). This base featured four cylinders, each measuring 50 mm in height and 15 mm in diameter, which would connect to the platform holding the materials to be tested securely in place (as shown in Figure 30 c). Furthermore, for fixation purposes, a material holder was incorporated into the design (despicted in Figure 30 b). Both components designed for fixing the material feature a hole with a diameter of 20 mm.

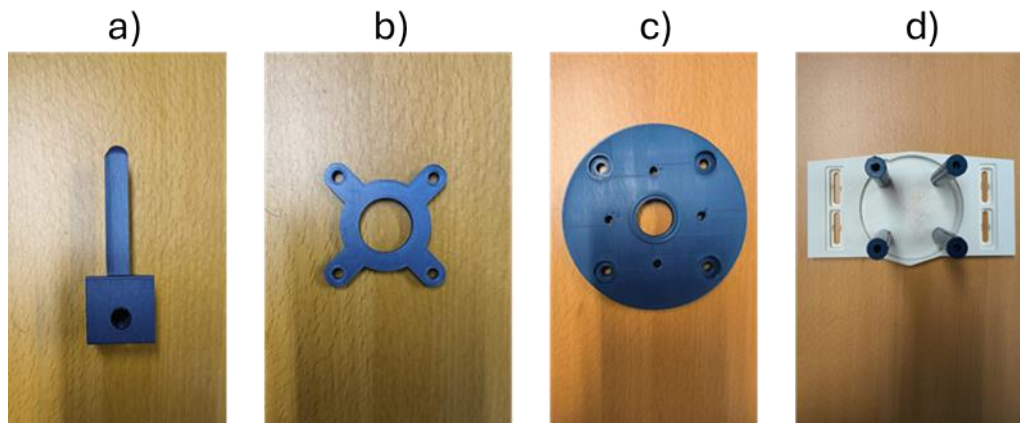


Figure 30 Ball burst test equipment. a) ball, b) holder, c) platform and d) base.

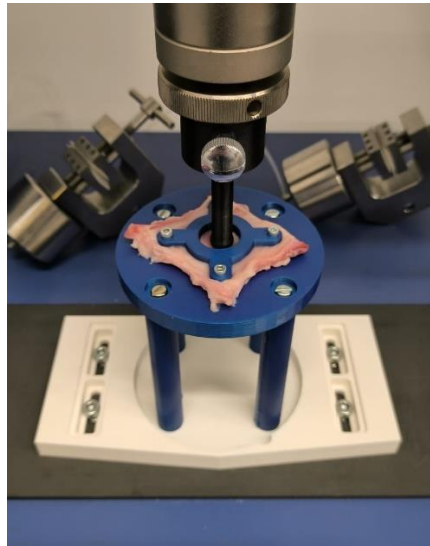


Figure 31 Ball burst machine assembly.

As mentioned earlier, the 3D printed ball had a consistent descent rate of 10 mm/min. This controlled descent rate ensures that the force applied to the material is systematically increased over time, allowing for a gradual buildup of pressure on the specimen.

Data acquisition and analysis were facilitated by the Emperor Software, enabling the visualization and storage of obtained graphs from each test. This comprehensive approach allowed for a thorough examination of the burst strength and structural performance of the materials under consideration.

3.5 Computational Modelling

For the simulations, the material properties derived from uniaxial tests were assigned to accurately represent the nature of the materials. Each component (mesh, tissue and the ball burst equipment) was created separately in the simulation environment.

Interactions between different components were defined to simulate the cohesive behavior during the Ball Burst test. This involves capturing how the mesh and tissue interact and respond to the applied pressure.

Additionally, boundary conditions, such as constraints and loading conditions, were carefully set to mimic the real-world scenario of the ball burst test. These conditions are crucial in ensuring the accuracy of the simulation and obtaining meaningful results.

It is important to emphasize that three simulations were conducted for each ball burst test: one involving only tissue, one involving only the mesh and another with both components, where the tissue was positioned on top of the mesh.

Before diving into the explanation of the simulation and its components, it is essential to note that this simulation was run using the explicit method in ABAQUS software due to its complexity, as the standard mode was not effective. Additionally, it's worth noting that simulations were exclusively performed on meshes with a square diameter of 0.24 mm.

3.5.1 Material Properties

In order to accurately simulate the behavior of the materials in the model, it's essential to have precise data on their mechanical properties. The uniaxial tests play a key role in this process, providing valuable insights into parameters such as the Young's Modulus and stress-strain characteristics. Other important factor is the density of the material. By extracting this data allows a comprehensive understanding of how materials respond to forces and deformations.

Young's modulus (E), or modulus of elasticity, is a characteristic of the material that allows determining the ease with which it stretches and deforms, based on the ratio between stress (σ) and strain (ϵ). Stress is defined by the force exerted per unit area, and strain corresponds to the extension applied to the object per unit length, as shown in the equation (Eq. 1). Typically, Young's modulus is expressed in megapascals (MPa).

$$E = \frac{\sigma}{\epsilon} = \frac{F \times l}{A \times \Delta l} \quad (3)$$

In addition to Young's modulus, determining Poisson's ratio is necessary for simulations. Poisson's ratio reflects the relationship between width and length changes when a material experiences force. It's calculated as the ratio of expansion fraction to compression fraction. For

isotropic materials, Poisson's ratio usually ranges from -1 to 0.5. For biodegradable polymers like PCL, Poisson's ratio is approximately 0.3. [109]

It is important to mention the results presented are averages from three uniaxial tensile tests on each material, technical PCL fibers and vaginal tissues. This ensures a reliable representation of the materials' mechanical behavior in the simulation.

The graphic in Figure 32 illustrates the average experimental values obtained from the uniaxial tensile test conducted on a PCL fiber with a diameter of 0.24 mm.

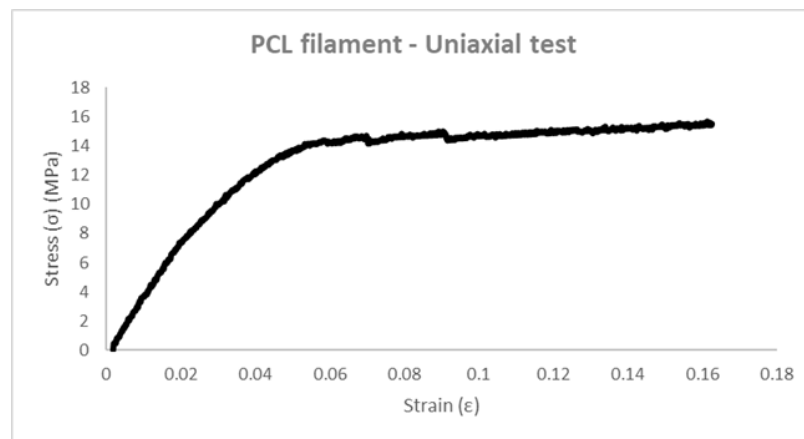


Figure 32 Stress-strain curves experimental results of PCL fiber.

From the Stress-Strain response, the Young's modulus can be determined by creating a line that overlays the elastic zone of the fiber (Figure 33). The slope of this line corresponds to the Young's modulus value.

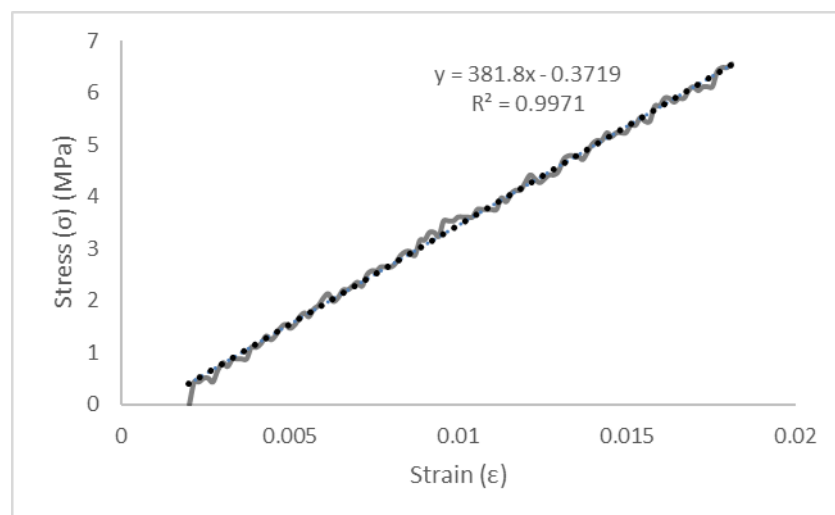


Figure 33 Young's modulus line.

