Division of Biomedical Engineering
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Design and Development of a Speculum-Free Digital Cervical Cancer Screening Device

In partial fulfilment of the requirements for the degree of
Master of Science in Biomedical Engineering
by coursework and dissertation

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02 July 2024

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Acknowledgements

The author would like to would like to acknowledge the following contributions:

The University of Cape Town and merSETA for funding me throughout my dissertation. Moreover, the MSc Biomedical Engineering Program for giving me the privilege of being accepted into the program.

My supervisor, Prof Sudesh Sivarasu, and the MedTech laboratory for creating an innovative environment that allows us, as students, to learn about all the aspects of the medical devices industry. The freedom to explore different avenues and get exposure to the various aspects of medical device development.

My co-supervisor, Dr Rakiya Saidu, for all her valuable input into the design of the device from a clinical perspective. Dr Nomonde Mbatani and the gynaecologists at the Groote Schuur Hospital colposcopy clinic for taking the time to participate in the validation testing and providing me with the location and equipment I needed to perform the test.

And finally, my fiancé, Vonny, and all my friends and family for supporting me throughout the project. From my colleagues at the MedTech Lab, my flatmates, parents, and (soon-to-be) in-laws, I appreciate all the time and support from each of you. These two years will always be remembered as the time when I was "almost finished".

And now I am.

Abstract

Title Design and development of a speculum-free digital cervical cancer screening device.

Introduction Cervical cancer poses a significant global health challenge, particularly in low- and middle-income countries (LMICs), where the disease remains a leading cause of cancer-related deaths among women. Despite the success of cytology-based screening programs in developed nations, implementing effective screening in resource-constrained environments has proven challenging. Visual Inspection with Acetic acid (VIA), a cost-effective alternative, has limitations due to subjective diagnosis, hindering large-scale implementation. This research addresses the need for improved cervical cancer screening in LMICs through the design and development of a speculum-free digital screening device. Recognising the potential of digital technology to enhance VIA's diagnostic accuracy, the project aims to create a device that combines the simplicity and cost-effectiveness of VIA with digital advancements.

This research aims to develop a speculum-free cervical cancer screening device that matches the diagnostic accuracy of the standard screening tool while enhancing usability. The objectives include the development of the device, verification guided by ISO 8600 standards for medical endoscopes and ISO 14971 risk assessment, and validation of the developed device's diagnostic performance and usability through a simulated clinical study.

Materials and Methods The design and development of the cervical cancer screening device, the CerviScreen, used rapid prototyping and testing principles. Comprising five subsystems—housing, visualisation, liquid application, dilation, and decontamination—the subsystems were independently designed and subsequently integrated. The dilation subsystem, developed to enable speculum-free screening, simplifies the screening process and prioritises patient comfort. The device offers a less invasive screening procedure, providing real-time video images, controllable lights, and an acetic acid application system for cleaning the cervix and inducing the acetowhitening effect for diagnosis.

The first verification phase tested the dilation subsystem's compliance with engineering specifications and selected the optimal dilation cup design. Subsequently, the complete device underwent verification using tests aligned with ISO 8600 standards and auxiliary tests done by predicate devices. The second verification phase assessed the risk of the device to identify and mitigate usability and functionality risks. Validation involved simulating a cervical cancer screening procedure using a female pelvic training model in a gynaecology clinic. This comparative study assessed the CerviScreen's diagnostic accuracy against the colposcope, with experienced gynaecologists conducting diagnoses, as well as the usability of the device. Ethics approval (Reference number: HREC REF 570/2023) was obtained for this validation study.

Results and Analysis Five experienced gynaecologists from Groote Schuur Hospital participated in the study, averaging 14±7.01 years of experience. The CerviScreen and colposcope demonstrated a diagnostic accuracy of 80%, indicating comparable accuracy. Usability, measured by the System Usability Score (SUS), scored 83.75, indicating 'good' usability. Post-test feedback from the participants reflected positive perceptions regarding device usability and features.

Conclusion The speculum-free digital cervical cancer screening device fulfilled all design requirements to complete an entire screening procedure. It was validated to have diagnostic accuracy equivalent to that of the standard device and good usability in the simulated screening environment. While the validation testing strength lay in utilising highly experienced gynaecologists, limitations arose from inaccuracies introduced by the simplified anatomy and pathology of the female pelvic model and cervices. Despite positive results and feedback, future testing on more accurate human anatomy is essential to establish the device's efficacy. Ongoing work involves refining specific design aspects based on input from the validation study.

Table of Contents

List of Figures

List of Tables

List of Acronyms

AI	Artificial Intelligence
ASC-H	Atypical Squamous Cells, cannot exclude High-grade Squamous Intraepithelial Lesion
ASC-US	Atypical Squamous Cells of Undetermined Significance
CD	Compressed Deformation
CF	Collapsing Factor
CIN	Cervical Intraepithelial Neoplasia
DOV	Direction of View
ES	Engineering Specification
FEA	Finite Element Analysis
FEM	Finite Element Model
FOV	Field of View
HIC	High-Income Countries
HIV	Human Immunodeficiency Virus
HLD	High-Level Disinfection
HPV	Human Papillomavirus
LMIC	Low- and Middle-Income Countries
LRS	Low-Resource Setting
ISO	International Organization of Standardization
NAT	Nucleic Acid Test
PCR	Polymerase Chain Reaction
PCB	Printed Circuit Board
SAHPRA	South African Health Product Regulatory Authority
SCJ	Squamocolumnar Junction
SIL	Squamous Intraepithelial Lesion
SLA	Stereolithography
STD	Sexually Transmitted Disease
SUS	System Usability Scale
SV	Side-view
TZ	Transformation Zone
VIA	Visual Inspection with Acetic Acid
WD	Working Distance
WHO	World Health Organization

1 Introduction

1.1 Background and Problem Identification

In 2020, cervical cancer affected a total of 604,127 women worldwide, with a fatality rate of 57% (Bruni L, 2021b). Despite being highly preventable and treatable, cervical cancer ranks as the fourth most common cancer among women globally. Low- and middle-income countries (LMICs) bear a significant burden, accounting for 85% of global incidence and 90% of deaths (WHO, 2020). Among the regions most affected is Sub-Saharan Africa, where cervical cancer stands as the leading cause of cancer-related deaths in women (Bruni L, 2021a). The primary cause of cervical cancer is the sexually transmitted Human Papillomavirus (HPV) (Bruni L, 2021b). Notably, the co-occurrence of HPV and Human Immunodeficiency Virus (HIV) substantially increases the risk of cervical cancer, making women with an HPV infection six times more likely to develop the disease (WHO, 2020). This combination of HPV and HIV contributes significantly to the prevalence and severity of cervical cancer in LMICs.

Cervical cancer prevention relies on a three-pillar strategy of vaccination, screening, and treatment (WHO, 2020). While all three components are available in LMICs, screening remains the most challenging to implement effectively in national prevention programs (Yimer et al., 2021). The difficulty lies in incorporating high-quality screening technology within resource-constrained environments. Typically, cervical cancer screening involves a two-step process: primary screening to confirm the presence of cancerous cells or HPV infection, followed by secondary screening for final diagnosis (WHO, 2020). Developed countries with established screening programs have substantially reduced cervical cancer incidence and mortality by over 70% through Pap Smear or HPV-DNA tests followed by colposcopy diagnosis, with or without biopsy (Bedell et al., 2020).

Despite the success of cytology-based screening programs in developed countries, implementation in LMICs remains a challenge due to the dependence on laboratory infrastructure, expensive equipment, expert cytopathologists and gynaecologists, and the need for regular screenings (Bedell et al., 2020). As an alternative in low-resource settings, Visual Inspection with Acetic acid (VIA) followed by immediate treatment of the patient has been developed for mass screening programs (Sankaranarayanan et al., 2004). VIA involves visually inspecting the cervix for cancerous lesions by applying acetic acid, which causes cancerous cells to turn white—a process known as acetowhitening (Prendiville & Sankaranarayanan, 2017). Unlike colposcopy, VIA is performed with the naked eye, eliminating the need for a colposcope and colour filters to visualise the cervix's transformation zone up close (Denny et al., 2005). VIA offers advantages in resource-constrained settings: it is cost-effective, easy to perform, resource-efficient, and provides immediate results (Sankaranarayanan et al., 2004).

However, VIA has a significant drawback that has hindered its large-scale implementation—the diagnosis is subjective and heavily reliant on the clinician conducting the screening. This subjectivity leads to considerable variations in the sensitivity and specificity of VIA results, resulting in lower performance than other screening tests (Sankaranarayanan et al., 2004; Sarian et al., 2005). Recent advancements in digital optical technology and artificial intelligence (AI) have shown promise in overcoming VIA's variable diagnostic accuracy (Sami et al., 2022). Preliminary studies indicate that digital imaging can enhance VIA's diagnostic accuracy by offering improved visualisation capabilities, quality control measures, digital documentation, and connections to telecommunication platforms that enable offsite experts to assist in

diagnosis. AI-based cervical cancer diagnosis tools developed for these devices have also demonstrated the potential to significantly improve the sensitivity and specificity of VIA procedures, making the screen-and-treat process feasible on a large scale (Sami et al., 2022).

1.2 Project Rationale

Digital screening solutions aim to address the primary challenge faced by VIA—the diagnostic variability—while retaining the key features contributing to its success in LMICs, such as simplicity and low cost. These solutions show promise as an effective response to VIA's low diagnostic accuracy, although further research is needed to validate these findings (Sami et al., 2022). However, studies that examine the effectiveness of implementing these digital solutions in resource-constrained settings are scarce (Rossman et al., 2021). Piaggio et al. (2021) proposed a framework for designing resilient and effective medical devices in low-resource settings, which can be used to evaluate current digital screening devices compared to traditional VIA (Piaggio et al., 2021). The areas where the current devices are inferior include cost, consumable requirements, the number of components, and training needs.

Based on the criteria outlined by Piaggio et al. (2021) and considering current solutions' identified strengths and weaknesses, this project aims to design and develop a speculum-free, digital cervical cancer screening device suitable for large-scale screening programs in LMICs. The project will focus on something other than improving the screening accuracy of VIA, as existing digital screening devices have shown feasibility with digital technology. Instead, the project will prioritise developing a digital screening device with specific design features to facilitate implementation on a large scale in resource-constrained settings. By doing so, the device will be as implementable as VIA in LMICs while allowing for the integration of additional assistive digital screening tools in the future that can significantly improve diagnostic accuracy.

1.3 Research Question

This leads to the following research question: *Can a speculum-free cervical cancer screening device be designed and developed to achieve diagnostic accuracy comparable to the standard-of-care screening device, and how does its screening and usability performance compare to the standard of care in a clinical setting?*

1.4 Aim and Objectives

Aim: Develop a speculum-free cervical cancer screening device that achieves diagnostic accuracy similar to the standard-of-care screening device but with improved usability.

Objectives: The aim will be achieved through the following objectives:

1. Develop a device to perform a speculum-free cervical cancer screening procedure.
2. Conduct engineering tests on the newly developed device, guided by ISO 8600 standards for medical endoscopes and endotherapy devices, to ensure compliance with minimum standards for a colposcopy device.
3. Validate that the proposed device has equivalent diagnostic performance and improved usability to the standard of care screening tool in a clinical setting through comparative testing.

1.5 Scope and Limitations

The project scope is to develop a proof-of-concept device and demonstrate that it can successfully perform a cervical cancer screening procedure in a simulated clinical environment. The device will not be tested on human patients but on a medical training model to test its functionality and usability. Thus, the device will be developed according to the relevant medical device regulatory standards for medical endoscopes.

1.6 Dissertation Outline

This dissertation documents the research, development, and testing processes followed to complete the project. Figure 1 represents the flow of the chapters of the dissertation, with each block briefly explaining the contents of each chapter. The dissertation begins with an introduction to the research project, which identifies the problem, sets the research aim and objectives, and the scope of the research. In Chapter 2, an overview of cervical cancer is given in terms of epidemiological, anatomical, and physiological aspects. Then, an in-depth literature review is conducted on cervical cancer prevention, screening, and technological solutions. The review explores the various existing solutions used and then proceeds to evaluate each solution using a framework to guide the design of medical devices for low-resource settings. This evaluation provides insights into the solution required to solve the identified problem.

The knowledge and insights gained in Chapter 2 are used in Chapter 3 to guide the design of the cervical cancer screening device. Chapter 3 details the concept and engineering specifications that were eventually considered in the final prototype device design, and Chapter 4 details the development of the final prototype. Chapter 5 describes the verification testing and risk assessment procedures followed to test the device and ensure it meets all the engineering specifications identified in Chapter 3. Following the verification testing, Chapter 6 presents the final validation study used to test if the device met the project objectives in Chapter 1. The results are analysed and discussed in Chapter 6, after which the conclusion and future recommendations are discussed in Chapter 7.

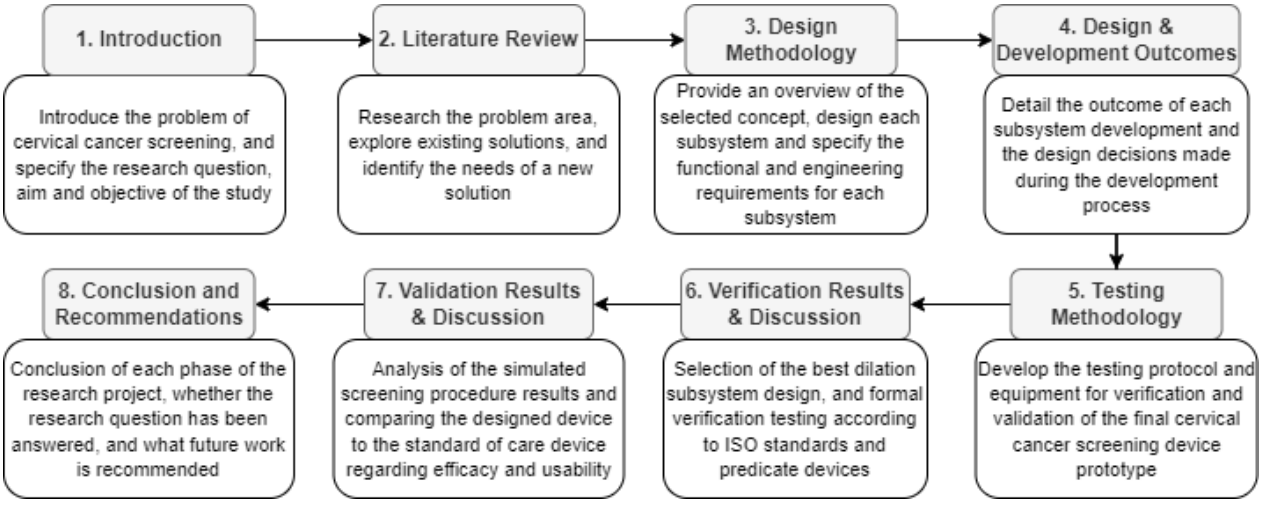

Figure 1: Dissertation Overview

2 Literature Review

2.1 Cervical Cancer Fundamentals

2.1.1 Epidemiology

Cervical cancer is predominantly attributed to Human Papillomavirus (HPV) infection, with 95% of malignant cervical lesions testing positive for HPV DNA. HPV is a sexually transmitted disease (STD) that affects both men and women, and its prevalence is so widespread that the majority of sexually active individuals are at risk of infection at some point in their lives. In approximately 90% of cases, the body's immune system can naturally clear the infection. However, in cases where the virus persists in women, it can lead to chronic infections, resulting in the development of precancerous lesions that may eventually progress into invasive cancer (Small et al., 2017; WHO, 2022).

HPV comprises more than 100 strains, categorised into low-risk (LR) and high-risk (HR) types. While multiple HR-HPV types can develop into cervical cancer, two specific strains, namely HPV-16 and HPV-18, are responsible for 70% of precancerous lesions and cervical cancer cases (Small et al., 2017). Several risk factors increase the likelihood of cervical cancer, including immune system disorders like HIV, co-infection with other STDs, engaging in sexual activity with multiple partners, smoking, oral contraceptive use, and socioeconomic status (Herbst, 2015).

2.1.2 Anatomy and Physiology

The cervix is a pivotal female reproductive organ located within the pelvic region, forming the connection between the vaginal canal and the uterine cavity, as shown in Figure 2. It is essential to understand the detailed anatomy and physiology of this organ to grasp the complexities of cervical cancer.

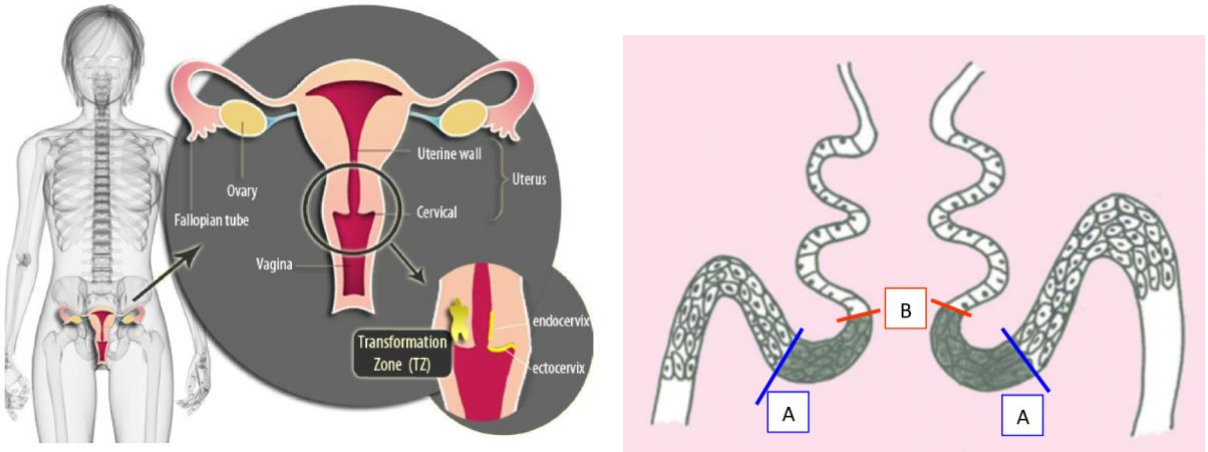

Figure 2: Female reproductive system anatomy, location of the cervix (left) (Herfs et al., 2012), and the transformation zone (right)(Prendiville & Sankaranarayanan, 2017).