The plasticity values were determined by generating a curve that represents the plasticity zone (Figure 34). This curve allows us to capture the material's behavior beyond the elastic region and understand its response to increasing stress. The obtained values, crucial for accurately representing the behavior of PCL in ABAQUS simulations, are summarized in Table 3.

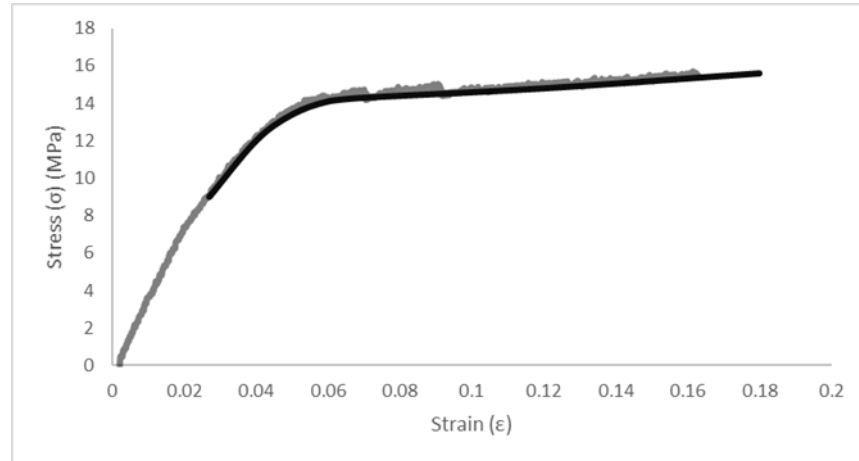


Figure 34 True stress- strain curve.

It's crucial to note that the values presented in the previous graphs and table are the true stress-strain values, not engineering values. This distinction is important for accurate representation and analysis, as true stress-strain consider changes in the specimen's cross-sectional area and length throughout the testing process. Engineering stress and engineering strain, on the other hand, assume constant original dimensions and may result in different trends and interpretations.

Table 3 PCL mechanical properties.

Density	Elastic		Plastic	
Mass Density	Young's Modulus	Poisson's Ratio	Yield Stress	Plastic Strain
1.14E-09	382.00	0.30	9.0	0.000
			12.0	0.013
			13.4	0.023
			14.1	0.033
			14.3	0.043
			14.8	0.093
			15.6	0.153

Figure 35 presents the results of uniaxial tensile tests conducted on sow's vaginal tissues, featuring a width of 10 mm, a length of 50 mm, and a thickness of 4 mm. The stress-strain curves were assessed using Abaqus software with various hyperelastic constitutive models, ultimately revealing the Arruda-Boyce model as the most accurate approximation.

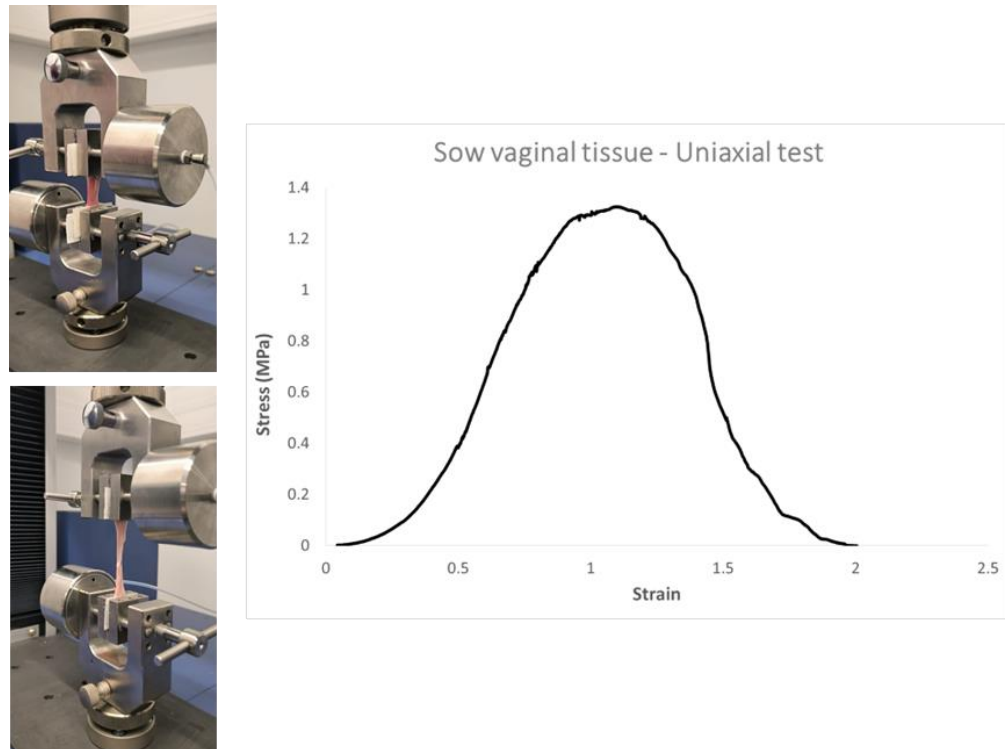


Figure 35 Stress-Strain curves experimental results of sow's vaginal tissue.

Soft tissues exhibit a nonlinear elastic response due to their microstructural arrangement. This microstructure can change under different physiological conditions, influencing the tissues' mechanical behavior. Comprising components like elastin, collagen fibers and ground substance (including proteoglycans and water), these soft tissues display highly nonlinear elastic behavior. Various attempts have been made to model the mechanical behavior of soft tissues, particularly focusing on their nonlinear elasticity. [110]

The nonlinear behavior of soft tissues is commonly described using constitutive models based on the theory of hyperelasticity. Hyperelastic models are employed to capture the intricate mechanical responses of soft tissues under different loading conditions. [110]

Among the hyperelastic models, the Arruda and Boyce model is often used in finite element modeling to predict the mechanical response of tissues. [110]

The equation (4) used in the Arruda-Boyce hyperelastic model combines material constants and microstructural behaviours to predict how elastomeric materials will respond to deformation. This equation is used to calculate the potential strain energy, denoted as U , in the model. [111]

$$U = \mu \sum_{i=1}^5 \frac{C_i}{\lambda_m^{2i-2}} (\bar{I}_1^i - 3^i) + \frac{1}{D} \left(\frac{J_{e\ell}^2 - 1}{2} - \ln J_{e\ell} \right), \quad (4)$$

where the coefficients C_1 through C_5 are defined as:

$$C_1 = \frac{1}{2}, C_2 = \frac{1}{20}, C_3 = \frac{11}{1050}, C_4 = \frac{19}{7000}, \text{ and } C_5 = \frac{519}{673750}. \quad (5)$$

The strain energy density's deviatoric portion is derived from Arruda and Boyce's work from 1993. This model is also referred to as the eight-chain model, as it was developed based on a representative volume element where eight springs extend from the centre of a cube to its corners. The coefficients $C_1 \dots C_5$ are calculated through a series expansion of the inverse Langevin function, which arises in the statistical treatment of non-Gaussian chains. The series expansion is truncated after the fifth term. The coefficient λ_m signifies the locking stretch, which is the point at which the slope of the stress-strain curve will rise significantly. The initial shear modulus, μ_0 , is related to μ through the expression. [111]

$$\mu_0 = \mu \left(1 + \frac{3}{5\lambda_m^2} + \frac{99}{175\lambda_m^4} + \frac{513}{875\lambda_m^6} + \frac{42039}{67375\lambda_m^8} \right). \quad (6)$$

The Arruda-Boyce potential relies solely on the first invariant. This means that the eight chains are stretched equally when subjected to a general deformation state. The elongation is directly represented by the first invariant, which is defined as $\bar{I}_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2$. If the Arruda-Boyce form is selected, the user has the option to specify the coefficients as functions of temperature. Alternatively, Abaqus can perform a fit of the test data provided by the user to determine the mechanical parameters. [111]

The constants used in the Arruda-Boyce hyperelastic model were utilized to characterise the vaginal tissue of the sow, as shown in Table 4.