The cervix consists of three regions, each with a distinct epithelial lining. The innermost region, the endocervix, is characterised by a lining of simple columnar epithelial cells. These cells play a crucial role in producing mucus that aids in fertility by facilitating the passage of sperm into the uterus while simultaneously acting as a protective barrier against potentially harmful microorganisms (Small et al., 2017). In contrast, the outer region of the cervix, the ectocervix, features a lining of stratified squamous

epithelial cells (Prendiville & Sankaranarayanan, 2017). This tissue type is more robust and resilient, providing durability to withstand the mechanical and microbial stresses associated with the vaginal environment. The transition between these two different cell types occurs at a critical juncture called the squamocolumnar junction (SCJ). The SCJ moves dynamically from the endocervix to the ectocervix. As the SCJ moves to lie on the ectocervix post-adolescence, it becomes the new SCJ, and the region between the original SCJ and the new SCJ is called the transformation zone (TZ). The new SCJ and original SCJ are denoted as A and B on the right of Figure 2, respectively, with the TZ between them. This region holds particular importance as it is susceptible to various cellular changes and is often the site where cervical abnormalities, including precancerous lesions, first manifest (Prendiville & Sankaranarayanan, 2017).

Beneath the layers of squamous epithelial cells in the ectocervix lies the basal layer, composed of a single layer of basal cells anchored firmly to the basement membrane. These basal cells serve as a reservoir of undifferentiated cells that can divide and differentiate into the specialised cells lining the ectocervix. This regenerative process is vital for continuously replenishing the ectocervix as it naturally sheds its surface layers, akin to a self-renewing protective barrier (Prendiville & Sankaranarayanan, 2017).

2.1.3 Pathophysiology

An HPV-infection originates when the human papillomavirus penetrates the epithelia at the SCJ to infect the basal cells of the squamous epithelium. From the moment of infection, there is a prolonged precursor stage during which the virus attempts to infect the basal cells, but the immune system fights against the infection. During this precursor stage, the immune system clears 90% of HPV infections. If the immune system cannot clear the infection, the virus will infect and alter the genome of the basal cells. This results in the amplification of specific genes in the cells that aid the replication of viral cells, which results in the infection of more basal cells. As shown in Figure 3, this process of HPV infection in the epithelial cells continues for years and eventually develops into various stages of lesions and, ultimately, invasive cancer (Prendiville & Sankaranarayanan, 2017).

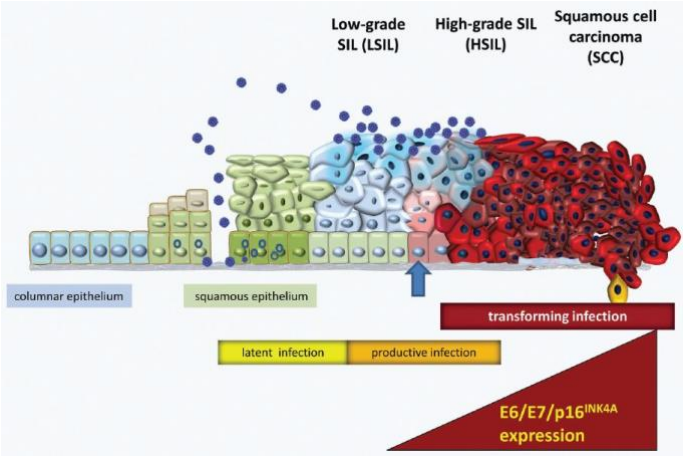

Figure 3: HPV Infection Development (Prendiville & Sankaranarayanan, 2017).

The cervical cancer lesions that develop as the HPV infection progresses are typically classified via cytology and histology methods. The difference between the methods is that cytology studies the cells, and histology studies the tissues. Both approaches use microscopes to classify the extent (or severity) of the epithelium's squamous intraepithelial lesion (SIL). As shown in Figure 3, the lesions are classified as low-grade SIL, high-grade SIL, or squamous cell carcinoma (where the cancerous cells have broken through the basement membrane). Another naming convention used for cervical lesion classification is to refer to

the epithelial abnormalities as cervical intraepithelial neoplasia (CIN), and assign the lesions severity grades of CIN1, CIN2, CIN3, and invasive cancer (Prendiville & Sankaranarayanan, 2017).

2.1.4 Clinical Presentation

As mentioned above, in the early stages of development, the HPV infection remains latent for a prolonged period. During this period, the patients show no symptoms of the infection. If a patient does not go for a regular cervical cancer screening, the first signs of symptoms appear at a relatively advanced stage of invasive cancer. At the advanced stage, the most common symptom is abnormal vaginal bleeding (Herbst, 2015). In advanced cases, when the disease is in the invasive cancer stage and has started infecting surrounding structures, symptoms such as rectal bleeding, loin pain, oedema, and haematuria can be observed. Treatments for precancerous lesions include cryotherapy, surgical excision, laser therapy, and photodynamic therapy. Treatments for invasive cancer include surgery, chemotherapy, radiotherapy, and palliative care (Small et al., 2017).

2.2 Cervical Cancer Prevention

To mitigate the incidence, morbidity, and mortality associated with cervical cancer, the World Health Organization (WHO) has outlined a comprehensive three-level protocol for prevention and control. The initial level, primary prevention, focuses on girls aged 9 to 14 years who receive the HPV vaccination alongside comprehensive education about practising safe sexual behaviour, refraining from smoking, and the importance of male circumcision. Secondary prevention involves the screening of all women aged 30 and above, as well as women with HIV starting from age 25. Screening must employ a test that is equivalent or superior to an HPV test, and if the results are positive, immediate treatment is imperative. The third and final level of control is dedicated to all women requiring treatment for invasive cervical cancer, with options including surgery, radiotherapy, chemotherapy, or palliative care (WHO, 2022).

Overview of prevention strategies and the WHO guidelines

In 2020, the WHO launched a global strategy that aims to eliminate cervical cancer as a public health problem (WHO, 2022). The strategy is based around the 90-70-90 targets that must be met by 2030 to put countries on a path towards eliminating cervical cancer. These targets aim for (WHO, 2020):

- 90% of girls fully vaccinated with the HPV vaccine before the age of 15,
- 70% of women screened with a high-performance test by the age of 35 and again by 45 years of age,
- 90% of women identified with cervical cancer receive treatment (either for precancer or invasive cancer).

This strategy highlights the three critical aspects of any cervical cancer prevention program – HPV vaccination, screening, and treatment. If these targets can be reached by 2030 and maintained, mathematical models estimate that cervical cancer incidence will be reduced by 97% within 100 years and save tens of millions of lives in LMICs (WHO, 2020).

Primary prevention – HPV vaccine

The viral origin of cervical cancer makes it possible to develop an HPV vaccine that can prevent HPV infection. Currently, there are three different HPV vaccines available, with the first vaccine receiving FDA approval in 2006. These vaccines aim to immunise girls and women against the most persistent and

high-risk HPV types, HPV-16 and HPV-18 (NCI, 2022). These vaccines have proven to be the most effective long-term intervention to prevent HPV infection and all stages of cervical cancer. However, for optimal efficacy, the vaccine needs to be administered before the individual becomes sexually active and gets exposed to HPV, which is why the WHO recommends that girls between the ages of 9 and 14 years receive the vaccination (WHO, 2020).

Secondary prevention – screening and treatment of precancerous lesions

Despite the high efficacy of the HPV vaccine, it does not replace or reduce the need for women to be screened for cervical cancer. The primary goal of screening is to identify women with precancerous lesions that need to receive treatment (WHO, 2020). There are several screening methods, and as technology advances and the global emphasis on women's health increases, newer screening methods are emerging that could possibly replace the traditional methods. The most important commonly used screening methods will be discussed in greater detail in the next section.

In addition to the screening procedures, the WHO included the treatment of precancerous lesions as part of secondary prevention. Thermal ablation and cryotherapy methods are the two recognised treatment modalities accepted by the WHO for treating lesions (WHO, 2020). These treatments are safe and effective and can be performed in outpatient settings.

Tertiary prevention – treatment of invasive cancer and palliative care

Tertiary prevention focuses on the treatment of invasive cancer and palliative care. The treatment for invasive cervical cancer requires timely further examination and testing after the initial diagnosis is made, and these procedures typically happen in higher levels of the health system (WHO, 2020). Once the diagnosis is confirmed, the appropriate treatment is performed, typically involving surgical excision followed by the appropriate treatment, depending on the cancer stage. The most effective therapy after surgical excision is radiotherapy, with or without chemotherapy.

Disparities between LMICs and HICs in terms of prevention strategies

This proposed three-stage prevention strategy has proven to be highly effective in reducing cervical cancer incidences and mortality in high-income countries. This inspired the WHO to set the 90-70-90 targets, which are primarily aimed at resource-restricted LMICs (Davies-Oliveira et al., 2021). However, these targets are ambitious, with many HICs finding it difficult to reach the vaccination and screening coverage targets.

The disparities between cervical cancer prevention in HICs and LMICs regarding each of the three primary pillars of prevention are significant. A systematic review found that the average global cervical cancer screening adherence rate in 2019 for women aged 20-69 years was 33.66%, but that HICs and LMICs have average adherence rates of 75.66% and 24.91%, respectively (Zhang et al., 2022). These adherence rates vary from being as high as 82.57% in Denmark to as low as 11.70% in South Africa. Thus, as it stands, the global cervical cancer screening rates still fall far short of the target of 70% set by the WHO.

A comprehensive understanding of all the associated factors that are barriers to cervical cancer screening is needed to attempt to increase adherence rates. Petersen et al. (2022) carried out a systematic review that grouped these barriers to screening into five groups: individual/person, cultural and religious, social, health system, and structural barriers. Each of these categories contains several associated factors that are barriers to screening, but the study found that four primary barriers underpin all the rest:

1. **Lack of information and education.** Limited information and education about cervical cancer and screening, along with misconceptions about the cause of cervical cancer and the screening process, lead to a lack of awareness and understanding of screening's importance.
2. **Inadequate readiness of healthcare systems.** Many healthcare facilities lack the necessary resources, clear policies, or proper implementation of existing policies related to cervical cancer and screening, which hinders access to screening services.
3. **Limited access to healthcare services.** In many LMICs, the lack of universal health coverage and affordability creates obstacles to accessing healthcare, including cervical cancer screening. Geographic barriers and additional costs, such as transportation, further impede access.
4. **Cultural and gender norms.** Societal norms and gender inequalities deprioritise the health needs of women, both at institutional and community levels. Patriarchal norms that favour the needs of men and boys over women and girls impact investment in women's health and contribute to inequities in healthcare and women's access to care. Factors like partner approval, religious/cultural restrictions, and traditional prohibitions also act as barriers to screening uptake.

The study highlights the scale of the multidisciplinary interventions that are required to successfully improve cervical cancer screening uptake to achieve the WHO's goals and eliminate cervical cancer. One intervention that could immediately contribute to increasing screening uptake is increasing access to screening services. Some factors contributing to the current lack of access include a lack of capacity in healthcare systems, limited facilities, equipment and materials shortages in rural areas, high travel and screening costs for patients, and lengthy screening and treatment pathways (Petersen et al., 2022). In the context of cervical cancer, the lack of capacity refers to the limited number of experts, such as gynaecologists, and the poor technical skills of healthcare providers to perform the procedures.

2.3 Cervical Cancer Screening

The primary goal of cervical cancer screening is to prevent invasive cancer by identifying precancers that can be treated. Despite the increasing global HPV vaccination efforts and its effectiveness, cervical cancer screening will continue to be an essential part of cervical cancer control (Wentzensen et al., 2016). HPV vaccination is highly effective in protecting people against the high-risk types of HPV which cause most cervical cancers. However, HPV vaccines do not protect people against all types of HPV, nor do they guarantee that cervical cancer will not develop. For this reason, regular cervical cancer screening will still be necessary to detect minor changes in the cervix over time to identify potential issues early, when they are most treatable.

The standard screening process can be summarised into three sequential phases: primary screening tests, secondary screening/triage tests, and management of abnormal tests (Botha & Dreyer, 2017). However, due to the disparities in screening successes between LMICs and HICs, this screening process has been expanded to include two options that can be used based on the screening setting. The first option is that the three-phase screening algorithm remains in place in well-resourced settings. However, in limited-resource settings, a two-phase screening procedure is used where patients with positive primary screening results should be treated immediately (WHO, 2022). The four leading screening solutions that are widely used include the Pap Smear, visual inspection with acetic acid (VIA), HPV tests, and colposcopy-guided biopsy. Each of these will be discussed in this section, along with the commercially available products associated with each screening technique.

2.3.1 Pap Smear

A Pap smear, also known as a Pap test or cervical cytology, is a well-established and widely used screening method for cervical cancer. When implemented in national screening programs that have the resources to achieve high coverage, patient follow-up, additional tests, and subsequent disease management, this cytology screening methods have been very successful in reducing cervical cancer incidence and mortality (WHO, 2020). The steps involved in a Pap smear are:

1. **Sample Collection:** During a Pap smear, a healthcare provider collects a small sample of cervical cells from the patient's cervix. This is typically done using a specialised spatula or brush to scrape or swipe the cervix's surface gently.
2. **Sample Preparation:** The collected cervical cells are placed on a glass slide or in a liquid-based medium. Liquid-based cytology has become increasingly common, allowing for more efficient and accurate sample processing.
3. **Laboratory Analysis:** The collected cervical cell samples are analysed in a laboratory. In the laboratory, trained cytotechnologists or pathologists examine the cells under a microscope. During these microscopic examinations, healthcare professionals look for abnormalities in the cervical cells, including size, shape, and structure changes. These can be indicative of precancerous or cancerous conditions.
4. **Reporting and Follow-Up:** Based on the cytological findings, the Pap smear result is categorised into one of five different categories, namely "normal," "atypical squamous cells of undetermined significance" (ASC-US), "low-grade squamous intraepithelial lesion" (LSIL), "high-grade squamous intraepithelial lesion" (HSIL), or "atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion" (ASC-H).
5. **Further Evaluation and Treatment:** Follow-up procedures may be recommended depending on the Pap smear result. For example, if abnormal cells or precancerous changes are detected (e.g., LSIL, HSIL), further evaluation procedures, such as colposcopy and biopsy, may be advised to confirm the diagnosis and determine the extent of cervical abnormalities. Treatment, if necessary, can then be initiated.

Some of the critical strengths of Pap smears are the effectiveness at detecting precancerous lesions at an early stage, they have a well-established track record and have shown to be effective, and sample collection is simple and non-invasive (Shrute Kannappan, 2021). However, some significant limitations are the high rate of false negatives, variability in interpretation based on technician experience, the significant infrastructure and laboratory network required, and the need for multiple follow-up tests (Bedell et al., 2020). These limitations are among the primary reasons why the Pap smear has yet to be implemented with the same success in LMICs as in HICs.

2.3.2 Visual Inspection with Acetic Acid (VIA)

VIA is a straightforward and cost-effective method used in the initial screening of cervical cancer and precancerous lesions. During VIA, a patient undergoes a pelvic examination in which a speculum is inserted into the vagina to visualise the cervix. A solution containing 5% acetic acid (vinegar) is then applied to the cervix, temporarily causing any abnormal areas to turn white in a process called acetowhitening (Prendiville & Sankaranarayanan, 2017; Sankaranarayanan et al., 2004). Healthcare providers inspect the cervix, either with the naked eye or a colposcope, a magnifying device. The appearance of white patches or lesions following the acetic acid application may indicate potential issues since it is a characteristic

feature of precancerous lesions to turn white as the acetic acid coagulates the excessive proteins (Shrute Kannappan, 2021).

VIA is particularly well suited for resource-limited settings and regions where access to healthcare may be challenging. It is a vital component of the screen-and-treat or single-visit approach to cervical cancer screening, where women are screened and, if necessary, immediately treated during a single healthcare visit (Denny et al., 2005). VIA is highly applicable to this approach due to its simplicity and immediate results. The test results are either true or false for the presence of visible cancerous or precancerous lesions. If visible abnormalities or lesions are detected during VIA, they can be documented and assessed immediately. Women identified with abnormal findings through VIA may become candidates for immediate treatment, which can include cryotherapy, thermal ablation therapy, loop electrosurgical excision procedure (LEEP), or other appropriate methods for removing or treating precancerous lesions.

The strengths of this approach are that it minimises the need for multiple healthcare visits, reduces the risk of loss to follow-up, and ensures timely intervention, particularly in underserved or remote areas (Bedell et al., 2020). It also requires less infrastructure and equipment to perform the procedure, and the results are simple and immediate. However, the primary limitation of VIA is the high rate of false-positive results that lead to overtreatment and further complications (Sankaranarayanan et al., 2004). The primary cause of the low specificity is false diagnoses of other diseases, such as cervicitis, that also cause a reaction similar to the acetowhitening reaction when acetic acid is applied. An additional limitation of the procedure is the highly subjective nature of the results since it relies on the observer's interpretation to make a qualitative diagnosis, leading to significant variability in diagnostic accuracy.