Table 4 Arruda-Boyce hyperelastic mechanical parameters for sow's vaginal tissue

μ	μ_0	λ_m	D
1.30098754	1.30098825	1034.07055	0.00

3.5.2 Part Conception

The initial step in the simulation involves creating its components. The goal is to meticulously replicate the experimental test, which requires the mesh, a ball, two supporting plates to simulate clamping and the sow's vaginal tissue.

To initiate the creation of the mesh, it was crucial to model first its fiber (Figure 36 a)), an 8-node linear brick, reduced integration, hourglass control (C3D8R). This deformable fiber, with a diameter of 0.24 mm and a length of 40 mm, served as the base component.

In the context of melt electrowriting (MEW) printing, constructing the mesh required a layered approach, with each layer meticulously crafted atop the other. This necessitated a systematic procedure, commencing with the fiber as the base and progressively building upon it to form the mesh structure. By arranging the fiber in a linear pattern, spaced at intervals of 1.74 mm, a mesh measuring 40x40 mm was obtained. This process was then replicated to produce the second layer. Finally, by assembling these two layers, the intricate mesh structure was realized (Figure 36 b)).

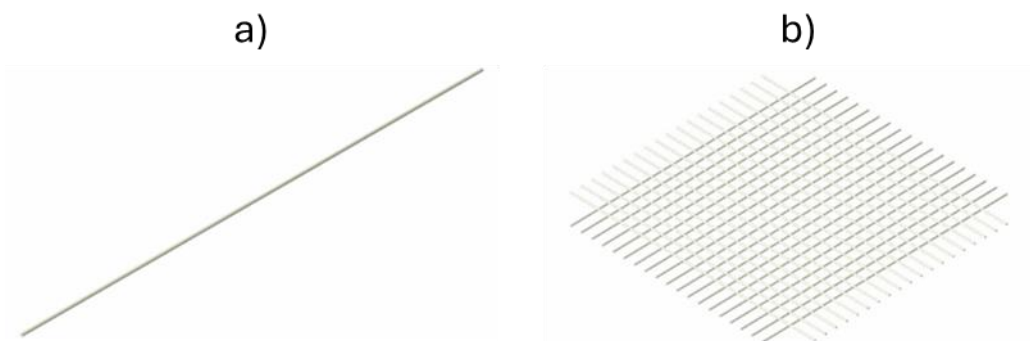


Figure 36 Geometric models of the a) fiber and b) mesh.

The ball (Figure 37 a)) is a 3D rigid analytical sphere with a diameter of 11.5 mm. This sphere will descend to penetrate the material, providing us with the Force-Punch graph that represents the material properties.

The plate (Figure 37 b)) is a 3D analytical rigid component with a thickness of 2 mm and a diameter of 40 mm. Two plates, one upper and one lower, will be used to simulate clamping and supporting the material under study. Therefore, a 20 mm hole is incorporated in the center for the ball to pass through. In Figure 37 c) we can see an assembly of the ball and the plates with a mesh.

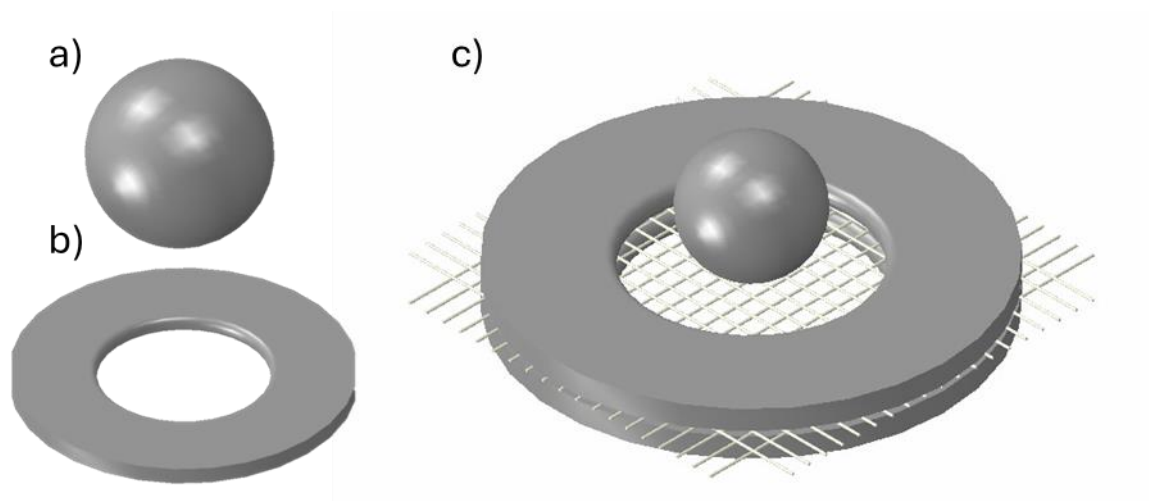


Figure 37 Geometric models of the a) ball, b) plate and c) Ball burst test with mesh.

Analytical rigid surfaces are geometric surfaces that are linked to a reference node for rigid body motion control. The use of analytical rigid surfaces offers distinct advantages in contact modeling, allowing for precise representation of curved geometries through parameterization with curved line segments. This results in smoother surface descriptions offering a more accurate approximation of the physical contact constraint. Additionally, employing analytical rigid surfaces can contribute to decreased computational costs associated with the contact algorithm.

To precisely depict the region where the ball interacts with the sample, the vaginal tissue samples (Figure 38) were modeled as a 4 mm disk using 8-node linear brick elements (C3D8). It is important to note that in the simulations the mesh will be below the tissue.

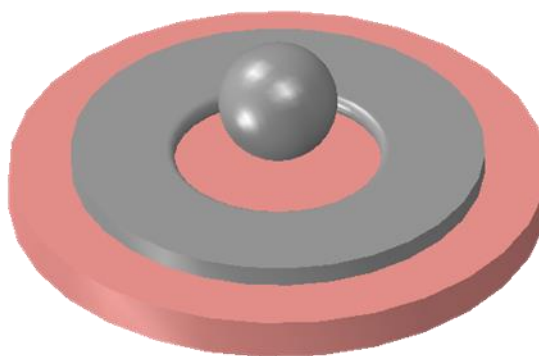


Figure 38 Geometric model with tissue.

3.5.3 Interactions and Boundary Conditions

Before addressing the interactions and boundary conditions, it's essential to explain that these simulations will be composed of 3 steps to ideally simulate reality. The first step involves the descent of the upper plate until it makes contact with the sample to be tested. Subsequently, upon contact, the upper plate becomes encased, simulating the fixation of the samples. After this, the ball begins its descent.

These steps are designed to closely mimic the actual conditions of the ball burst test (Figure 39 and Figure 39), providing a more realistic simulation of the interaction between the components.

In these simulations, there will be three to four types of interactions: Ball-Sample, Upper Plate-Sample, Lower Plate-Sample and if both materials are present, Tissue-Mesh interaction. All of these interactions will be surface-to-surface interactions frictionless.

The boundary conditions are a crucial factor in making the simulation as close to reality as possible. In the initial step, the horizontal sides of the samples and the lower plate are fixed. As the simulation progresses, the upper plate descends until it reaches the sample, at which point an encasement is created vertically on the upper plate. Finally the ball begins to descend.

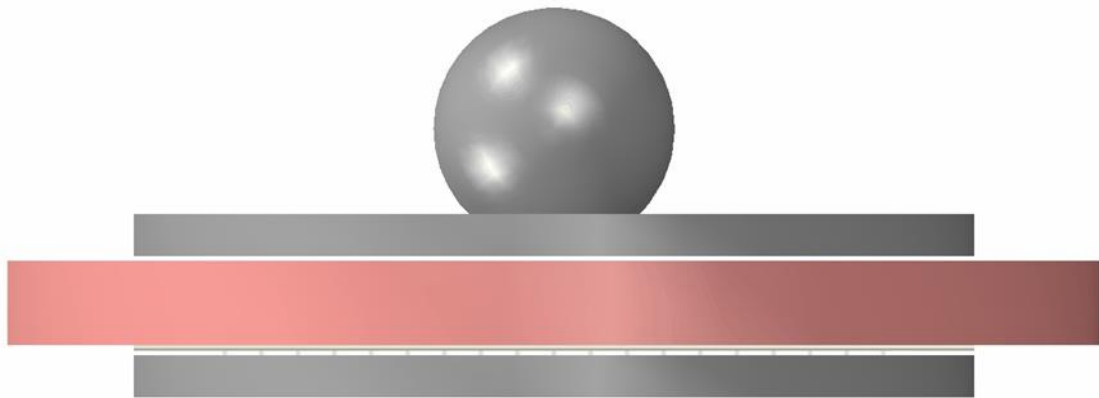


Figure 39 Geometric models were used for the Ball burst test simulations.

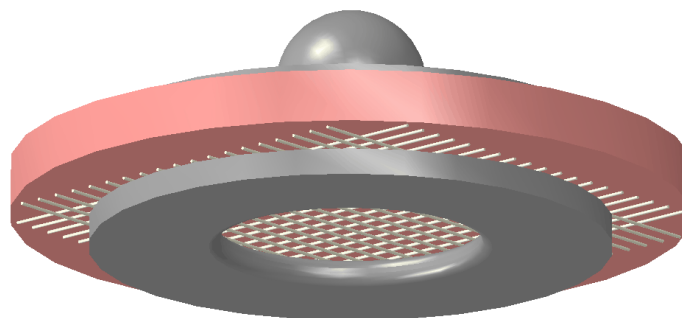


Figure 40 Different view of the geometric model.

Chapter 4

Results and Discussion

Chapter 4 starts with the presentation of the ball burst test results. Subsequently, the outcomes obtained from the computational models are analysed. As mentioned earlier, simulations were exclusively conducted for meshes with 240 μm , sow's vaginal tissue and the combination of both. The simulation results are presented through images and graphics.

Comparative analyses will be presented between these results and others articles related to the same topic.

4.1 Ball Burst Test Experimental Analysis

In this chapter, the results derived from the ball burst tests performed on meshes characterized by square and cross configurations, with fiber diameters of 240 μm and 160 μm , respectively will be explored. We also examine the behavior of sow's vaginal tissue in isolation and in combination with both types of meshes (240 μm square and cross). The tests of all samples were conducted until there was complete rupture of the material. The force vs punch curve was drawn and analysed.

4.1.1 Mesh

The results obtained from the ball burst tests conducted on meshes with varying diameters and configurations (Figure 41) provide valuable insights into the performance of these materials under pressure conditions.

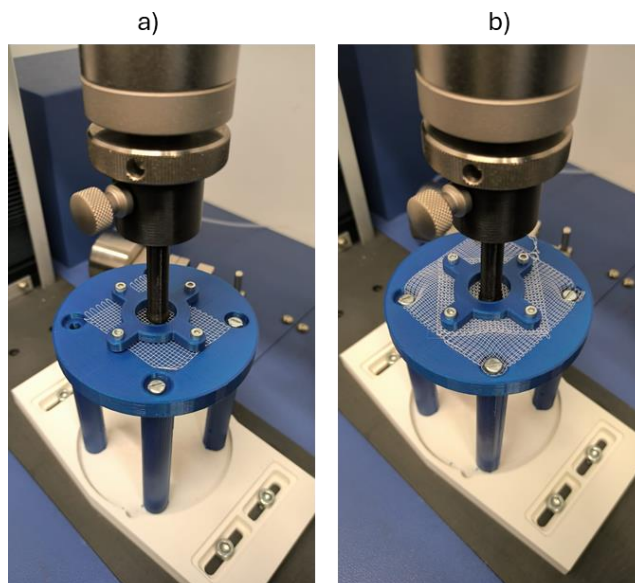


Figure 41 Ball burst test on different meshes configurations. a) Quadratic b) Cross.

Figure 42 visually presents the force-punch response that corresponds to the average of 3 trials conducted in the ball burst test for each mesh configuration. The top row displays the square meshes with diameters of 160 μm (Figure 41 a)) and 240 μm (Figure 41 b)), while the bottom row showcases the cross-shaped meshes with diameters of 160 μm (Figure 41 c)) and 240 μm (Figure 41 d)).

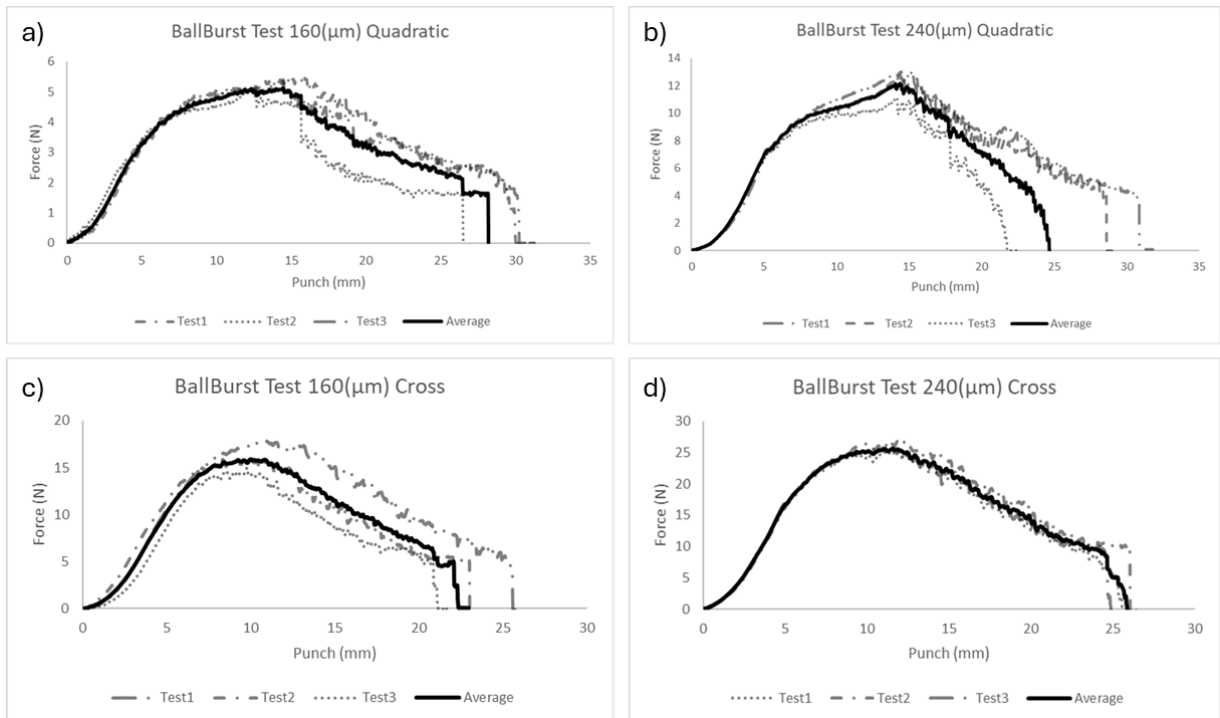


Figure 42 Force-punch curve obtained from ball burst test on meshes. a) 160 μm Quadratic, b) 240 μm Quadratic, c) 160 μm Cross and d) 240 μm Cross

In Figure 43, a comparison of the averages from the four tests reveals distinct patterns in the behavior of the tested meshes. It is noteworthy that the abbreviation 'Q' is assigned to square meshes and 'X' to cross meshes.

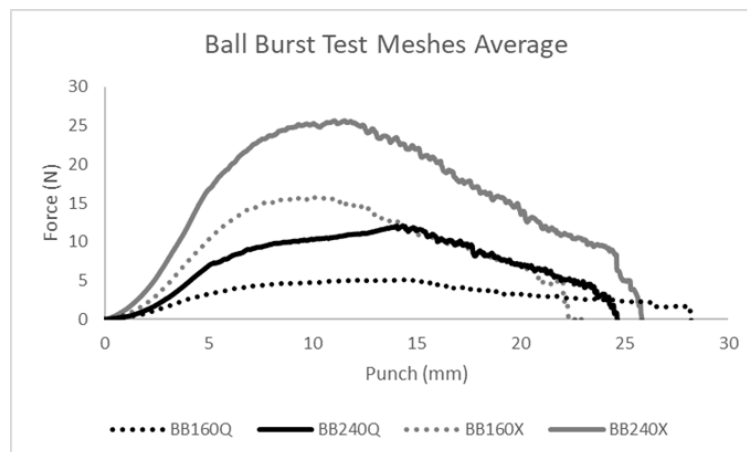


Figure 43 All meshes force-punch curves with averages.