Recent advancements in digital technology have aimed to enhance VIA's effectiveness. Digital colposcopes and high-resolution imaging systems like the *MobileODT EVA*, *Gynocular*, and *Callascope* have been introduced to improve VIA's visualisation and diagnostic capabilities (Bedell et al., 2020). These technologies enable healthcare providers to capture and store detailed images of the cervix, which can aid in documentation and allow for remote consultations and long-term monitoring of patients. Integrating digital technology has improved the accuracy and reliability of VIA results, contributing to more effective cervical cancer screening and management.

2.3.3 Nucleic Acid-based Test

Polymerase Chain Reaction (PCR) and nucleic acid tests (NATs) have emerged as powerful and sensitive methods for cervical cancer screening, particularly in the detection of high-risk HPV infections. PCR is a laboratory technique to amplify and detect specific DNA sequences (Bedell et al., 2020). In the context of cervical cancer screening, PCR is employed to identify the presence of high-risk HPV DNA in cervical samples. The process involves the following steps (Shrute Kannappan, 2021):

1. **Sample Collection:** A healthcare provider collects a cervical sample (typically via a Pap smear or swab) from the patient's cervix, or the patient collects a sample.
2. **DNA Extraction:** DNA is extracted from the collected cervical cells.
3. **PCR Amplification:** Using specific primers, PCR amplifies the DNA region associated with high-risk HPV types. This amplification process makes it easier to detect even small amounts of HPV DNA.
4. **Detection:** The amplified DNA is then subjected to detection methods, such as gel electrophoresis or fluorescence-based assays, to determine the presence or absence of high-risk HPV types.

These screening methods are highly sensitive and specific in detecting high-risk HPV infections. When high-risk HPV types are detected, healthcare providers can promptly initiate appropriate follow-up and management strategies, such as colposcopy, to assess the extent of cervical abnormalities and guide treatment decisions.

This approach's high specificity and sensitivity has led the WHO and national health departments to adopt HPV DNA testing as part of a new screening protocol in combination with cytology-based methods, such as Pap smears. This new protocol aims to improve the accuracy of cervical cancer screening and replace cytology-based procedures entirely in the future (WHO, 2020). Molecular tests are particularly valuable for identifying high-risk HPV infections in women, even when no significant cervical abnormalities are present. This enables early intervention and monitoring to prevent the progression of cervical lesions to cancer.

This technology has been clinically proven to be effective in primary screening for HPV, with numerous kits receiving FDA approval, such as *Xpert HPV Assay, Cervista HPV HR, Roche Linear Array, Cervista HPV 16/18, Hybrid Capture 2, and Cobas HPV test,* to name a few (Prakash et al., 2016). These systems have also been used extensively in South Africa in HIV and TB screening programmes and, more recently, for COVID-19 screening.

One of the most significant advantages of HPV testing as a co-testing or primary testing modality is the simple sample collection method, which the patient can perform via self-swabbing. This makes the approach highly beneficial in low-resource settings since it allows more women to be screened without needing expert gynaecologists and cytologists to screen every patient. However, one major limitation is the high cost of the equipment, maintenance requirements, and the high cost of consumables required per test (Bedell et al., 2020).

2.3.4 Colposcopy and Colposcopy-guided Biopsy

Colposcopy and colposcopy-guided biopsy are crucial components of cervical cancer screening and play a vital role in the early detection of cervical abnormalities. Colposcopy is a specialised and magnified examination of the cervix, typically recommended for women who have received abnormal Pap smear results or tested positive for high-risk HPV (Eugen et al., 2017). During a colposcopy, a healthcare provider uses a colposcope, which is a binocular microscope with a light source, to inspect the cervix's surface closely. This magnified view allows the healthcare provider to identify unusual or abnormal areas, such as precancerous lesions, that turn white after applying 3-5% acetic acid or abnormal blood vessels and vascular patterns (Prendiville & Sankaranarayanan, 2017).

A colposcopic biopsy may be performed if suspicious areas are identified during the colposcopy. A biopsy involves the removal of a small tissue sample from the abnormal area of the cervix. The tissue sample is sent to a laboratory for histological analysis to determine whether the cervical cells are precancerous or cancerous. Thus, colposcopy and colposcopic biopsies are critical in providing a more detailed and precise assessment of cervical health beyond what a Pap smear or HPV test alone can offer. If abnormal cells are confirmed, healthcare providers can develop appropriate treatment plans to prevent the progression to invasive cancer.

2.4 Evaluation of Screening Solutions

One of the main factors contributing to the overall poor state of the healthcare system in LMICs is the poor design of medical devices (MDs) for the contexts in which they operate. A common-known problem is that up to 80% of medical technologies are donated to LMICs, but between 70-90% are broken or non-operational (Piaggio et al., 2021). This problem originates from the fact that these MDs are designed for healthcare standards in HICs that cannot be achieved in LMICs, which means that the infrastructure and knowledge to use and maintain these technologies are unavailable. To overcome this problem, efforts are being made to improve the design process of medical devices to make them more resilient to low-resource settings. The most popular term for this new design concept is 'frugal biodesign' (Harris et al., 2020; Sivarasu, 2019).

Another concept also being promoted in conjunction with 'frugal biodesign' is called 'reverse innovation', which is the flow of ideas and technology from LMICs to HICs (DePasse & Lee, 2013). This principle is well established in the business world, and attempts have been made to apply this thinking model to healthcare technologies and innovation. This concept promotes the idea that HICs can benefit from innovative healthcare technologies and practices developed for LMICs due to their improved cost, quality of care, access, and effectiveness (Harris et al., 2020). Thus, by thinking about cervical cancer screening solutions through the lens of 'reverse innovation' and applying 'frugal biodesign' principles, the design strengths and weaknesses of current screening solutions can be identified, and innovative improvements can be made.

2.4.1 Evaluation Matrix Overview

Piaggio et al. created a framework that could guide the design of medical devices for low-resource settings (Piaggio et al., 2021). The framework is based on essential criteria that need to be considered when designing healthcare technologies that are resilient yet effective in these settings. In the research, they initially identified, classified, and weighted the criteria based on literature reviews and then by relevant scholars and experts from 19 different countries. The result of this study was a framework that can be used to holistically assess medical devices to see if they are compliant and well-designed for low-resource settings or to start a new innovative design project. In this research, the framework was utilised to analyse the existing cervical cancer screening solutions to identify commonalities between solutions and understand their effectiveness in LMICs. These findings were used to guide the project towards an appropriate solution. The screening solutions that were analysed include the three primary solutions that the WHO promotes: HPV-DNA testing, Pap Smear, and VIA, along with some of the emerging digital technologies on the market, such as the Gynocular, MobileODT EVA, Pocket Colposcope, and Callascope.

The evaluation matrix framework developed by Piaggio et al. and used for the analysis can be found in Appendix A, including the detailed list of components and decontamination methods considered for each screening solution. Identifying and clarifying these components and decontamination methods are critical since the solutions in their entirety need to be analysed, including the peripheral products and infrastructure required to perform the screening and decontamination post-screening. For example, suppose only the primary components that are used in a pap smear at the point of care, i.e. sample collection swab kit, are considered. In that case, evaluating the resilience of the pap smear screening procedure in low-resource settings will be significantly different since the expert laboratory, cytopathologists, and microscope needed to make the diagnosis would not be considered.

In the matrix, a qualitative score is given to each solution for each criterion based on the component of the solution with the worst score. For example, the Pap smear requires 'specialised personnel' to perform the maintenance since the microscope has specialised operator and maintenance requirements, even though the other components, such as the sample collection kit, require minimal to no maintenance. The scoring legend used for the criterion is shown in Figure 53 on page 93, which uses a 3-point Likert scale. These results were converted to a score of 1 to 3, with 1 being the lowest score and 3 the highest score, and the scores across all the criteria were summed for each screening solution. The evaluation matrix results are shown in Table 1 below, which shows the solutions that were evaluated and how their total scores compare against each other. Based on the Likert scale used, the higher the total score of the solution, the more suited it is for cervical cancer screening in low-resource settings.

2.4.2 Evaluation Matrix Outcomes

The detailed evaluation matrix from which the summary table was generated is shown in Figure 52 to 54 in Appendix A. These figures present the scores given to each screening solution, and how these scores were converted and added to calculate the totals shown below. The highest-scoring solution (i.e. that is the most well-suited to screening in low-resource settings) was VIA/VILI, and this is consistent with what the literature research has shown thus far. The criteria that set the VIA/VILI solution apart from the rest were maintenance frequency, maintenance complexity, need for consumables, need for spare parts, compatible consumables/spare parts, and limiting the number of components/spare parts. This solution also performed the best for all cost metrics, including initial, maintenance, and running costs.

Table 1: Total scores and rankings of the various cervical cancer screening solutions using the evaluation matrix.

Medical Devices		**Ranking Without Cost**		**Ranking With Cost**	
Category	**Solution**	**Total**	**Ranking**	**Total**	**Ranking**
Existing solutions	**Pap Smear**	40	8	44	8
	VIA/VILI	57	1	66	1
	HPV-DNA Test (PCR)	42	7	45	7
	Colposcopy	46	5	51	6
New solutions	**Gynocular**	48	2	53	4
	MobileODT EVA	48	2	55	3
	Callascope	46	5	53	4
	Pocket Colposcope	48	2	56	2

The new digital visual screening solutions that enhance VIA or colposcopy, such as the MobileODT, Gynocular, Callascope, and POCKET Colposcope performed second best along with normal colposcopy. These solutions had very similar overall scores, with some minor differences in specific criteria based on the unique features of each. On average, the strengths of this group of solutions over the solutions that ranked lowest were their low installation requirements, portability, compactness and robustness, low reliance on power sources, and minimal to no need for sample preparation.

The solutions that had the lowest scores and are thus the worst suited for low-resource settings were the Pap Smear and PCR HPV-DNA Test, with the Pap Smear having the lowest score. Although research and historical data show that these two solutions are highly effective in screening for cervical cancer, they have some key aspects that make their implementation difficult. The most significant weaknesses of the two solutions are their high installation requirements, low portability, low compactness and robustness, high reliance on power sources, and need for specialised sample preparation.

The cost evaluation for the different solutions was difficult to quantify with a high degree of confidence due to the lack of information available. No research or information could be found that accurately assesses and compares the cost of the different solutions, including initial cost, maintenance cost, and running cost. Thus, a subjective judgement was made to categorise the costs into three groups (high, medium, and low) based on the researcher's understanding of each solution from the literature and compared to the solution with the lowest cost, VIA. The initial cost groups were given ranges within which the costs fall, since some information about some of the solutions could be found. For the other two cost categories, maintenance and running costs, the grouping allocation is based purely on understanding the solution, such as how technical and specialised the components are and what the consumables are per screening.

Subjectively, the screening solution with the highest cost across all three criteria is the HPV test, and the solution with the lowest cost is the VIA. According to the study by Piaggio et al., the initial cost is less important than the maintenance and running costs for low-resource settings. With this in mind, the Callascope device with its single-use probe scores worse than the other low-cost solutions for running costs, even though the other solutions that use speculums have to decontaminate more equipment after each screening. In addition to the cost aspect, the single-use probe of the Callascope is not practical in logistically and space-constrained environments where screen-and-treat procedures would typically be performed. The HPV-DNA test has the highest cost across all three cost criteria, but for this solution, the critical cost criterion that is the most important and needs to be reduced the most is the cost per individual screening. The HPV-DNA test will always have the highest costs compared to these point-of-care and low-cost solutions. However, its primary goal is to be an effective primary screening solution that can do mass screenings, making the high initial and maintenance costs less significant factors.

2.5 Design Requirements

A review of the literature has explained what cervical cancer is, how it develops, and what can be done to reduce the burden that it is currently placing on women and healthcare systems, especially in LMICs. The literature has shown how successful prevention programs have been in HICs but that these strategies do not effectively translate to low-resource settings. This has forced governments and organisations like the WHO to come up with new strategies that are more fitting to LMICs, such as the screen-and-treat approach. However, until recently, the problem with this approach has been that the available screening solutions have been ineffective in LMICs, which has led to the development of promising new screening solutions such as HPV-DNA testing and low-cost digital VIA devices. An evaluation of these new solutions, along with the traditional screening solutions, was conducted to determine if they would be more effective and ultimately successful in LMICs.

A few critical barriers to effective implementation on a large scale were identified using the "*Framework for designing medical devices resilient to low-resource settings*" by Piaggio et al. to evaluate the solutions. The HPV-DNA test has shown significant promise as a better primary screening tool that can replace the Pap Smear and will likely do so in the near future. On the other hand, digital VIA or colposcopy solutions are needed to fill the gap as triage or primary screening devices in low-resource settings where HPV-DNA tests are hard to implement effectively. Some of the most significant implementation barriers to digital VIA devices are the number of components and consumables required per patient, which need to be decontaminated each time, the maintenance and running costs, and the complexity of some of the solutions. The speculum was also identified as a barrier to the patients and the healthcare system, which

must either keep providing new single-use speculums or continuously decontaminate them after each use. However, these solutions have strengths such as high portability and compactness, low initial costs, little to no reliance on grid power, and use of the VIA procedure as the basis of their diagnostic method.

Based on this, it seems clear that there is a need for a cervical cancer screening device that has the following attributes: is digital and speculum-free, functions based on the VIA procedure, is easy to use, and is optimised to perform a primary screening or triage procedure in low-resource settings. Moreover, if the design is successful in low-resource settings, it would also be practical and valuable in well-resourced healthcare settings to perform the same procedures. The essential design requirement of such a device is summarised in Table 2 below. These are the high-level requirements that the final solution has to satisfy to be an effective cervical cancer screening solution in low-resource settings.

Table 2: Identified design requirements based on literature research.

Design Requirements	Source
Portable, compact, and robust	This is the most significant design criterion when designing medical devices for low-resource settings (Piaggio et al., 2021).
Digital	Digital VIA has several benefits over unassisted VIA, so the new visual screening solutions are all digitally based (Sami et al., 2022).
Point-of-care test	In resource-constrained settings where HPV testing is not feasible, the WHO suggests a screen-and-treat approach using VIA (WHO, 2020).
Triage test	WHO suggests that a strategy of screening with an HPV test followed by triage with VIA should be followed if both are available in a screening programme (WHO, 2022).
Easy to use and to learn to use	One of the major strengths of the VIA procedure that makes it so feasible in low-resource settings is its simplicity, allowing a wide range of medical practitioners to perform the screening (Bedell et al., 2020).
Scalable – not limited by a reliance on infrastructure to increase screening rates	One of the major problems with current screening methods is the infrastructure required at screening centres, such as the decontamination processes required after each screening (Bedell et al., 2020).
Simplified decontamination procedures	Decontamination is a prominent component of a medical device's continuous cost (running cost), which is why it is a more critical design consideration than the initial cost (Piaggio et al., 2021)
Low-to-no reliance on grid power	The new digital screening solutions* are all battery-powered, and reliance on external power sources is the main criterion for considering external factors when designing medical devices resilient to low-resource settings (Piaggio et al., 2021).
Speculum-free	It was identified as an element of current screening solutions that increases the number of components and decontamination requirements. It also increases running, maintenance, capital costs, and the need for spares (Piaggio et al., 2021).
Uses fewer consumables per screening	This is one of the significant strengths of the traditional VIA procedure, which makes it feasible in low-resource settings (Bedell et al., 2020)
Reduced cost – maintenance, running and capital costs	The two most important criteria to consider when designing a medical device for low-resource settings are the maintenance and running costs (Piaggio et al., 2021).
Minimal number of components	Every additional component increases the running costs, maintenance costs, need for spares and infrastructure required to sustain the screening solution (Piaggio et al., 2021)

*Predicate devices: Gynocular , MobileODT EVA , Callascope , Pocket Colposcope.

3 Design Methodology

This chapter outlines the design methodology used to develop a cervical cancer screening solution to address and meet the design requirements identified from the literature review. The chapter contains the overview of the design concept that was developed into the final prototype and the different subsystems that the concept was broken into to guide the development process towards the design outcomes. The design requirements identified in Table 2 on page 15 are the system-level requirements, and the functional requirements of each subsystem were developed to ensure that the subsystems performed their intended function within the system. These functional requirements were broken down further and used to identify the engineering specifications that had to be met for the subsystem to perform that function.

3.1 Conceptual Design

The device concept was a handheld point-of-care screening device that was based on the diagnosis fundamentals of the VIA screening procedure. The design philosophy of the concept was to use technological advancements in imaging and processing to improve the VIA screening method and encase these digital systems in a device designed to be effective and successful in low-resource environments. This concept aimed to fill the role of either being used as a primary screening device in a screen-and-treat setting in low-resource settings or as a triage device after a positive HPV or Pap test and before a complete colposcopy examination and biopsy is done.