As anticipated, meshes with a 240 μm diameter exhibit a significantly higher capacity to withstand force, showing almost a 10N difference when compared to their 160 μm counterparts. This proportional increase in strength aligns with expectations, considering the direct relationship between fiber diameter and applied force.

Upon evaluating mesh configurations, a notable discrepancy emerges in the results. Cross-configured meshes demonstrate a force applied twice as much in 240-micrometer meshes and three times as much in 160-micrometer meshes. This substantial difference can be attributed to the way these meshes were printed.

Analysis of the G-Code reveals a fundamental difference in the manufacturing process: while square meshes were built with only two layers, cross-configured meshes were printed with four layers. This variation in mesh structure may have significant impacts on force distribution and resistance capacity during the ball burst test.

4.1.2 Tissue

The results of the ball burst test on the sow's vaginal tissue (Figure 44) were obtained from three tests, with the tissue having nearly the same dimensions in both cases, measuring 50x50 mm and 4 mm in thickness. It is important to mention that special attention was given to select a uniform location of the sample for testing.

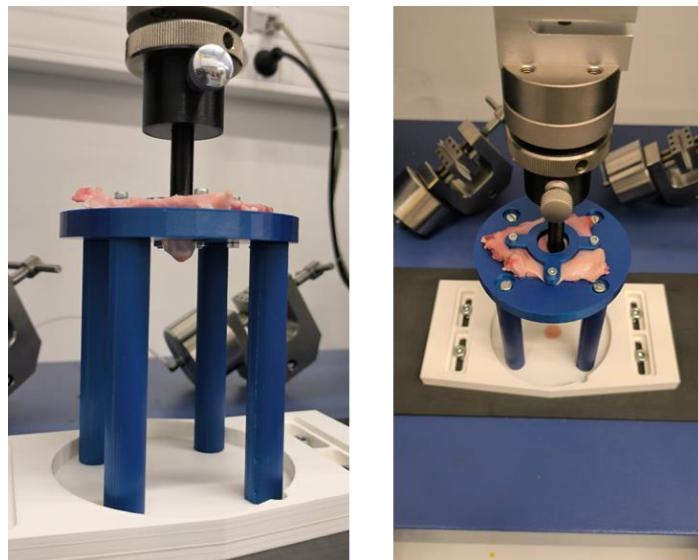


Figure 44 Ball burst test on sow's tissue.

These results are presented in Figure 45, which shows the force-punch curves of the vaginal tissue.

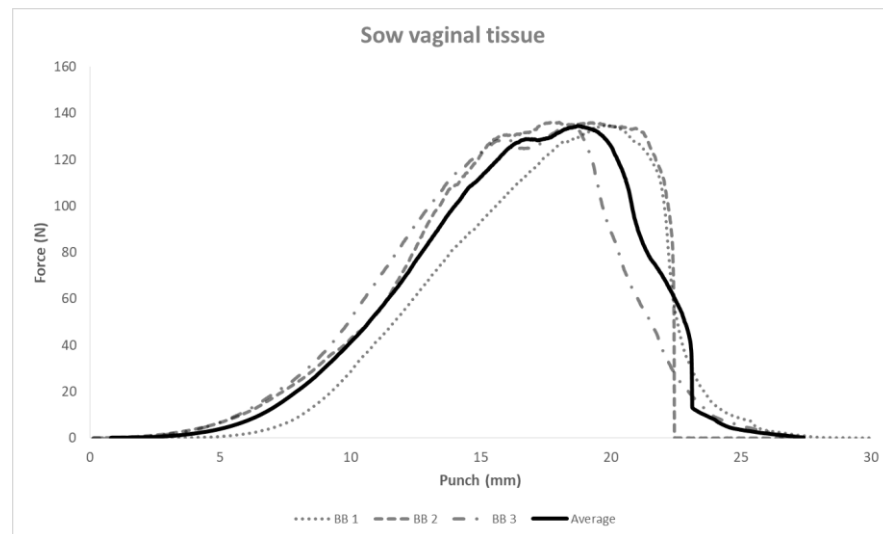


Figure 45 Tissue force-punch curves with average.

A comparison of these results with those from Catarina's dissertation [112] can be insightful. In her thesis, ball burst tests were conducted using sow's vaginal tissue with and without cog threads. Interestingly, in the tests without cog threads, two distinct results (with the names of test1 and test2) were observed, as depicted in Figure 46. One result closely resembles those obtained here (140 N), while the other differs significantly (180 N). This notable variation could be attributed to differences in how tissue thickness was considered. In our study, we consistently maintained a tissue thickness of 4 mm, which may not have been the case in Catarina's tests. Another factor to consider is whether a uniform tissue location was selected in Catarina's experiments. These factors could have contributed to the observed differences.

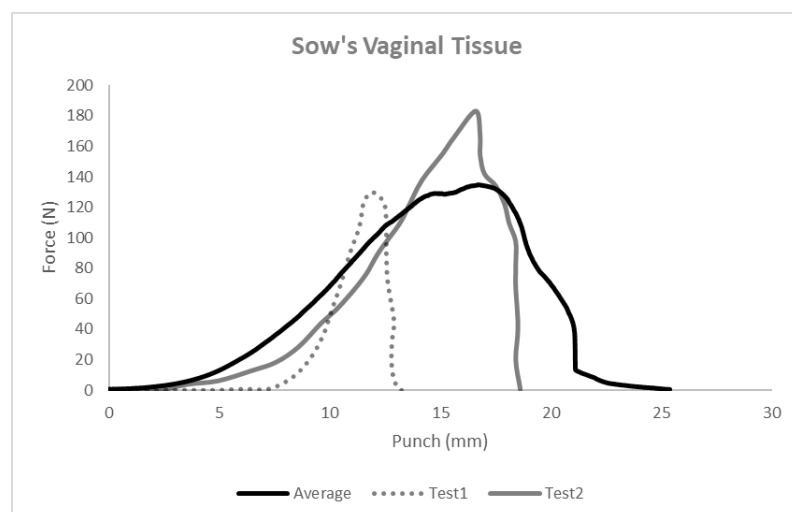


Figure 46 Comparison of ball burst test results on tissue with Catarina's study. (adapted from [112])

Another ball burst test, this time involving sheep tissue, was conducted by Rynkevicius et al, 2019.[113] In this test, specimens were obtained from three groups of sheep at various stages of their life cycle: virgin, pregnant, and parous ewes. Subsequently, ball burst tests were performed on these specimens, all possessing similar tissue structures. The force-punch curve of the virgin sheep vaginal tissue reveals a considerable discrepancy when compared to the sow's vaginal tissue, with the former exhibiting a force of 45 N compared to 140 N for the latter. This substantial difference underscores the distinct mechanical properties between the vaginal tissues of different animal sources, highlighting the importance of considering such variations in biomechanical studies and surgical interventions involving pelvic organ prolapse repair.

4.1.3 Tissue with Mesh

As mentioned earlier, tests were exclusively conducted between tissue and mesh with a diameter of 240 μm , featuring both square and cross configurations (Figure 47). Figure 48 displays the obtained results and the cross-configured meshes exhibit higher resistance to the applied force.

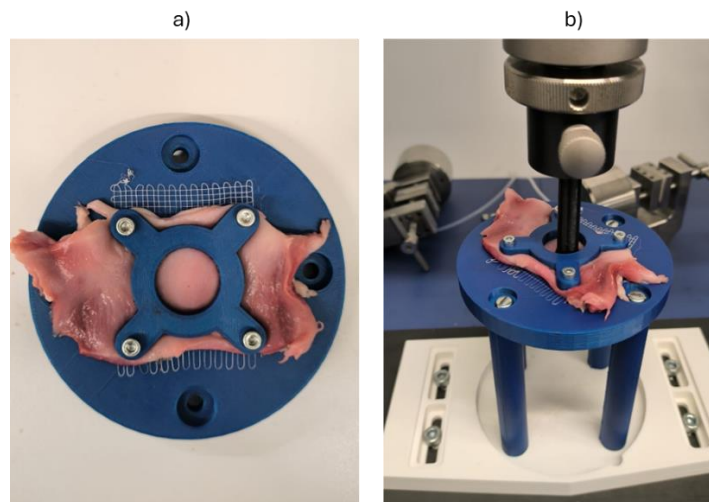


Figure 47 Ball burst test on sow's tissue with quadratic mesh. a) before test b) during test.

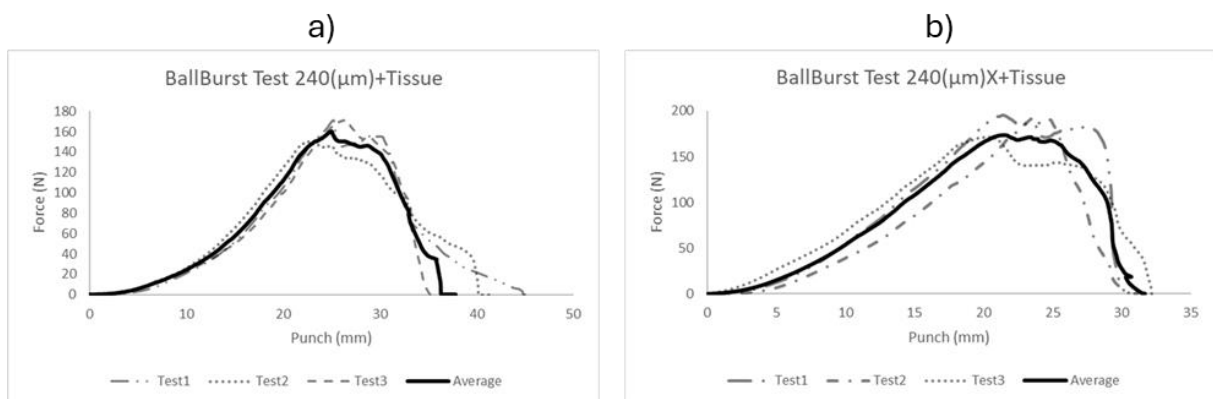


Figure 48 Mesh and Tissue ball burst tests: a) quadratic mesh and b) cross mesh.

The influence of meshes on the tissue can now be analyzed (Figure 48). The meshes indeed contribute to an increase in tissue resistance, with a 14% enhancement in the square configuration and a 21% improvement in the cross configuration. This emphasizes the role of mesh structure in reinforcing the overall strength of the tissue-mesh composite.

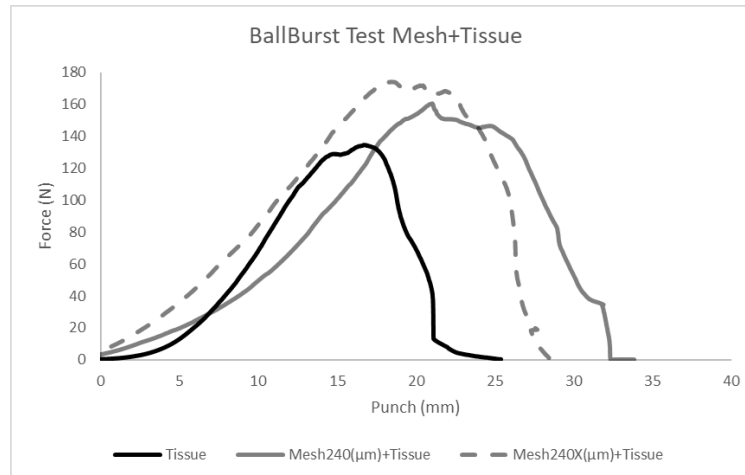


Figure 49 Mesh and tissue force-punch curves with averages.

Comparing again with Catarina's dissertation [112], where tests were conducted with sow's vaginal tissue and cog threads (Figure 49), we can observe that the cog threads exhibit higher values (200 N) compared to the cross meshes (175 N). Although different reinforcement approaches were employed to strengthen the vaginal canal, it was discovered that the level of reinforcement remained consistent.

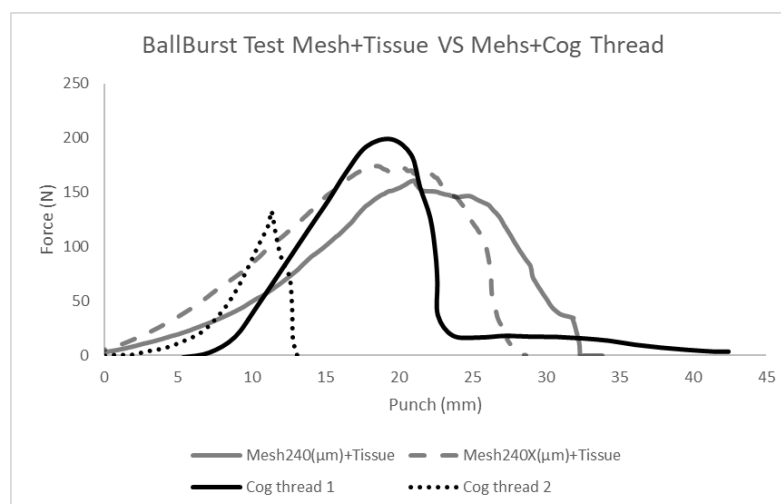


Figure 50 Comparison of ball burst test results on tissue with meshes with Catarina's study. (adapted from [112])

Our work also supports the findings of Katarina Knight et al, 2022 [84], where ultra-lightweight synthetic meshes with a square pore were implanted onto the vaginas of rhesus macaques in a non-deformed configuration and ball burst tests were performed. The meshes were classified as 1) square pore (Stable), 2) diamond pore (Unstable), and 3) Predeformed pore (pores intentionally collapsed and mesh wrinkled prior to implantation). We can see that in this study, the tissues exhibited an increase in stiffness with the placement of the meshes. Additionally, we noted variations in the maximum force across different mesh configurations, indicating differing stiffness values associated with each configuration.

4.2 Ball Burst Test Computational Model

In this chapter, the results obtained from the simulations will be presented. It is important to note that simulations were only conducted with square meshes with a diameter of 240 μm , with the tissue and with the tissue combined with square meshes with a diameter of 240 μm . The primary objective is to try to obtain results closest to real-world scenarios. The results will be presented and analyzed through a combination of images and graphs, allowing for a comprehensive evaluation of the simulated outcomes.

4.2.1 Mesh

In Figure 51, we can observe the numerical model of the ball burst test on the mesh in action. One of the main issues encountered in this simulation was the fact that the mesh was composed of two layers. At times during the simulation, these layers would twist due to the pressure from the upper plate, causing them to overlap. This was resolved by not applying any force to the upper plate, causing them to overlap. This was resolved by not applying any force to the upper plate (which simulates the tightening) and instead fixing the plate against the mesh backing.



Figure 51 Numerical model results on the ball burst test conducted on meshes.

The numerical results obtained from this simulation are visible in Figure 52, alongside the experimental results. We can observe similarities in the elastic zone of the material. However, the simulation fails to attain the maximum force value, primarily due to discrepancies in the assigned properties of PCL. Despite achieving a relative error of 14%, which isn't excessively high, it underscores the importance of refining material properties or potentially redesigning the geometry, such as importing it from SolidWorks, for greater accuracy.