The design focused on building all the components required for the screening procedure into a single housing that has a small form factor and could function without a speculum. Thus, to function without a speculum, the concept made use of an insertion probe that needed to be inserted into the vaginal canal and positioned in front of the cervix. The final concept is broken down into its functional blocks to identify each function, component, and engineering specifications. The individual functionality of the functional blocks, shown in Figure 4 below, would ultimately combine to create a complete device that could perform an entire cervical cancer screening procedure. These functional blocks were referred to as subsystems and were detailed as follows:

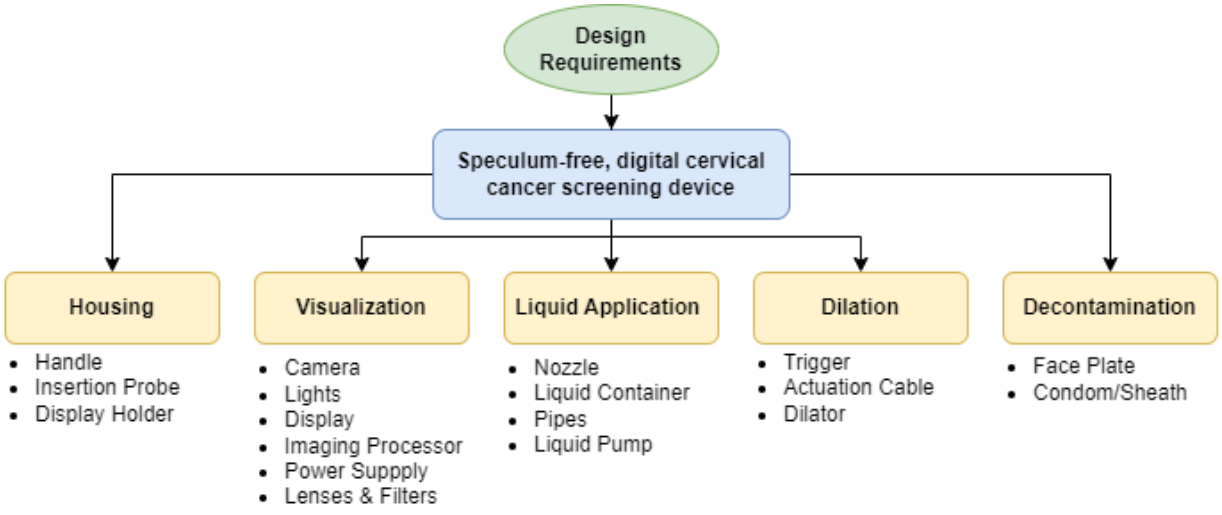

Figure 4: Function blocks (subsystems) into which the device was broken down for design and development and the elements constituting each subsystem at the end of the design phase.

The following sections detail the design of each of these subsystems. It explains the rationale behind the design decisions and the literature used to support them. Through this process, the overall conceptual design of the device was established and finalised, from which the various iterations and embodiments of this concept were generated in the development phase.

3.2 Subsystem Design

3.2.1 Housing Subsystem Design

The function of this subsystem was to house and support all the other subsystems and provide an intuitive and ergonomic platform for the user to interact with. The housing consisted of three components: the insertion probe, handle, and display holder. The insertion probe was needed due to the decision to pursue a speculum-free design. This design decision was based on the information found in the literature that highlighted several problems with the requirement for speculum use, such as patient discomfort, reducing the number of components, and sterilisation requirements. In the context of screening in low-resource settings where the correct decontamination equipment is not always available, reducing the number of times a speculum needs to be decontaminated would allow more patients to be screened. A more in-depth literature review of the vaginal speculum follows in Section 3.2.4 on page 19 below.

To optimise the design for patient comfort, the diameter of the insertion probe needed to be kept to a minimum. Consequently, the handle was required to house the large components from the other subsystems while being small enough for one-handed operation. Additionally, the layout of the components and user controls on the handle needed to accommodate both left- and right-handed operators. The display holder was attached to the handle to compact the device and reduce the number of loose components during screening. The display holder needed to position the display to make it comfortable for the operator to see the entire display and interact with the controls on the display. The functional requirements that were developed to achieve this functionality are listed in Table 3, along with the accompanying engineering specifications that were identified.

Table 3: Housing subsystem functional requirements and engineering specifications (ES).

ES No	Functional Requirement	Engineering Specification	Value
1.1	Probe needs to be inserted into the vaginal canal up to the cervix.	Maximum insertion width/diameter	<=20mm[1]
1.2		Minimum probe insertion depth	100mm[1]
1.3	Device needs to be one-hand operated.	Maximum weight	<1kg[2]
1.4		Maximum width at maximum cross-section50	<50mm[3]
1.5	The operator must position the display in their preferred position for visualisation and usability.	Adjustable display holder	Yes/No

[1](Barnhart et al., 2006).

[2]Predicate devices 510(k) submission documents: MobileODT EVA, Gynocular, POCKET Colposcope.

[3] The device is designed to be one-hand operated, thus it needs to comfortably fit in the operator's palm when their hand is cupped. Therefore, the value is taken as half the palm length of the lower 5th-percentile female (Gordon et al., 2014). Female palm length is used since it is shorter than male palm length.

3.2.2 Visualisation Subsystem Design

This subsystem was one of the critical subsystems of the concept since its primary function is to allow the user to visualise the cervix. To achieve this function, the subsystem required the integration of four systems smaller subsystems: imaging, illumination, power supply, and display systems.

The probe-based design of the device required that the imaging and illumination components that needed to interact with the cervix be as small as possible to minimise the size of the insertion probe. Additionally, between these two systems, there needed to be the ability for the operator to apply a green filter to the image of the cervix seen by the operator. The green filter is applied to assist with examining delicate vessel patterns by removing the background redness of the cervix and allowing the vessels to stand out as black lines (Prendiville & Sankaranarayanan, 2017). Thus, the filter could be a physical filter positioned between the light source and the cervix, between the cervix and the camera, or a software filter applied to the displayed image.

In addition to being small, the camera and lights are needed to provide the operator with a high-resolution image of the cervix to identify the small features and abnormalities used to make a diagnosis accurately. The camera, image processor, and display combination had to display a real-time video to the operator. Finally, the operator also had to be able to adjust the brightness of the light source during the procedure to find the optimal intensity. The functional requirements that were developed to achieve this functionality are listed in Table 4, along with the accompanying engineering specifications that were identified.

Table 4: Visualisation subsystem functional requirements and engineering specifications (ES).

ES No	Functional Requirement	Engineering Specification	Value
2.1	Imaging and illumination system components need to be close to the cervix	Working distance (WD)	20-50mm[1]
2.2		Minimum Field of View @ minimum WD	>70°[1]
2.3		Minimum illumination beam diameter @ minimum WD	>30mm[1]
2.4		Direction of view	0 degrees[2]
2.5	Imaging and illumination system needs to provide a clear and high-resolution image of the cervix	Limiting resolution @ maximum working distance	>11lp/mm[2]
2.6		Image distortion	<3%[2]
2.7		Illumination intensity @ maximum working distance	>1000Lux[2]
2.8		Illumination colour	White light[2]
2.9		Adjustable illumination intensity	Yes/No[2]
2.10	A green filter needs to be applied to the image of the cervix	Has a physical green filter	Yes/No[2]
2.11	The operator needs to be able to zoom in on areas of interest	Digital magnification	>5x[2]
2.12	The image of the cervix needs to be displayed in real-time	Minimum frame rate	30fps[2]
2.13	Screen multiple patients before needing to be recharged	Minimum battery life	2 hours[2]

[1] Vaginal canal length and cervix diameter (Barnhart et al., 2006).

[2]Predicate devices 510(k) submission documents: MobileODT EVA, Gynocular, POCKET Colposcope.

3.2.3 Liquid Application Subsystem Design

The liquid application subsystem had two functions: cleaning the cervix from mucus or other obstructions and 'washing' the cervix with acetic acid to induce the acetowhitening effect. In clinical practice, a soaked cotton swab or a spray bottle was used to apply the acetic acid and wash away the mucus. If all the mucus was not removed, the acetic acid would not reach the epithelium and cause a false impression of non-uptake (Prendiville & Sankaranarayanan, 2017).

For integration with the insertion probe, a spray bottle concept was used for this subsystem, which allowed a nozzle to be placed in the probe that was connected to a finger-actuated pump and liquid reservoir contained in the handle. The spray from the nozzle needed to be strong enough to remove the mucus from the cervix but also have a wide enough spray pattern to allow the operator to cover the entire cervix with the acetic acid with multiple sprays. The functional requirements that were developed to achieve this functionality are listed in Table 5, along with the accompanying engineering specifications that were identified.

Table 5: Liquid application subsystem functional requirements and engineering specifications.

ES No	Functional Requirement	Engineering Specification	Value
3.1	Store the liquid in the device to avoid the need for an external container	Liquid capacity	Enough for 10 screenings[1]
3.2	Cover the cervix in acetic acid	Covering efficacy	Cover all four quadrants of cervix[2]
3.3		Able to remove mucus on cervix	Yes/No[2]

[1] (Barnhart et al., 2006)

[2] Basic requirement for a screening procedure (Prendiville & Sankaranarayanan, 2017).

3.2.4 Dilation Subsystem Design

3.2.4.1 The Vaginal Speculum

Based on the information gathered from various sources, the speculum has been identified as a critical part of current screening methods, but it is an element of the screening process that needs to be improved on. In the context of cervical cancer screening, the vaginal speculum is used to dilate the vaginal canal to enable visualisation of the cervix and create a working channel for the instruments used during the procedure. However, the speculum is also used in several other medical procedures and pelvic examinations to perform a similar function.

The vaginal speculum is a widely used medical instrument that has been a staple in gynaecological examinations for more than a century. The vaginal speculum, in its modern form, can be traced back to the 19th century. Dr. James Marion Sims' invention of the Sims speculum in the mid-1800s represented a significant advancement in gynaecological instrumentation. This initial design consisted of two curved blades, which, when opened, allowed visualisation of the cervix and vaginal walls. The concept was later refined into various shapes and sizes, including the Graves speculum shown in Figure 5.

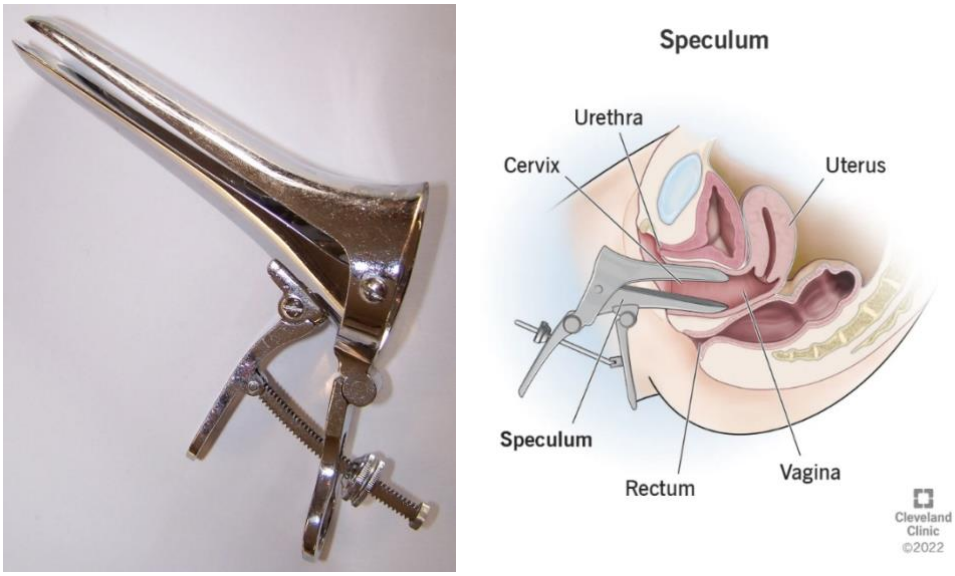

Figure 5: Example of a Grave's or Duckbill speculum (left) and how it is used (right) (Clinic, 2022).

The Strengths and Weaknesses of the Current Speculum Design

Despite minor improvements, the traditional speculum design introduced in the 18th century has stayed the same. This is an indication that it is fundamentally a good design, but it has several persistent issues that could be solved by modern technology. Some of the key strengths of the design that contribute to its long-standing success are (Asiedu et al., 2017):

1. **Simplicity:** Both in design and functionality, the device is simple and effective, making doctors reluctant to try a new device that is more complex to operate.
2. **Strength:** It is strong enough to withstand the high pressures imposed by the vaginal walls during an examination.

In recent years, minor improvements have been made to the speculum, such as manufacturing them out of plastic to make them single-use and more pleasant for the patient as opposed to a cold metal speculum and adding built-in lights to make the procedure easier for doctors. However, there are still several weaknesses with the design, which can be categorised into four main areas:

1. **Patient discomfort:** Research suggests that the speculum is a primary source of discomfort during pelvic exams, which contributes to lower uptake of procedures such as regular cervical cancer screening (Asiedu et al., 2017). Thus, addressing this issue is crucial for enhancing the patient experience and increasing the uptake of pelvic examinations.
2. **Decontamination requirements:** Multi-use specula need to go through a multistep decontamination process every time they are used, which requires a variety of specialised equipment and resources (Sellors J.W, 2003).
3. **Suboptimal fit to female anatomy:** Current speculum designs dilate the entire vaginal canal evenly, despite pressure distribution studies indicating that the highest-pressure zone is concentrated in the mid-region rather than around the cervix (Guaderrama et al., 2005). Furthermore, the natural anterior-posterior curvature of the vaginal canal is not accounted for by the straight and rigid speculum (Cacciari et al., 2017), further increasing pressure on the vaginal walls during dilation.
4. **External visualisation dependence:** Current visual examination procedures rely on external imaging technologies, such as the colposcope or the naked eye, to inspect the internal

reproductive organs. Thus, a uniformly sized and straight line of sight is required along the entire vaginal canal (Asiedu et al., 2017).

5. **Lack of self-examination and self-insertion capabilities:** In some scenarios, a speculum design with these capabilities can be beneficial, such as women preferring self-insertion to increase comfort (Asiedu et al., 2017).

In response to these limitations of the traditional speculum, several alternative approaches have been explored to improve the design (Wong & Lawton, 2021). Some designs aimed to use different materials to make soft speculums or plastic speculums, while others tried a complete redesign using fundamentally different dilation concepts. Devices like the *FemSpec* and *Vadascope* used air pressure to expand the vaginal canal once the device was inserted. However, these air-based expansion concepts had various problems, such as the difficulty of providing and maintaining enough pressure, limited visualisation of the vaginal walls and being too complex. Other devices like the *Callascope* use a special inserter that only dilates the area around the cervix and allows for easier self-insertion by the patient (Foundation, 2023). Although this ability for self-insertion is highly desirable and well-received by women and doctors, the large insertion size still doesn't address the discomfort patients feel during insertion and removal, and the single-use design makes it impractical in low-resource settings.

3.2.4.2 New dilation concept

The primary function of the dilation system is to physically displace tissues or objects obstructing the cervix to allow visual and physical access to the screening equipment housed in the insertion probe. The concept uses a soft, remotely dilated cup whose shape and functionality were inspired by silicone menstrual cups. Silicone menstrual cups are used as an alternative to tampons and pads for capturing and collecting menstrual fluid (Manley et al., 2021). A menstrual cup uses a simple design and elastic silicone rubber material to allow the cup to collapse into a smaller size for insertion into the vaginal canal, as shown in Figure 6a and b below. Once inserted, the cup can be released to automatically expand and return to its circular shape (Figure 6c), effectively dilating the canal (Figure 6d). To remove the cup, it collapses once more to break the seal that has formed and is pulled out (Figure 6e).

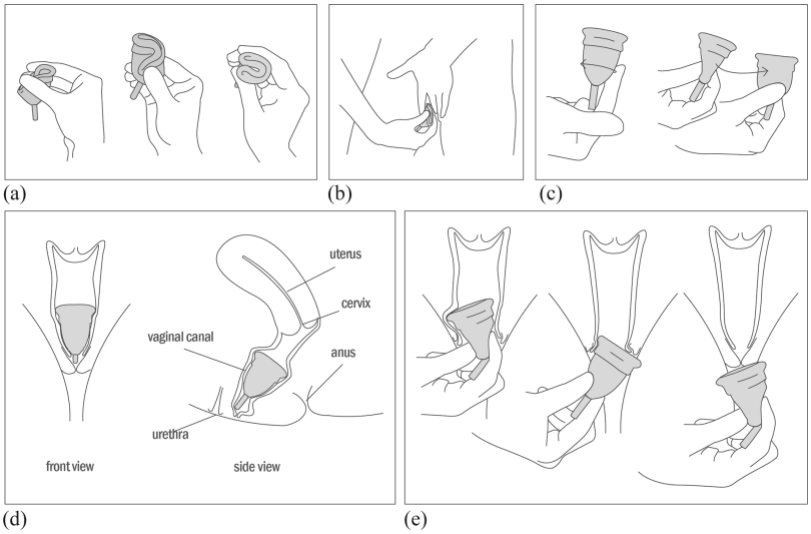

Figure 6: Menstrual cup use (Manley et al., 2021).

Using the menstrual cup as the design inspiration offers several advantages, such that it is used effectively for a very similar purpose, the design and operation are straightforward, it is soft and flexible, and it might be less intimidating since women are somewhat familiar with it. The proposed device, referred

to as the dilation cup, follows analogous steps to menstrual cup operation but is optimised for vaginal dilation during screening procedures. Thus, the following capabilities needed to be incorporated into the cup design:

- Attachment of the cup to the tip of a mounting probe.
- Provision of an unobstructed working channel beyond the probe's tip for instrument access to the target area.
- Actuation (collapsing) the cup from a distance without physical contact with the cup.
- Easy decontamination of the cup after use.

For the modified cup to achieve these capabilities, two aspects of the cup design needed to be decided on. These include deciding on the collapsed shape that the cup should be designed to achieve and the actuation mechanism that will allow the operator to actuate the cup from a distance and without physical contact.

The actuation mechanism refers to the mechanism that allows the operator to collapse and dilate the cup from a distance without having to manipulate the cup physically. Thus, moving forward in the report, 'cup actuation' refers to the movement (collapsing and dilation) of the cup caused by the operator using the actuation mechanism. Several different cup actuation concepts were generated, including a two-piece sliding mechanism over the entire probe and cup, embedding wires and meshes inside the cup walls, shape-memory and 4D printing materials, and attaching cables/wires to multiple points on the cup to pull on. The concept selected was to connect a single wire to the cup that can be pulled on to collapse the cup into the desired shape. This concept was selected because of its simplicity in design and manufacturing.

To select the desired collapsed shape, the large variety of different ways to fold menstrual cups for insertion was considered, as well as what folding pattern is the most feasible with the selected actuation mechanism. The decision was made that the "Punchdown fold", shown in Figure 7 below in its collapse state, was the most appropriate folding pattern for the cup, allowing it to be remotely actuated using a single cable. This typical folding pattern requires pushing the cup's back lip down towards the centre and then squeezing the side to create a thin, conical profile that can easily be inserted into the vaginal canal. These design decisions regarding the actuation mechanism and the collapsed shape are the primary inputs that guided the design of the new dilation cup.

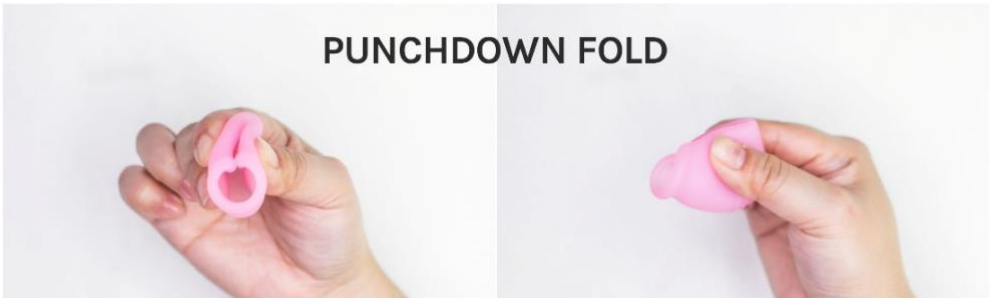

Figure 7: Demonstration of the 'Punchdown Fold', which is the chosen collapse shape of the dilation cup (Baladad, 2022).

The functional requirements that were developed to achieve this functionality are listed in Table 6, along with the accompanying engineering specifications that were identified.

Table 6: Dilation subsystem engineering specifications.

ES No	Functional Requirement	Engineering Specification	Value
4.1	Provide a clear, unobstructed working channel around the cervix	Minimum dilated diameter	30mm[1]
4.2		Maximum radial compression to withstand in dilated state	50kPa (0.5 bar)[3]
4.3		Maximum allowable compression under maximum compression in dilated state	25%[4]
4.4	Reduction in size for insertion and removal	Maximum insertion diameter	25mm[2]
4.5		Maximum actuation force to collapse cup and hold it in the collapsed state	7N[5]

[1]Average size of cervix (Barnhart et al., 2006).

[2]Narrowest part of the vaginal canal at the level of the vaginal introitus is 26.15mm on average. (Barnhart et al., 2006)

[3]Maximum pressure that can be exerted by high-pressure region of the vaginal canal (Cacciari et al., 2017).

[4]Cup should not reduce the field of view by more than 25% when placed under maximum pressure.

[5]Comparing the strength of the thumb and index finger for both flexion and extension Yu et al. (Yu et al., 2009) found that the thumb is the weakest in extension, only capable of an average maximum force of 13.6N. Thus, since either of these digits are commonly used in finger actuated systems this value was selected, and a 100% safety factor was added to account for friction losses and that the maximum force is not required for actuation.

3.2.5 Decontamination Subsystem Design

3.2.5.1 Current Decontamination procedures

The Spaulding classification system categorises medical instruments and devices into three main groups based on their level of patient contact and intended use (Sellors J.W, 2003). Critical (C) items, such as surgical instruments that directly touch sterile body tissues or the vascular system, require sterilisation before each use to prevent infection transmission. Semi-critical (SC) items, like endoscopes or dental instruments that contact mucous membranes or non-intact skin, necessitate high-level disinfection to eliminate most microorganisms. Non-critical (NC) items, such as blood pressure cuffs or stethoscopes that only contact intact skin, pose the lowest risk of infection, and typically undergo low-level disinfection. This classification framework guides healthcare facilities in determining appropriate decontamination and sterilisation procedures for different instruments, ensuring patient safety and effective infection control. The decontamination procedures for the different instruments used during a standard colposcopy examination are shown in Table 7 below (Sellors J.W, 2003).

Table 7: Decontamination procedures for the primary instruments used during a colposcopy examination procedure.

Instrument	Category	Processing	Suggested Procedure
Vaginal speculum and vaginal side-wall retractor, forceps	C	Decontamination and cleaning followed by sterilisation or HLD	Autoclaving or disinfection with boiling water
Colposcope head, stand, torch light	SC	Intermediate or low-level disinfection	Wipe with 60-90% ethyl, isopropyl alcohol

3.2.5.2 New Decontamination Procedure Concept

The decontamination subsystem's function is to protect the patient from cross-infection (Gray et al., 2012). The decontamination process for each colposcopy examination is extensive and consists of multiple steps and several different types of processes to decontaminate all of the equipment involved. This extensive decontamination process needs to be simplified in developing a device that can be used as a triage device to pre-screen higher volumes of patients.

The probe-based design of the device lends itself to a similar decontamination process used by transvaginal ultrasound probes. This process uses a probe cover during the examination and then cleans the probe post-examination using high-level disinfection (HLD) techniques. The probe covers used are either commercial, designed explicitly by manufacturers for ultrasound probes or condoms. A study by Basseal et al. found that the breakage rates of modern commercial covers perform slightly better than condoms, despite both not being 100% effective and still resulting in occasional contamination of the probe (Basseal et al., 2020).

Like transvaginal ultrasound probes, the insertion probe is also classified as a semi-critical device according to the Spaulding classification system because of the contact with intact mucus membranes. Thus, despite the probe cover used during the screening process, classifying the device as semi-critical justifies the need for at least an HLD process following the examination (Gray et al., 2012). Multiple HLD techniques exist, such as chemical baths using glutaraldehyde or ortho-ophthalaldehyde, disposable wipes utilising chemicals such as chlorine dioxide, or automated chemical-free devices that use ultraviolet-C radiation (Kyriacou et al., 2022).

The decontamination process for the device is based on the process followed by the transvaginal ultrasound probes, which means that it will consist of a single-use probe cover that is pulled over the probe during the examination, and then post-examination, the probe and handle will be cleaned using an appropriate HLD technique. By using this process, the goal of simplifying the decontamination process is achieved by reducing the number of tasks to two, as well as the number of equipment that needs to be cleaned and consumables required. The functional requirements that were developed to achieve this functionality are listed in Table 8, along with the accompanying engineering specifications that were identified.

Table 8: Decontamination subsystem engineering specifications.

ES No	Functional Requirement	Engineering Specification	Value
5.1	Attaches to the insertion probe.	Secures to the tip of the probe	Yes/No[2]
5.2		Creates a watertight barrier over the probe and cup.	Yes/No[1]
5.3	Interfaces with the components mounted in the probe (camera, light pipes, and spray nozzle)	Does not degrade the camera resolution to below the allowable threshold.	Yes/No[2]
5.4		Does not increase the image distortion to below the allowable threshold.	Yes/No[2]
5.5		Does not reduce the illumination intensity to below the allowable threshold.	Yes/No[2]

[1] Basic test to see if condoms are torn.

[2] No reference.

4 Design and Development Outcomes

This chapter details the outcomes of the design and development process. This process formed part of the overall design methodology to develop the final prototype that met the functional requirements and engineering specifications identified in Chapter 3. This design methodology is outlined in Figure 8 and consists of design, development, and verification. Integrating these two aspects of the design methodology created the iterative design loop to develop the final prototype used in the validation study.

The flow diagram in Figure 8 explains the technical design and development of the constituent subsystems, which was supplemented by design inputs from the verification aspect of the design methodology. The verification aspect included engineering verification conducted on the subsystems and the subsequent device risk assessment. The risk assessment formed part of the requirement imposed on medical device development by *ISO 14971:2019 Medical devices - Application of risk management to medical devices,* to ensure that the medical device was safe to use and could perform its intended purpose. The risk assessment is discussed further at the end of the verification chapter (Chapter 5) and provided in full detail in Appendix G.

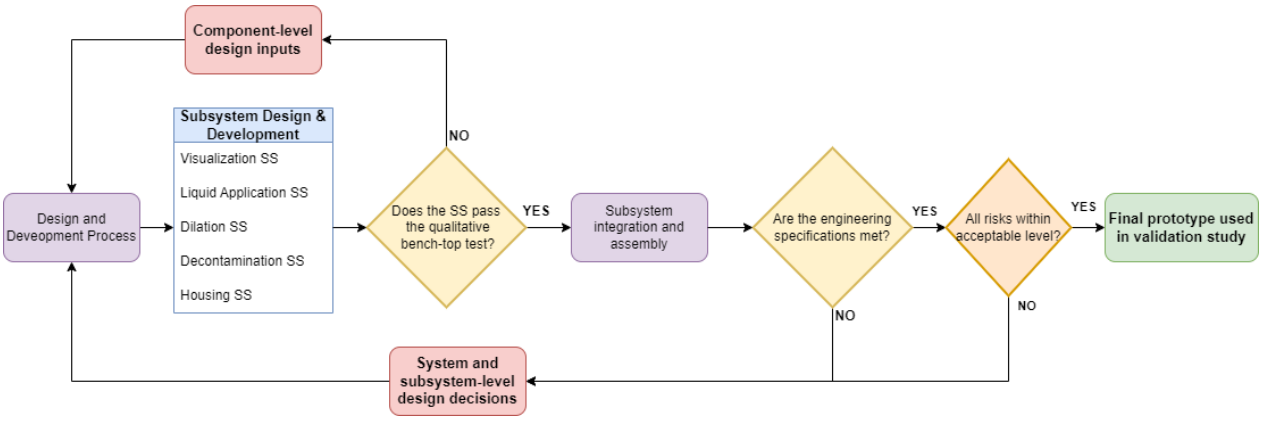

Figure 8: The design methodology used to develop the final cervical cancer screening device.

The final prototype development resulted from several iterations of the design methodology Figure 8. Appendix B shows the evolution of the prototype leading to the final version. Each complete design iteration, driven by design inputs generated from engineering tests and risk analysis, produced a prototype and contributed to the development of the subsequent prototype. However, this chapter focuses on this final prototype to explain the development of each subsystem, how it functions, and how the various subsystems integrate. This final prototype was used for the verification and validation testing that follows in the next chapters.

Although not discussed in this chapter, prototype 5 was a crucial milestone in the design process, resulting in critical design decisions that led to the final prototype. Prototype 5, shown in Figure 59 in Appendix B, was the 'proof-of-concept' device that verified that the concept could achieve the project's aim if developed further. Thus, this prototype underwent more rigorous preliminary testing, leading to several crucial design decisions. Appendix C contains the detailed testing protocols and results from these preliminary tests. However, as part of the detailed subsystem development in this chapter, the relevant design inputs from these tests are highlighted for each subsystem.

4.1 Visualisation Subsystem Outcomes

4.1.1 Subsystem Design Overview

The primary function of the visualisation subsystem was to provide the operator with a real-time and high-quality view of the cervix. This subsystem was critical as the VIA screening procedure heavily relied on visualising the cervix and identifying small features, textures, and colour changes. Four smaller subsystems were identified based on the unique function they needed to perform to allow the complete visualisation subsystem to perform its critical function successfully. These systems were the imaging, illumination, power supply, and display systems, and each of them was individually designed and developed in this section.

4.1.2 Camera Selection

The camera selection was a critical part of the device development since it captured the real-time video of the cervix displayed to the operator, which directly affects the ability of the device to make an accurate diagnosis. Thus, the following criteria were considered to select a suitable camera:

- **Image quality** – Table 4 on page 18 lists the ES required for image resolution, distortion, and frame rate.
- **Lens selection** – The selected lens had to allow the camera to have the desired field of view at the expected working distance, as listed in Table 4 on page 18.
- **Compatibility** – The output of the camera module had to be compatible with smartphones and computers for them to be used for image processing and display.
- **Size and Cost** – The camera had to be small and low-cost, which meant that a compromise had to be made between the size and cost since the cost of small cameras increases exponentially as the size decreases.

Figure 9: The MISUMI TD-B31105A-77-01 CMOS camera (MISUMI, 2023)

After analysing these criteria and the engineering specifications surrounding the imaging system, a mini-USB camera was selected as the most suitable camera for this project. The camera selected for the final prototype was the MISUMI TD-B31105A-77-01 CMOS camera (MISUMI, 2023), shown in Figure 9 above, purchased from MISUMI Electronics Corporation in Taiwan. The summary of the technical specifications of the camera is shown in Table 9 below.

Table 9: Technical specifications of the MISUMI TD-B31105A-77-01 camera (MISUMI, 2023).

Parameter	Specification
Sensor	1/6'' Colour CMOS 1080p (2MP)
Frame rate	30fps MJPEG 1920x1080
Lens	1.83mm / F 5.0
Depth of field (FID)	20 – 16 – 30mm
View angle	0° (Front view)
Dimensions	4.9mm (Diameter) x 17mm (Length)
Cable length	300mm (250mm and 50mm)
Cable connector	Nano 4p (OD 1.7mm)
USB Connector	USB 2.0 Type A
LED	None

4.1.3 Illumination System Design

The illumination system's function was to illuminate the cervix to allow the camera to capture a real-time image of the cervix. The need for a green filter in the light path led to the design decision to have a separate system that provides the illumination and not have the lights mounted directly onto the camera. A physical colour filter instead of a digital colour filter was used to simplify the design process and mitigate the development of a software application that performs the filtering since both methods achieved the same outcome. Thus, the requirement for a physical colour filter resulted in an illumination system consisting of three smaller subsystems: the light source, the power source, and the light filter.

4.1.3.1 Light source subsystem design and component selection

The function of the light source subsystem was to generate light and illuminate the cervix. The size restrictions due to the small diameter of the insertion probe and the need to add a physical colour filter in the light pathway between the light source and the cervix determined that the light source needed to be placed in the housing. This placement allowed more space to develop a filtering system without affecting the size and complexity of the insertion probe design. However, that necessitated the light to be transported along the length of the insertion probe to the probe's tip to illuminate the cervix. The light source selection took the following criteria into account:

- **Light type** – The light source had to be compact and have low power requirements.
- **Size** – Although the light source would be mounted in the handle, it still needs to be small enough not to increase the handle's size above the point where it could be held in one hand. The engineering specification for the maximum width of the housing is 50mm (ES 1.4 in Table 3 on page 17). Thus, the light source had to be less than 40mm in diameter to allow space for mounting it in the handle.
- **Colour** – the light source had to produce white light (ES2.6 in Table 4 on page 18).
- **Power** – Power consumption had to be minimised to prolong the device's battery life.
- **Luminous Flux** – A flux of >1000lux was required for the entire working distance range of 20-50 mm (ES2.7 in Table 4 on page 18). A 4x safety factor was applied to this specification due to the expected losses in transporting the light along the length of the insertion probe, resulting in at least 4000lux required at the 20mm working distance.
- **Dimmable** – the illumination brightness had to be adjustable by the operator.

Using these criteria and the engineering specifications related to the light source, the light source selected as the most suitable for this application was an LED. The OSCONIQ C2424 1 Star White 5000K CRI90 LED

(Solutions, 2023) from Intelligent LED Solutions, shown in Figure 10, was selected and purchased from RS Components. The LED was selected for its compact size, performance characteristics, and ability to be dimmed by controlling the supply current. Table 10 summarises the technical data of the LED.

Table 10: Technical specifications of the OSCONIQ C2424 1 Star 5000K LED (Solutions, 2023).

Parameter	Specification
Dimensions	20 x 20 x 2.2 mm (L x W x H)
Power @ max current	1.96W
Maximum current	700mA
Colour	White (5000K)
Flux at 700mA	240lumen (4500lux)
Dimming	Current controlled
Heatsink	*Required above 350mA

The selected heatsink attached to the LED to dissipate the heat is a 20x20x6mm aluminium heatsink. A thermal gap pad was added and compressed between the LED and the heatsink to reduce the thermal resistance between the LED and the heatsink (refer to risk A.5 in Appendix G). With the handle-mounted LED selected, the following criteria were considered to select the component that would transport the light from the LED to the tip of the probe:

- **Size** – Similar to the size requirements of the camera, the component must be small to minimise the probe diameter.
- **Flexibility** – To simplify the design and assembly of the housing and probe the component needed to be flexible.
- **Losses** – Minimal luminous intensity loss as the light is transported along the length of the insertion probe.

The selected component that was suitable for this application and met these criteria is a light pipe, which is shown in Figure 10 below. Light pipes are conduits filled with clear material, typically optical-grade silicone or glass, that guide light from a source to a target location with minimal losses. The working principle they are based on is total internal reflection, which allows the light to enter the conduit at one end and propagate along the length of the conduit until it exits the conduit at the other end. This allows a significant portion of the light intensity to be retained, so they are commonly used with LEDs to direct light. The selected light pipe was the 1304.1005 MENTOR PCB Mounted Flexible LED Light Pipe (Mentor, 2024) by Mentor GmbH, which has a diameter of 2.2mm and was purchased from RS Components.

Figure 10: The OSCONIQ C2424 1 Star 5000K LED (left) (Solutions, 2023) and a flexible lightpipe (right) (Mentor, 2024).