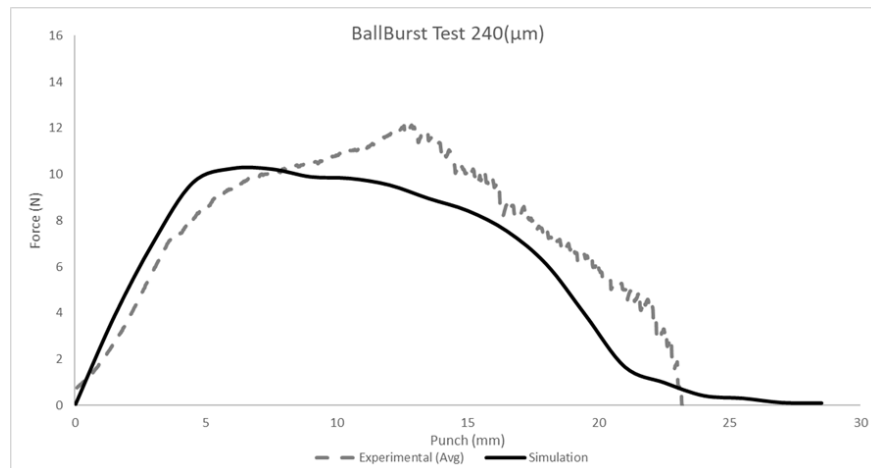


Figure 52 Comparison between ball burst test experimental and numerical results on 240μm quadratic mesh.

This disparity underscores the complexity of accurately simulating the intricate behavior of biodegradable meshes under varying mechanical loads, emphasizing the need for further refinement and validation of computational models to enhance their predictive capabilities.

4.2.2 Tissue

Figure 53 showcases the simulation's output of the ball burst test on tissue samples, demonstrating a close resemblance to real-world behavior. This visual similarity suggests the simulation effectively captures tissue responses under applied forces.

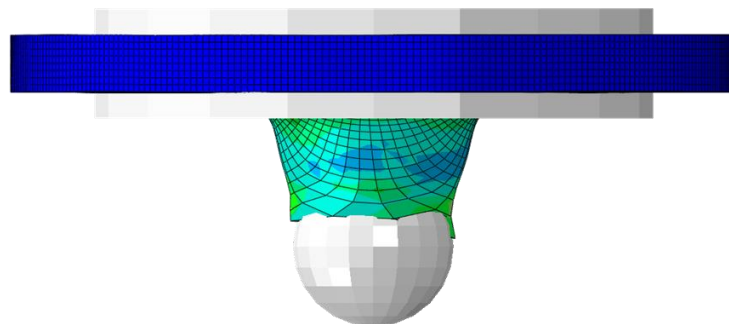


Figure 53 Numerical model results on the ball burst test conducted on tissue samples.

The comparison between the numerical and experimental results of the ball burst test is shown in Figure 54, indicating a close agreement up to the maximum force. However, the simulation results indicate a more rapid decrease in force after this point, suggesting potential discrepancies in either the mechanical properties of the tissue or the precision of the numerical model, particularly at greater displacements.

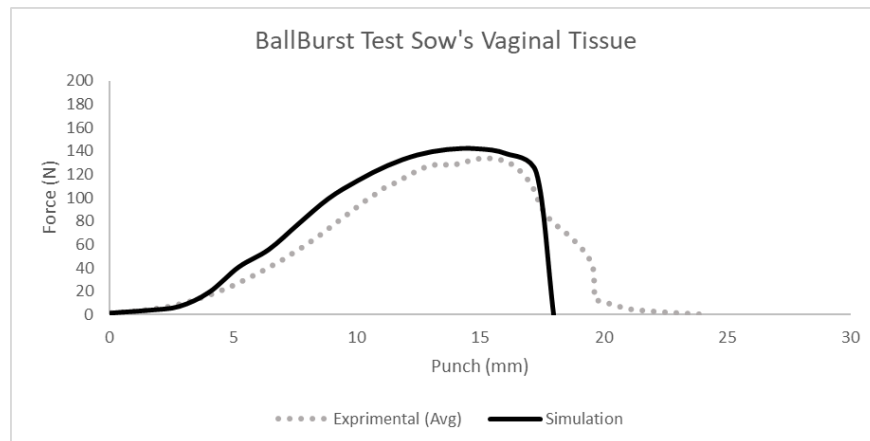


Figure 54 Comparison between ball burst test experimental and numerical results on tissue samples.

In this analysis there was an approximation between the experimental and computational parts, being the difference of 6.5%. Concluding that the computational model is replicating well the behavior obtained in the experimental analysis. However, adjustments can be improved, particularly in the material properties. Specifically, refining the parameters related to tissue behavior could lead to a closer match between the numerical predictions and experimental observations.

4.2.3 Tissue with Mesh

The simulation with both tissue and mesh together will be visualized. As seen in Figure 55, due to the prolonged simulation time, it was not possible to capture a ruptured figure. It's worth noting that we encountered numerous issues in this particular case, one of which mirrors that of the mesh: fiber overlap.

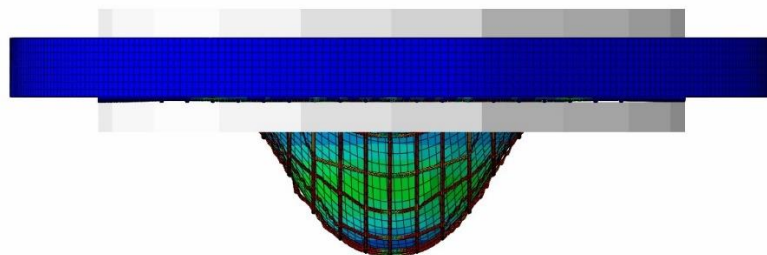


Figure 55 Numerical model results on the ball burst test conducted on tissue with mesh.

Regarding the obtained values, a significant discrepancy is evident, with an error double the maximum force (Figure 56). Unfortunately, the expected result was not achieved, potentially due to several factors, primarily the creation of the mesh geometry. Initially, the mesh was being reproduced as a single layer and in a wire element. However, as it's a single layer, certain points of the mesh wouldn't have double the diameter, as a real mesh would have with greater thickness. Therefore, we transitioned to creating a deformable solid 3D mesh, as seen in the current model. Surely, there must be a more suitable way to create this mesh. Undoubtedly, some properties of the mesh and tissue need improvement, which is another point to consider. Additionally, there may be errors in the boundary conditions that need to be addressed.

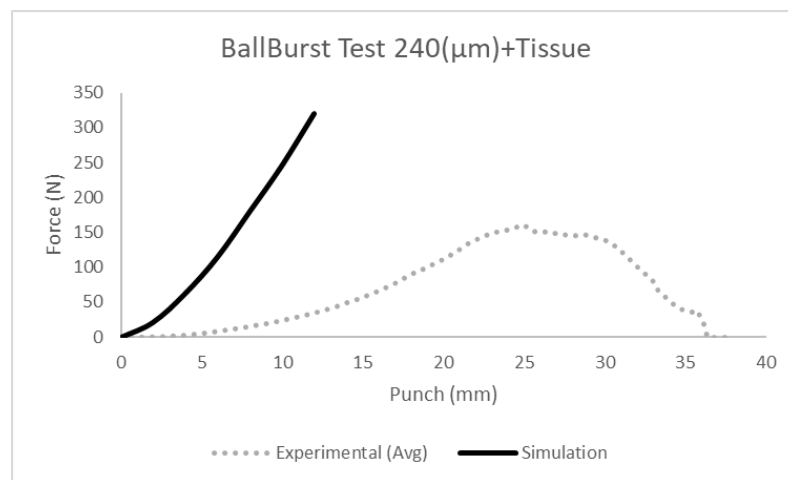


Figure 56 Comparison between ball burst test experimental and numerical results on tissue with mesh.

Chapter 5

Conclusions and Future Works

5.1 Conclusions

The principal goal of this dissertation is to achieve simulation results that closely match the findings from the corresponding ball burst tests. To accomplish this objective, several phases were undertaken, starting with an extensive literature review to familiarize myself with the issue of pelvic organ prolapse. The process involved the creation of the mesh, which required relearning G-code and acquiring skills to operate the MEW prototype. Additionally, uniaxial tests were conducted to obtain the properties of vaginal tissue and PCL. Finally, ball burst tests were performed to obtain results and compare them with the created simulation.

Regarding the experimentally obtained results, significant agreements with the literature are evident. It can be concluded that the placement of biodegradable PCL meshes in sow's vaginal tissue increases the maximum force by 14 to 20 percent in ball burst tests. However, concerning the computational model, it is observed that the simulations created for the meshes and tissue were largely successful, with adjustments needed only for sample properties. Conversely, the tissue with mesh simulation did not fare as well, exhibiting bigger errors when compared with the other two. In this case, it is necessary to review the model and identify the source of the error.