4.1.3.2 Power source subsystem design and component selection

The primary function of this subsystem was to power the LED, and the secondary function was to control the LED's luminous intensity (brightness). The selected OSCONIC C2424 1 Star LED could reduce its brightness by controlling the supply current, making it a current-controlled LED. A specialised LED driver provides this constant current control for high-powered LEDs, such as the one selected. The criteria used to select the most suitable LED driver to pair with the LED were:

- **Size** – Similar to the size restrictions imposed on the LED, the LED driver had to fit into the handle. Thus, the maximum allowable width of the LED driver was 40mm.
- **Operating mode** – The LED driver had to be a constant current source.
- **Output current** – 0 to 700mA, per the LED current range specification.
- **Input and output voltage** – Output voltage must be able to match the forward voltage of the LED, which is 2.7-3.2V. The input voltage range had to be higher than the output voltage.
- **Control type** – The LED driver needed to be capable of analogue and digital dimming to allow flexibility in selecting between a manual or software dimming method based on the most suitable option for the user interface design.

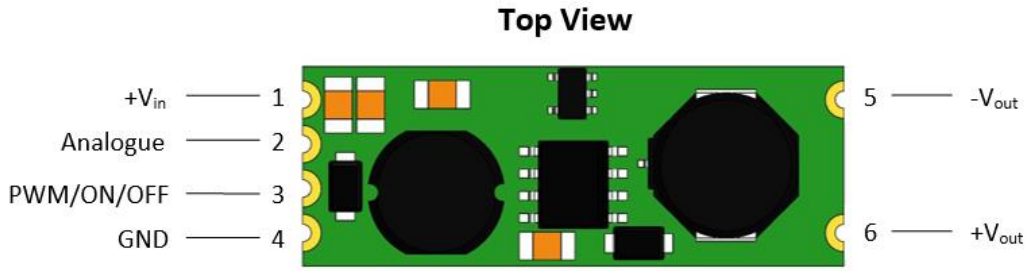

Figure 11: RCD-24/PL RECOM Constant Current LED Driver diagram with pinouts labelled (RECOM, 2024).

Based on these criteria, the LED driver selected to power and control the LED's brightness was the RCD-24/PL RECOM Constant Current LED Driver from RECOM Power (RECOM, 2024). It was a step-down constant current source that was designed to drive a high-power LED. Figure 11 shows a labelled diagram of the input and output pins of the LED driver, and the summary of its technical specifications is shown in Table 11.

Table 11: Technical specifications of the RECOM constant current LED driver (RECOM, 2024)

Parameter	Specification
Dimensions	31 x 11.4 x 6.6 mm (L x W x H)
Operating mode	Constant current source
Output current	0 – 700mA
Input voltage	4.5 – 36V
Output voltage	2 – 35V
Dimming control	Analogue (voltage-controlled) and digital (PWM control)
Mounting style	Pinless SMD

The final prototype used the analogue dimming control capability of the driver. A dimming control circuit was designed to provide an analogue voltage signal to the analogue input pin, labelled pin 4 in Figure 11. The analogue signal supplied to pin 4 controlled the current output of the LED driver, which adjusts the brightness of the LED. The assembly of the components used in the dimmer circuit is shown in Figure 12 as part of the exploded assembly view of the LED power source subassembly. The assembly layout was designed to minimise space and provide an ergonomic interface for the user to control the LED brightness. The large size of the LED dimmer wheel that attaches to the rotary potentiometer was designed such that the edges of the dimmer wheel protrude out of both sides of the handle to allow the operator to access the dimmer easily using the thumb of either hand. This configuration is clearly shown at the end of the chapter in the final device assembly, in Figure 17 on page 33.

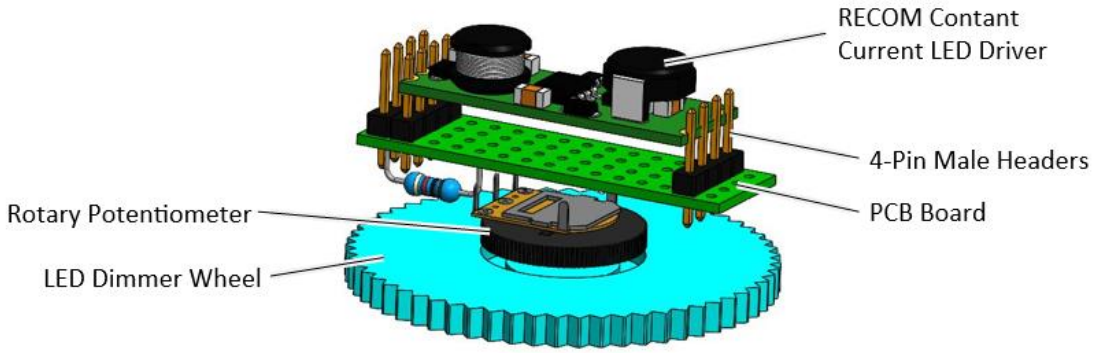

Figure 12: LED power source and dimmer circuit exploded assembly.

The dimmer circuit used a rotary potentiometer to adjust the input voltage from the power supply to an analogue output voltage ranging between 0V and $+V_{in}$. The input voltage range to pin 4 is 0-15V, and as shown in the graph in Figure 13 below, there is an inverse correlation between the input voltage signal on the analogue pin and the output current of the LED driver. Thus, the maximum brightness (fully ON) would be produced when the analogue input signal is 0V, and the LED is OFF when the signal is 4.2V.

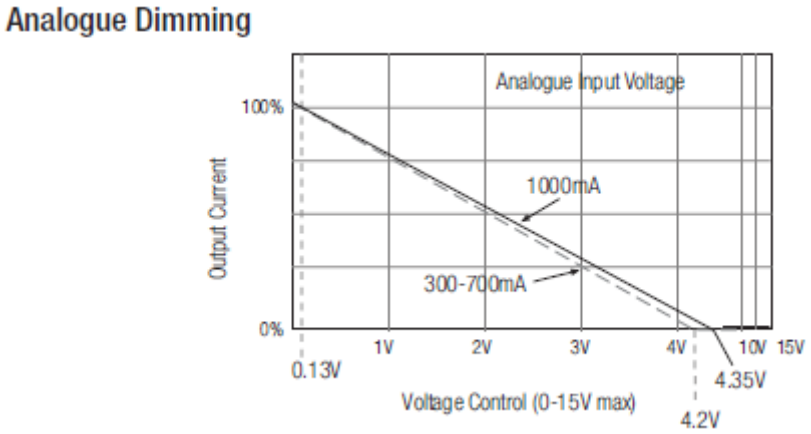

Figure 13: Analogue dimming control graph showing the correlation between the voltage control signal and the output current of the LED driver (RECOM, 2024).

The detailed circuit diagram of the dimmer circuit is shown in Figure 18 on page 33 at the end of this chapter, along with the complete electronic diagram for the final prototype.

4.1.3.3 Light filter subsystem design

The function of the light filter subsystem is to allow the operator to add and remove a green colour filter to the light that illuminates the cervix. The design used a physical colour filter instead of digitally filtering the image displayed to the operator. This design decision required the development of a mechanism that could position a physical colour filter in the light path between the LED and the lightpipe, while allowing the operator to remove the filter to visualise the cervix using the white light. Figure 14 below shows the assembly of the LED lightbox, which was the mechanism that provided this functionality to the final prototype. The figure includes the LED and the heatsink to show how they are mounted into the lightbox, although they are not part of the subsystem.

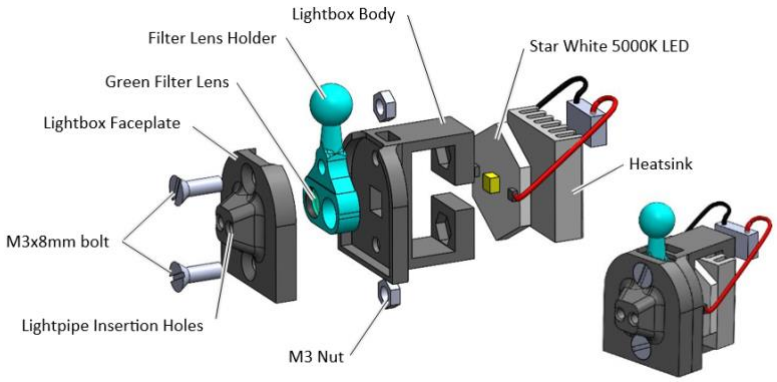

Figure 14: LED lightbox shown as a labelled exploded view and a full assembly view.

The LED and the heatsink were mounted to the body of the lightbox using fastening screws, and the light pipes were 'press-fit' into the centre of the lightbox faceplate. The two halves of the lightbox (the body and faceplate) were closed to create a sealed box. The 'Filter Lens Holder' was enclosed inside the sealed box and floated in position with the M3 bolt that was used to secure the two box halves. The filter lens holder could freely rotate around the axis of the M3 bolts inside the lightbox. This rotational freedom of movement allowed the upper tip of the filter lens holder to be pushed to one side or the other, which positioned one of the two holes between the LED and the light pipes. The two holes of the filter holder contained the green light filter and no filter, as seen in Figure 15 below. Thus, depending on the side to which the lens filter holder was rotated determined whether or not the green filter was in the LED light path. These two configurations are illustrated in Figure 15 below, showing the LED either visible and unfiltered through the clear hole (B) or filtered through the hole containing the green filter in (C).

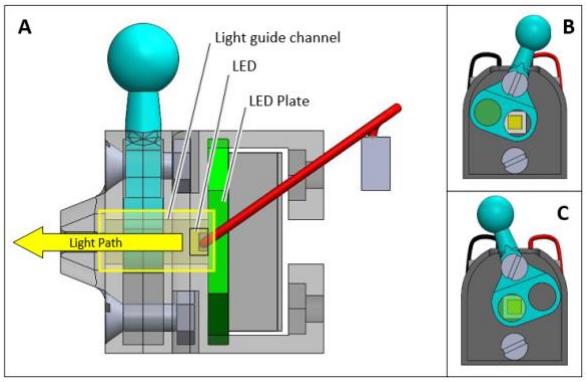

Figure 15: A) Illustration of the path that the light follows from the LED to the lightpipes, and the filter lens positions that places the clear hole (B) and the green filter (C) in front of the LED, resulting in either white light or green light illuminating the cervix.

Figure 15A shows a labelled side view of the assembled lightbox, with the light path and light guide channel identified. The light guide channels are features in the lightbox body and faceplate that direct the light through the filter lens holder to the lightpipes mounted in the faceplate. This prevented the light from filling the entire lightbox, limiting the reduction in luminance due to light 'leaking' out of the box. Thus, the light path labelled in Figure 15A illustrates the path the light took as it was emitted from the LED, passed through the hole in the filter lens holder, and into the guide channel in the faceplate where the lightpipes were connected. The lightpipes carried this light along the length of the probe's tip to illuminate the cervix.

4.1.4 Power Supply and Display System Selection

The function of this system was to provide all the previously mentioned electronic components that needed to be powered and to display the real-time video of the cervix to the operator. Based on the design inputs from the preliminary testing of the proof-of-concept device, the final prototype was developed using a smart device (smartphone, tablet, laptop, or computer) instead of a built-in power supply, processor, and display. In the proof-of-concept device, this built-in system consisted of a Lithium-ion battery and power control module that provided the power, a Raspberry Pi 4 as the processor, and an LED touchscreen display. The decision to move to a smart device-based concept had several benefits, such as reducing the number of components, decreasing the device size, and making the device more suited to low-resource settings by not limiting it to only working with specific and specialised components that are difficult to replace.

In addition to the smart device serving as the power supply, processor, and display, the final prototype used a USB hub to connect the smart device to the electronic systems. The ORICO Mini 3-in-1 USB Hub, shown in Figure 16 below, was selected for its small form factor (55x25x20mm), 3-port system (1xUSB3.0 and 2xUSB 2.0) and high data transfer rates. The camera and the LED driver were connected to two of the output ports, which provided power to both systems and a connection to transmit the video data from the camera to the smart device connected to the input port. Figure 17 shows the assembly diagram indicating these connections, and the detailed electronic diagram is shown in Figure 18. Another benefit of the smart device concept was that the final prototype could connect to any USB-enabled smart device through the USB hub. Thus, if the smart device has any software application installed that runs and controls the camera (*USB Camera V10.8.9* was used in this project), it can be used to perform the screening using the device (refer to risk A.3 in Appendix G).

Figure 16: The ORICO Mini 3-in-1 USB hub used (ORICO mini U32) (ORICO, 2024).

4.1.5 Final Visualisation Subsystem Assembly

The final assembly and electronic diagram of the visualisation subsystem that includes all the components mentioned in this section are shown in Figure 17 and Figure 18 below. Figure 61 in Appendix D shows the electronic connections required to produce the device's printed circuit board (PCB).

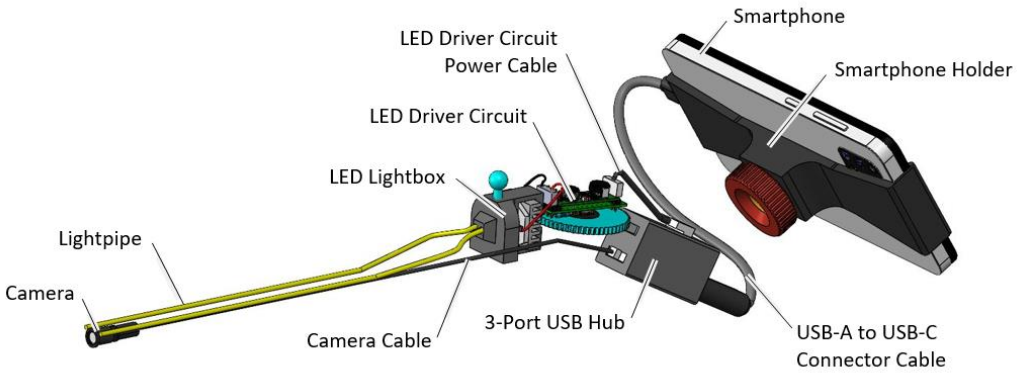

Figure 17: Visualisation subsystem complete assembly diagram with labelled components.

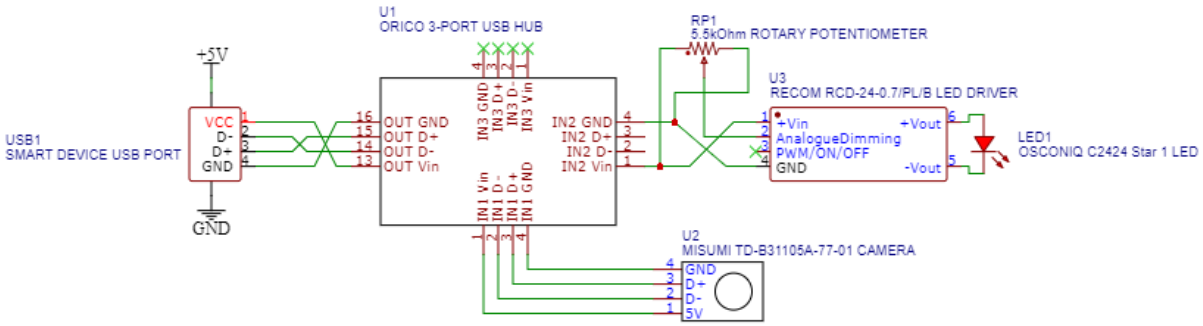

Figure 18: Visualisation subsystem electronic diagram to power the camera and LED and display the real-time image of the cervix on the connected smart device.

4.2 Liquid Application Subsystem Outcomes

The function of the liquid application subsystem was to spray liquid (acetic acid) on the cervix. The pump mechanism used in liquid spray bottles inspired the concept. Using this pump mechanism design allowed the pump and reservoir to be mounted in the housing where there is more space while pumping the liquid along a pipe that runs the length of the probe and out the nozzle mounted in the probe's tip. Thus, the subsystem consisted of three main elements:

- the reservoir that stored the liquid,
- the pump that moved the liquid from the reservoir along the pipe,
- the nozzle that sprayed the liquid onto the cervix.

The preliminary proof-of-concept testing generated an essential design input: the spray must have a velocity and strength sufficient to clean the cervix from mucus or liquid. Not achieving this would result in the acetowhitening reaction not taking place since the acetic acid would not come into contact with the cervical tissue.

4.2.1 Liquid Pump Design

The liquid pump's design used a combination of existing components and manufactured parts to develop an effective pumping system. The labelled diagrams in Figure 19 show the components of the liquid pump system. The pump was a repurposed pumping mechanism from a liquid spray bottle, and additive manufacturing methods were used to produce the additional components. The parts were manufactured from FormLabs Durable resin using stereolithography (SLA) 3D printing with the FormLabs 3+ printer. The component layout positioned the dispensing button in Figure 19 at the top of the handle in the area of the operator's thumb when holding the device. This layout allows the operator to actuate the pump with the same hand which holds the handle.

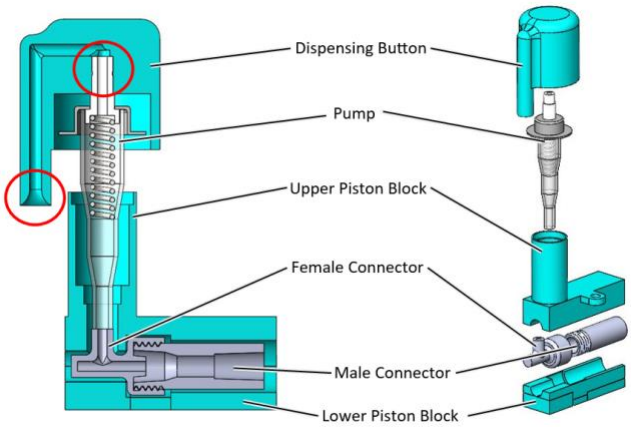

Figure 19: Labelled diagrams of the fully assembled pump system's cross-section (Left) and the exploded assembly (Right).

Based on input from the risk assessment, the design of the liquid dispensing button was optimised to connect securely to the neck of the pump using a clip-in mechanism and to allow the liquid pipe to be press-fitted into the arm of the dispensing button using a tapered channel, highlighted by the two red circles in Figure 19. These modifications created secure connections at the input and output of the dispensing button to prevent accidental fluid leakage inside the handle (refer to risk A.4 in Appendix G).

4.2.2 Final Liquid Dispensing Subsystem

Figure 20 shows the fully assembled subsystem as both a labelled cross-section view and a full assembly view. The fully assembled subsystem includes the reservoir, liquid pipe, and nozzle. One of the functional features of the subsystem was the refillable reservoir, which could be disconnected from the pump and removed from the housing for refilling. Refilling the reservoir with acetic acid was done by removing the filling cap and pouring the liquid into the reservoir. Once refilled, the cap was press-fitted back into position, and the reservoir was pushed back into position at the bottom of the handle. Two design improvements mitigated the identified risk of the operator incorrectly reconnecting the reservoir after refilling (refer to risk C.1 in Appendix G):

1. A Luer slip tip from a syringe formed the press-fit connection between the reservoir and the pump,
2. Clips added to the sides of the reservoir that clip into the handle prevented the reservoir from moving or falling out of position.

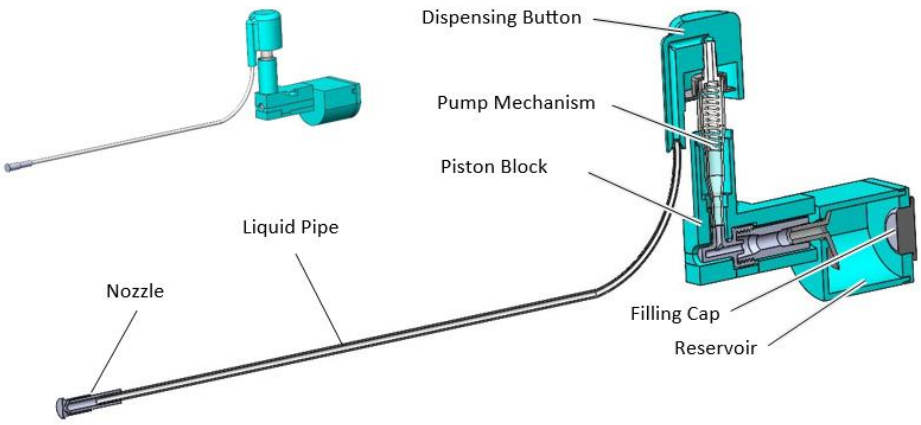

Figure 20: The liquid application subsystem complete assembly shown as a labelled cross-section and the entire assembly.

4.3 Dilation Subsystem Outcomes

4.3.1 Subsystem Overview

The primary purpose of the subsystem is to remove the need for a vaginal speculum to perform a screening. Thus, its primary function is to dilate the vaginal canal around the cervix to provide a clear working channel between the components in the tip of the insertion probe and the cervix. Secondarily, the dilation system aims to improve the patient's comfort and reduce the device's decontamination requirements between screening procedures.

The concept selected to fulfil these functions of the dilation subsystem was based on the design and functionality of a silicone menstrual cup. For the concept to work in this application, specific design modifications made to the standard menstrual cup added the following functionality to the dilation cup used on the device:

1. Fixing the cup to the tip of the insertion probe.
2. Providing a clear and unobstructed working channel between the tip of the insertion probe and the cervix.
3. Collapsing the cup from a distance without the operator having to touch it with their hands.
4. Easily decontaminated the cup after a screening procedure.

4.3.2 Dilation Cup Development Methodology

Figure 21 below illustrates the design and development methodology used to modify and optimise the cup design to achieve the desired functionality. Since the dilation cup is an essential feature of the device that enables speculum-free screening, it underwent an in-depth and multi-phase design and testing development process to create the best-suited cup design for this application. The process shown in Figure 21 combined finite element analysis (FEA), rapid prototyping, and testing to design a cup that could meet the engineering specifications in Table 6.

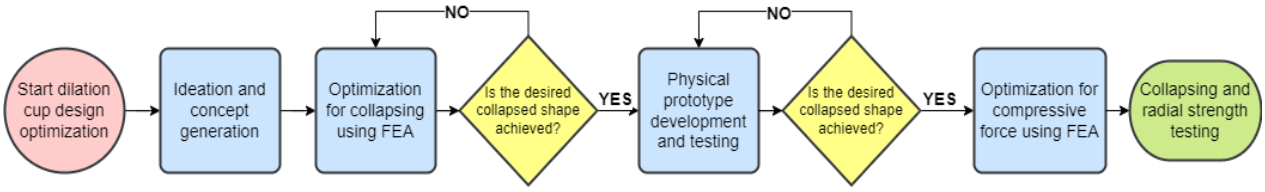

Figure 21: Dilation cup design and development methodology.

A qualitative FEA was performed since the primary interest of the analysis was to understand the structural behaviour of the cup and identify trends and patterns in the stress and deformation results. The FEA was only part of a multi-phase development process, so obtaining precise numerical data about the cup's performance, such as its radial strength, was unnecessary. These performance metrics were analysed later when the cup was physically manufactured and tested. Thus, the various stress and deformation visualisations generated from the FEA informed the design decisions and optimised the design.

4.3.3 Global Orientation and Segmentation of the Cup

This section aims to set the orientation of the cup and identify critical areas to ensure clarity throughout the development and testing sections of the dilation cup. Firstly, Figure 22a shows the cup orientation in three-dimensional space, with the primary and secondary coordinate systems and the two main axes of the cup labelled. Figure 22b labels the critical regions of the cup. The primary coordinate system was positioned in the centre of the cup's base, with the central axis running perpendicular to the base along the Y-axis. The secondary coordinate system was positioned at the point where the actuation force would be applied to the front wall of the cup. The actuation string axis runs along the Y-axis of the secondary coordinate system, intersecting the point where the actuation force is applied and the inner edge of the cup base on the primary XY-plane. The actuation force is applied along the axis in the FEA to ensure the accuracy of the analysis results by replicating the actual direction in which the initial force would be applied to collapse the cup.

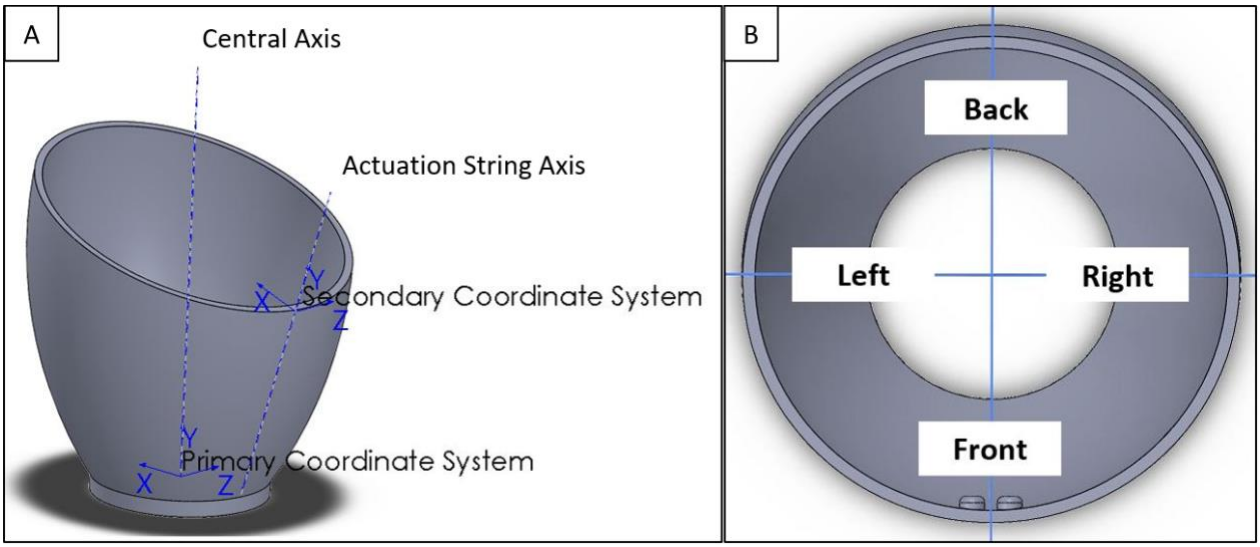

Figure 22: a) Primary and secondary coordinate systems and the two main axes of the cup used in the FEA, b) critical areas for reference, shown from the top view.

4.3.4 FEA Model Setup and Verification

This section details the development of the FEA model used to simulate the displacement and stress in the cup under various loads. The qualitative FEA was used as an iterative design tool to gain insights into the structural behaviour of the cup under various loads by analysing these stress and deformation results. The FEA software used for the cup design optimisation was COMSOL Multiphysics 6.0, and the software model of the dilation cup was designed using SolidWorks. The FEA model was created following the setup detailed in Table 12 below:

Table 12: FEA model setup parameters.

Specification	Model parameter
Spatial dimension	3 dimensional
Physical interface	Solid mechanics
Study Type	Stationary: • Geometric nonlinearity included. • Auxiliary sweep with 5% load increments. • Recalculate geometry at each step.
Imported geometry	SolidWorks part file (.sldprt-file)
Material properties	Hyperelastic material model for Elastosil M4601: • Hyperelastic model type: Yoeh-model. • Constants: C10 = 0.11, C20 = 0.02 (Pagoli, 2021)
Mesh generation	Automatically generated physics-controlled tetrahedral mesh with normal mesh size. The solver used mesh adaptation and error estimates to refine and adapt the mesh during the calculations.

The following global assumption and simplification was made in the model setup:

1. **Material properties:** For the large deformation analysis to work, a hyperelastic material model had to be applied to the cup. However, a hyperelastic model could not be found for any material typically used to manufacture menstrual cups, such as medical-grade silicone. Thus, a material with properties similar to silicone and with known hyperelastic material parameters was chosen. The selected Elastosil M4601 material is softer than the silicone used for menstrual cups. However, its stress-strain curve had a similar shape, meaning it had similar elastic characteristics, which was the critical material parameter the study was concerned with to achieve representative stress and deformation results of a cup manufactured with medical-grade silicone.

4.3.5 Phase 1: Cup Design and Optimisation for Collapsing

The abovementioned FEA model was used in Phase 1 to optimise the collapsing sequence and shape of the cup. The collapsing sequence refers to the events that occur as the cup deforms into its final collapsed shape. The analysis was performed by applying a tensile load to the pull pins in the direction that the actuation string applies the load and analysing the subsequent behaviour of the cup. This information and understanding of the cup behaviour was used in the iterative design process to improve the design and compare different designs until the desired collapsed state was achieved.

4.3.5.1 FEA Model Setup

The physics boundary conditions used for the cup collapsing analysis are:

1. **Fixed boundary condition:** cup base.
2. **Boundary load:** distributed force on the pull pin attachment features.
3. **Boundary load direction:** tensile force in the negative Y-axis only.

The following assumptions and simplifications were made in the analysis:

1. **Model symmetry:** The CAD model was halved along the XY-axis to enhance computational efficiency and reduce the number of nodes. By halving the cup along this axis, the assumption was made that the cup's deformation would be symmetrical. Thus, the 'Symmetry' boundary condition was applied to the cross-section of the cup wall on the XY-plane.
2. **Load direction:** The tensile load on the actuation pins was applied in the negative Y-direction along the actuation string axis. To achieve this load direction, the CAD model was imported such that the secondary coordinate system of the model aligned with the standard coordinate system of the software. Orienting the cup in this manner ensured that the actuation force was applied in the same direction as in a physical device. However, as the cup deformed and the actuation pins moved off the axis, the force did not remain collinear with the actuation axis. Thus, the force direction for the first half of the deformation is accurate. However, during the second half of the collapsing sequence, the force direction and, consequently, the deformation are less accurate.

4.3.5.2 FEA Results & Analysis

The qualitative FEA aimed to optimise the cup's design by considering the key parameters such as high-stress regions, stress transfer, and deformation shape, specifically at the beginning of the deformation. The analysis did not focus on the force applied to achieve the deformation since it was a qualitative analysis. The design aim was to mimic the pushdown fold shown in Figure 7 on page 22, which requires the front lip and wall of the cup to move outward and become narrower. The results of four main design iterations are shown in Figure 23 below, showing the stress in the cups at 50% and 100% of the maximum deformation achieved before the simulation failed.

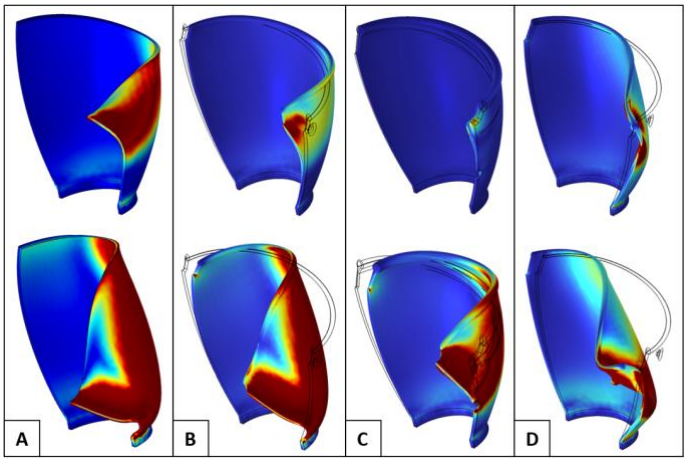

Figure 23: Phase 1 FEA results of the four main design iterations at 50% (top) and 100% (bottom) maximum deformation.

Iterations A, B and C have slight design differences, but they all have similar actuation directions. Their actuation direction was parallel to the XY plane and straight down towards the base of the cup. However, as the deformations show, this causes the back wall to move inwards towards the centre of the

cup and the cup to bulge sideways, opposite to the desired deformation. In iteration D, the actuation direction changed to be angled across the cup's centreline (XY plane), pulling the right pull pin and cup wall across and down towards the left of the cup.

The coloured stress patterns indicate the areas of high stress and how the stress was transferred along the cup walls. The light blue shading indicates how the stress transfer from the back wall towards the front wall of the cup changed for the different designs. The difference between iteration D and the rest is that more stress propagated towards the cup's front wall due to the different actuation angle. This resulted in more deformation of the front wall of the cup and a narrower collapsed profile. In the bottom row of images, the difference in deformation becomes apparent, with iteration D mimicking the elongated and narrower profile of the 'pushdown fold' concept significantly better than the other iterations. To summarise the insights gained from the analysis of the stress and deformation plots:

1. **Ineffective stress transfer:** Due to the material's flexibility, forces could be effectively transferred between different areas of the cup using thicker, stiffer rings. The only way to cause displacement of the front lip was to displace the back lip significantly.
2. **Cross-centreline pull:** The front lip could only be effectively displaced if the back lip collapsed past the centreline (XY-plane), resulting in an asymmetrical collapse.
3. **Influence of cup height:** Taller cups allow for more vertical displacement of the back lip, leading to more significant front lip displacement and a smaller collapsed cup size.
4. **Pull pin position and angle:** The pull angle refers to the angle of the actuation string between the base of the cup and the right pull pin. Adjusting the pull pin position and increasing the actuation angle reduced the stress forces on the pull pins and likely resulted in a lower force requirement to collapse the cup (which was tested in the dilation cup verification in section 5.2 on page 51).
5. **Staggered pull concept:** Actuating the pull pins at different times could result in a more effective collapse and cause the cup to fold in on itself (the right wall folds under the left wall) rather than collapsing symmetrically around the centreline.

Considering these insights, the cup design was optimised, resulting in the final FEM design shown in Figure 24. The key design features were wider pull-pin positions, added front wall pull-pin positions to assist in staggering the collapse, and notches in the front and back lip to direct the collapsing and folding points of the cup.

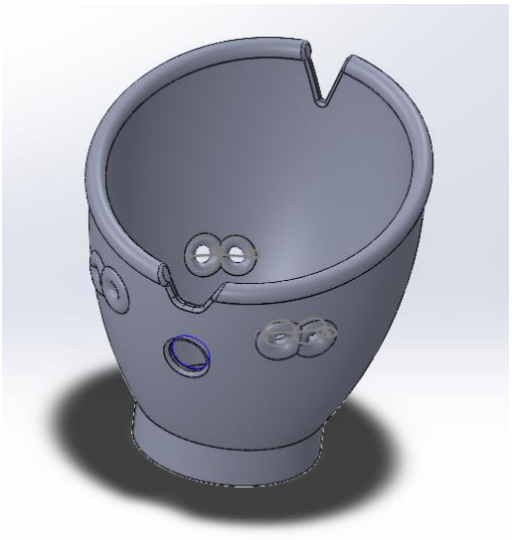

Figure 24: Phase 1 final design.