In conclusion, while this dissertation achieved significant progress in aligning simulation results with experimental findings, there are areas for further investigation and improvement. One aspect to consider is refining the computational model to better replicate real-world scenarios, particularly in the case of tissue with mesh simulations where a significant error was encountered. Additionally, exploring alternative approaches or techniques to address challenges encountered during the simulation process, such as optimizing mesh designs or refining material properties, could lead to more accurate results. Furthermore, conducting additional validation studies with a larger sample size or incorporating more sophisticated modeling techniques may enhance the reliability and robustness of the computational model. Overall, this research lays the groundwork for future studies aimed at improving the understanding and treatment of pelvic organ prolapse through computational modeling and simulation.

5.2 Future Works

Regarding future work, I believe it would be of great value to improve the computational models. This improvement could involve enhancing material properties, modifying part geometries, or even modifying the simulation entirely, especially the simulation of tissue with mesh.

Additionally, while the simulations of the mesh and tissue demonstrated promising accuracy, further investigation into the response of meshes with varying diameters and configurations could provide deeper insights. For example, experimenting with circular or hexagonal mesh geometries could offer valuable information on how different structural designs affect performance and interaction with the surrounding tissue.

Furthermore, investigating how varying scenarios and loading conditions impact mesh-tissue interactions could refine the predictive capacity of our models. This might entail simulating diverse physiological conditions or surgical scenarios to glean insights into the influence of factors like tension, mobility, and biological response on mesh performance and longevity.

Moreover, integrating advanced computational techniques, such as machine learning algorithms, could help refine the predictive accuracy of the models and enable personalized treatment planning. By analyzing large datasets of clinical outcomes and biomechanical data, machine learning algorithms could identify patterns and correlations that inform more precise patient-specific predictions and treatment recommendations.

Overall, the future of this research lies in the continued refinement and expansion of computational models, coupled with experimental validation, to advance our understanding of pelvic organ prolapse treatment and improve patient outcomes.

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Appendix A

G-Code for quadratic mesh with 80 μm

```
;END OF THE START GCODE
G0 F9000 X100.0 Y50.0 Z0
G0 F250
G1 F500 Y75.0 E4.0816
G1 X145.0 E0.09432
G1 Y76.58 E0.003312
G1 X100.0 E0.09432
G1 Y78.16 E0.003312
G1 X145.0 E0.09432
G1 Y79.74 E0.003312
G1 X100.0 E0.09432
G1 Y81.32 E0.003312
G1 X145.0 E0.09432
G1 Y82.9 E0.003312
G1 X100.0 E0.09432
G1 Y84.48 E0.003312
G1 X145.0 E0.09432
G1 Y86.06 E0.003312
G1 X100.0 E0.09432
G1 Y87.64 E0.003312
G1 X145.0 E0.09432
G1 Y89.22 E0.003312
G1 X100.0 E0.09432
G1 Y90.8 E0.003312
G1 X145.0 E0.09432
G1 Y92.38 E0.003312
G1 X100.0 E0.09432
G1 Y93.96 E0.003312
G1 X145.0 E0.09432
G1 Y95.54 E0.003312
G1 X100.0 E0.09432
G1 Y97.12 E0.003312
```

Appendix B

G-Code for quadratic mesh with 160 μm

```
;END OF THE START GCODE
G0 F9000 X100.0 Y50.0 Z0.5
G0 F250
G1 F500 Y75.0 E4.0816
G1 X145.0 E0.37656
G1 Y76.66 E0.013891
G1 X100.0 E0.37656
G1 Y78.32 E0.013891
G1 X145.0 E0.37656
G1 Y79.98 E0.013891
G1 X100.0 E0.37656
G1 Y81.64 E0.013891
G1 X145.0 E0.37656
G1 Y83.3 E0.013891
G1 X100.0 E0.37656
G1 Y84.96 E0.013891
G1 X145.0 E0.37656
G1 Y86.62 E0.013891
G1 X100.0 E0.37656
G1 Y88.28 E0.013891
G1 X145.0 E0.37656
G1 Y89.94 E0.013891
G1 X100.0 E0.37656
G1 Y91.6 E0.013891
G1 X145.0 E0.37656
G1 Y93.26 E0.013891
G1 X100.0 E0.37656
G1 Y94.92 E0.013891
G1 X145.0 E0.37656
G1 Y96.58 E0.013891
G1 X100.0 E0.37656
G1 Y98.24 E0.013891
```

Appendix C

G-Code for quadratic mesh with 240 μm

```
;END OF THE START GCODE
G0 F9000 X100.0 Y50.0 Z0.5
G0 F250
G1 F500 Y75.0 E4.0816
G1 X145.0 E0.84825
G1 Y76.74 E0.032799
G1 X100.0 E0.84825
G1 Y78.48 E0.032799
G1 X145.0 E0.84825
G1 Y80.22 E0.032799
G1 X100.0 E0.84825
G1 Y81.96 E0.032799
G1 X145.0 E0.84825
G1 Y83.7 E0.032799
G1 X100.0 E0.84825
G1 Y85.44 E0.032799
G1 X145.0 E0.84825
G1 Y87.18 E0.032799
G1 X100.0 E0.84825
G1 Y88.92 E0.032799
G1 X145.0 E0.84825
G1 Y90.66 E0.032799
G1 X100.0 E0.84825
G1 Y92.4 E0.032799
G1 X145.0 E0.84825
G1 Y94.14 E0.032799
G1 X100.0 E0.84825
G1 Y95.88 E0.032799
G1 X145.0 E0.84825
G1 Y97.62 E0.032799
G1 X100.0 E0.84825
G1 Y99.36 E0.032799
```

Appendix D

G-Code for cross mesh with 160 μm

```

;END OF THE START GCODE
G0 F9000 X100.0 Y50.0 Z0.5
G0 F250
G1 F500 Y75.0 E1.696932
G1 X151.46 E0.17903
G1 Y76.66 E0.005775
G1 X100.0 E0.17903
G1 Y78.32 E0.005775
G1 X151.46 E0.17903
G1 Y79.98 E0.005775
G1 X100.0 E0.17903
G1 Y81.64 E0.005775
G1 X151.46 E0.17903
G1 Y83.3 E0.005775
G1 X100.0 E0.17903
G1 Y84.96 E0.005775
G1 X151.46 E0.17903
G1 Y86.62 E0.005775
G1 X100.0 E0.17903
G1 Y88.28 E0.005775
G1 X151.46 E0.17903
G1 Y89.94 E0.005775
G1 X100.0 E0.17903
G1 Y91.6 E0.005775
G1 X151.46 E0.17903
G1 Y93.26 E0.005775
G1 X100.0 E0.17903
G1 Y94.92 E0.005775
G1 X151.46 E0.17903
G1 Y96.58 E0.005775
G1 X100.0 E0.17903
G1 Y98.24 E0.005775

```

Appendix E

G-Code for cross mesh with 240 μm

```

;END OF THE START GCODE
G0 F9000 X100.0 Y50.0 Z0.5
G0 F250
G1 F500 Y75.0 E4.0816
G1 X150.46 E0.951171
G1 Y76.74 E0.032799
G1 X100.0 E0.951171
G1 Y78.48 E0.032799
G1 X150.46 E0.951171
G1 Y80.22 E0.032799
G1 X100.0 E0.951171
G1 Y81.96 E0.032799
G1 X150.46 E0.951171
G1 Y83.7 E0.032799
G1 X100.0 E0.951171
G1 Y85.44 E0.032799
G1 X150.46 E0.951171
G1 Y87.18 E0.032799
G1 X100.0 E0.951171
G1 Y88.92 E0.032799
G1 X150.46 E0.951171
G1 Y90.66 E0.032799
G1 X100.0 E0.951171
G1 Y92.4 E0.032799
G1 X150.46 E0.951171
G1 Y94.14 E0.032799
G1 X100.0 E0.951171
G1 Y95.88 E0.032799
G1 X150.46 E0.951171
G1 Y97.62 E0.032799
G1 X100.0 E0.951171
G1 Y99.36 E0.032799

```