4.3.6 Phase 2: Physical Prototype Development and Optimisation

The second phase of the cup development and optimisation used physical prototypes to test the FEA results from phase 1 and further optimise the design for collapsing. This phase used rapid prototyping to manufacture and test physical prototypes. The *FormLabs Elastic 50A* resin was chosen for prototype manufacturing using the *FormLabs3* stereolithography (SLA) printer. The FormLabs Elastic 50A resin was selected as the material to use since it is designed to have the same properties as silicone and has material properties that are similar to the silicone used to manufacture menstrual cups. This additive manufacturing process using the FormLabs3 printer was selected for its advantages in reducing production time, having high accuracy and repeatability, and the ability to incorporate small design changes quickly and easily.

Informal testing was done on the manufactured prototypes using a handheld testing rig designed to replicate the dimension of the insertion probe onto which the cup was mounted. The mounting probe was 20mm in diameter and had internal actuation string hole positions to feed the actuation cable through. For testing, the cup was mounted on the rig, and an actuation string was attached to the pull pins of the cup. The cup's collapsing sequence and collapsed shape were evaluated by manually pulling the actuation string to collapse the cup. The key performance parameters that were evaluated during this informal testing included inspecting the fully collapsed cup size, the collapsing sequence, and the perceived force required to collapse the cup and maintain the collapsed shape.

The iterative process of printing, testing, and optimising the physical prototypes led to the following key findings and insights:

1. **Staged collapse concept:** Building on the insights of the 'staggered pull' concept from phase 1, the staged collapse concept used the two pull pins to fold the left and right walls of the cup over each other, as shown in Figure 25 below. Folding the sidewalls over the centreline effectively reduced both the actuation force and the size of the collapsed cup.
2. **Using a single actuation string**: The staged collapse sequence was achieved by running a single actuation string through the hole in the right wall and fastening it to the hole in the left wall. This caused the right wall to be displaced first when pulling the actuation string (Figure 25B), and as it crossed the centreline, the left pull pin displaced, folding over the top of the right wall (Figure 25C).

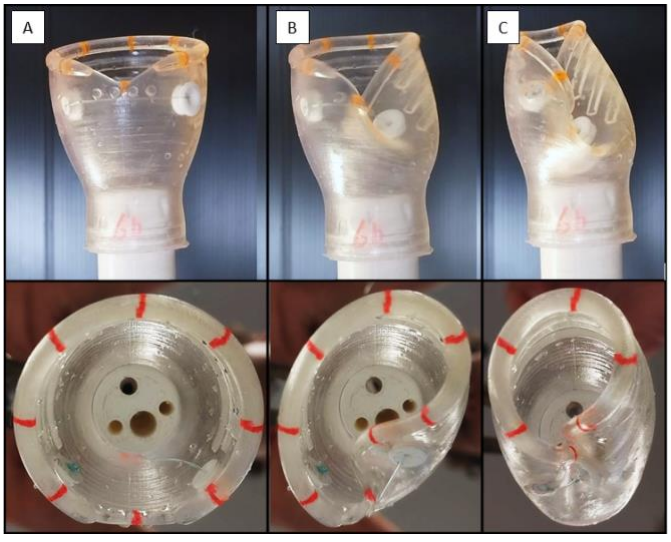

Figure 25: Dilation cup stagged collapse sequence. A) Before actuation - dilated cup. B) First collapsing stage - right wall fold. C) Second collapsing stage - left wall folds over right wall.

3. **Increased pull angle:** Increasing the pull angle by increasing the pull pin distance from the centreline reduces both the collapsed size and perceived activation force.
4. **Collapsed cup profile:** The elongated and narrower collapsed cup shape resulting from the staged collapse sequence creates a small diameter tip that gradually increases, likely making insertion more comfortable and straightforward in clinical applications.
5. **Radial reinforcement rings:** Adding internal radial reinforcement rings running horizontally along the cup's inner wall significantly increased the cup's radial strength and overall stability without affecting the activation force or collapse size.
6. **Back lip notch depth:** The notch in the back wall needed to be above the level of the actuation string that runs between the two pull pins on the cup's outer wall. If not, and the actuation string slips above the notch, the collapsing sequence fails since the back wall bends outwards instead of folding inwards.
7. **Material:** The FormLabs Elastic 50A material proved satisfactory for prototyping, with the cup enduring more than 50 complete collapses before failure (refer to risk B.4 in Appendix G).
8. **Pull hole reinforcement plugs**: To increase the lifespan of the cups PLA plugs were fit into the holes through which the actuation string runs and applied the force to the cup. Without these plugs the actuation string easily tore through the soft silicone cup material.

The final prototype design from this second design optimisation phase incorporated features such as wider pull pin positions, a staged collapse sequence, internal radial reinforcement rings and reinforcing the pull pins with PLA plugs to prevent the strings from tearing into the silicone (refer to risk A.14 in Appendix G).

4.3.7 Phase 3: Strength and Stability Analysis and Optimisation

The third optimisation phase consisted of a second FEA that focused on evaluating the cup's strength and stability against the radial forces that the vaginal walls would exert. This analysis aimed to identify structural weak points and design elements that could cause the cup to collapse against the external radial pressure and optimise the design accordingly. The analysis was performed using the same FEA model detailed in Table 12 on page 37 that was used for the collapsing sequence design but with changes to the boundary conditions.

4.3.7.1 FEA Model Setup

The physics boundary conditions used for the radial strength and stability analysis are:

1. **Fixed boundary condition:** cup base.
2. **Boundary load:** distributed pressure on the external cup walls.
3. **Boundary load direction:** positive pressure normal to the surface.

The following assumption and simplification was made in the analysis:

1. **Applied pressure:** Research has shown that the pressure profile of the vaginal canal is asymmetrically distributed around the circumference of the canal and not uniform along the length of the canal (Cacciari et al., 2017; Guaderrama et al., 2005). However, to simplify the FEA model, the same pressure is uniformly applied to all the external surfaces of the cup.

4.3.7.2 FEA Results and Analysis

The qualitative FEA aimed to optimise the cup's radial strength and stability design by identifying how different design features influence the deformation under a uniform compressive pressure load. The analysis consisted of 7 iterations of the cup design, shown in Figure 26 below, starting with a plain cup without any features to provide a benchmark, followed by the analysis of the final design from phase 2 and optimising it by making slight changes to specific features to see the effects it has on the deformation. The colours represent the amount of deformation of the different regions, with dark blue being the least deformation and red being the most deformation.

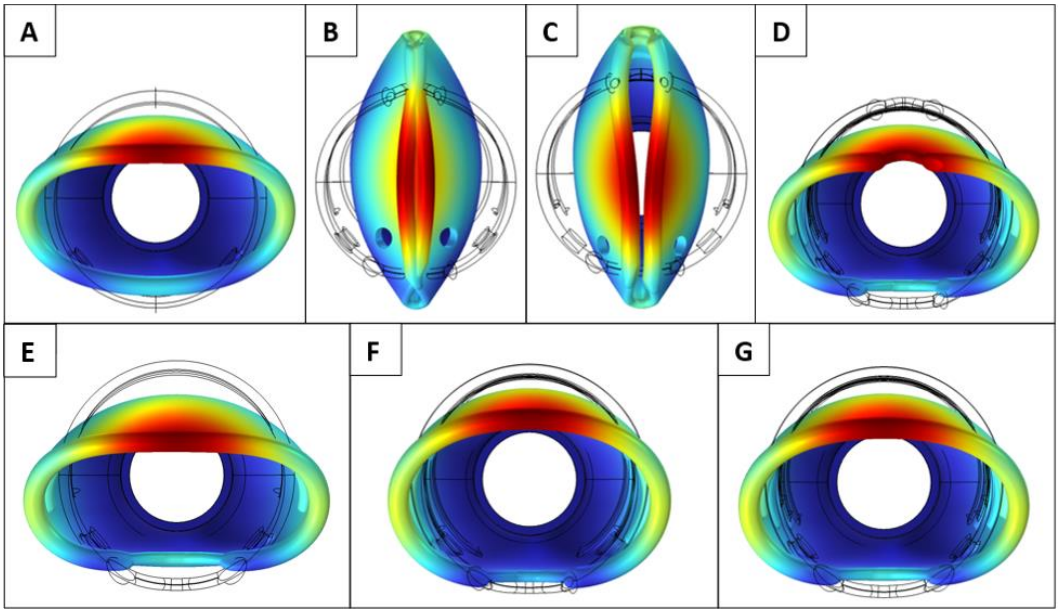

Figure 26: Phase 3 FEA results to optimise the cup for radial strength and stability.

All seven designs were placed under the same pressure load to compare the deformation to determine the strongest design. Only two design parameters were changed between the different iterations, with the rest of the features and sizes of the cup staying constant. These two design parameters are the notches in the lip on the centreline of the front and back walls and the horizontal reinforcement rings in the inner walls. The specific combination of design features and the maximum amount of deformation for each iteration is shown in Table 13 below.

Table 13: Phase 3 FEA maximum deformation results for the different iterations and their unique design features.

Iteration	Design Features	Maximum Deformation (mm)
A	No design features.	10.1
B	2 Rings (lower) and both front and back lip notch.	22.9
C	2 Rings (higher than B) and the same front and back lip notch.	17.1
D	3 Rings and both front and back notches.	9.73
E	1 Ring and only a back notch	12.4
F	2 Rings and only a back notch.	7.91
G	3 Rings and only a back notch.	9

Iteration A set the benchmark since it had no features that influenced the radial strength. Iteration B, the final design of phase 2, performed significantly worse and collapsed completely. The two reinforcement rings were moved higher to be above the midplane of the cup and as close to the top as possible to analyse the effect of the reinforcement rings' position on the strength. This increased the radial strength significantly and decreased the deformation. Adding a third ring in iteration D further decreased the deformation by almost half that of iteration C. Three iterations with only a back notch were made with one, two and three reinforcement rings, respectively, to analyse the effect of the number of rings on the cup's strength in more detail. The results showed an increase in strength from iteration E to F but an unexpected decrease from iteration F to G, i.e. more deformation in G than in F. Further inspection of the stress distribution plots of iterations F and G, shown in Figure 27 below, shows higher stress regions at the front notch and where the reinforcement rings end in iteration G, shown by the red dashed circles in Figure 27 below. This unexpected result was further analysed in the verification testing done on the cups in section 5.2 on page 51.

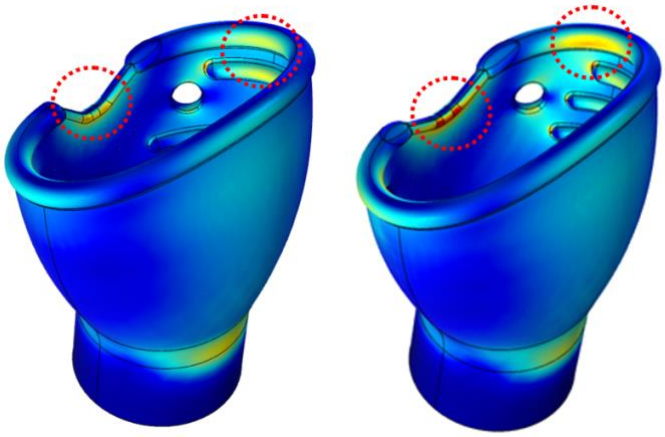

Figure 27: Stress distribution plot of iteration F (left) and G (right) showing the high-stress regions under external pressure loading.

In summary, the insights gained from the radial compression analysis were:

1. **Reinforcement rings effectiveness:** The internal reinforcement rings significantly increased the cup's radial strength, resulting in roughly half the deformation under that same pressure.
2. **Ring positions:** Shifting the rings higher up towards the lip of the cup further decreases the compressive deformation of the lip. The rings do not add any significant strength if they are below the midline of the cup.
3. **Lip notches:** Adding the notch in the back lip does not significantly affect the cup's stability and radial strength.
4. **Additional rings:** Increasing the number of reinforcement rings can increase the radial strength, but not in a linear relation and not necessarily with every configuration of features.

4.3.8 Final Dilation Cup Design

Considering these qualitative results, the final cup design was manufactured using the *FormLabs*3+ printer with the Elastic 50A resin and tested manually using the informal testing rig. This final informal test ensured that the changes did not adversely affect the physical cup's ability to collapse as designed. Based on this final test, the cup design was slightly adjusted, and the final result is shown in Figure 28 below.

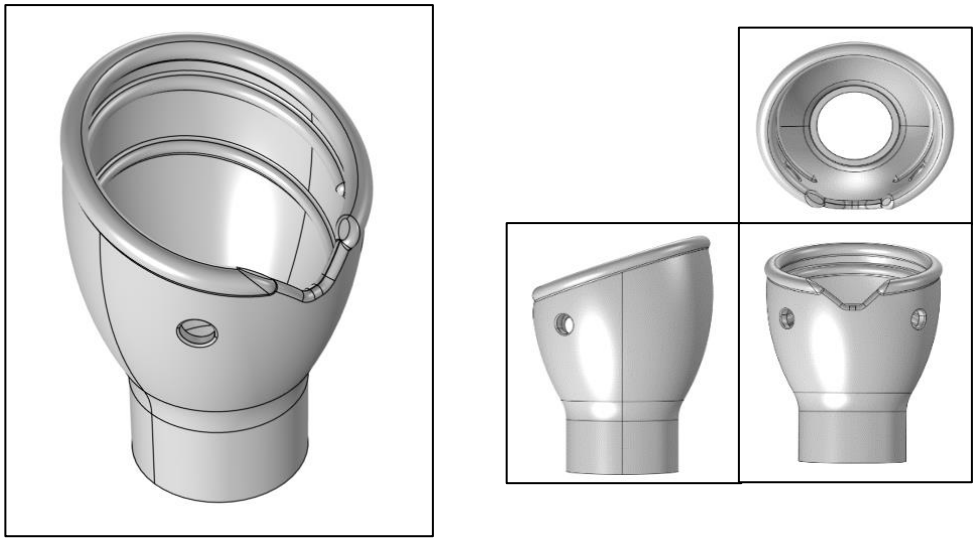

Figure 28: Final dilation cup after 3 phases of development and optimisation.

The most important design features that combine to create the final dilation cup design are:

- **Back lip notch only:** The front lip notch was discarded to improve the collapsed shape and create a smoother leading edge, and the back lip notch remained to help guide the collapse of the back wall.
- **Two radial reinforcement rings:** The two rings ensured high stability, radial strength, and elastic force to return to the dilated state once inserted while not significantly increasing the actuation force for collapsing.
- **Wide and shallow back lip notch:** A wide back notch allows for maximal vertical displacement of the lip during actuation. It needed to be shallow to ensure that the actuation string did not slip off the cup when it collapsed.
- **Large angle between pull pins:** The angle between the point where the actuation string applies the force needed to be as large as possible (100° in the final cup) to maximise the angle at which the actuation string is pulled. This large angle created the moment arm necessary to initiate the staged collapse sequence, allowed the cup to collapse further, and reduced the actuation force.
- **Staged collapse sequence:** The collapse sequence was optimised to collapse one side of the cup first and then the other over the top. This served two primary purposes: force reduction since only one side collapsed at a time, and it created a narrower and more elongated collapsed shape thwith a reduced insertion profile.

4.3.9 Complete Dilation Subsystem

The supplementary components of the dilation subsystem were the cup trigger, actuation string, and reinforcement plugs. These components assisted the dilation cup to perform its function of collapsing for insertion and removal. Figure 29 shows where the cup trigger was mounted to the bottom of the handle. The trigger slid in a slot in the handle to allow the operator to pull the trigger, i.e. move it further from the cup, which collapsed the cup. The actuation string attached the trigger to the cup so that the string displaced and applied the actuation force to the cup as the operator pulled the trigger. The actuation string passed through the reinforcement plugs attached to the cup at the points where the actuation string applied the force to the cup. These plugs were manufactured using PLA and reinforced the cup to provide a hard surface for the actuation string to interface with, preventing the string from tearing the silicone cup. Figure 29 shows the complete subassembly with all the components in position on the final prototype.

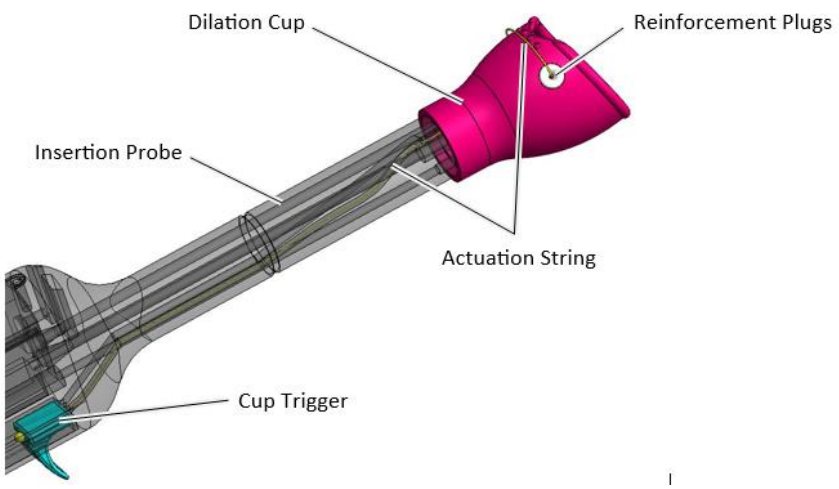

Figure 29: Assembled components of the dilation subsystem.

4.4 Decontamination Subsystem Outcomes

4.4.1 Subsystem Overview

The primary function of the subsystem was to protect the patient from cross-infection. The decontamination subsystem development focussed on the single-use probe cover since the second element of the decontamination process, the post-examination cleaning of the probe and handle, uses existing HLD cleaning techniques. The concept of a single-use probe cover originated from the sheaths used for the same purpose on transvaginal ultrasound probes, typically a condom or similar custom-produced sheath. However, a modified sheath with two elements was required for this application: a sheath and a faceplate.

The sheath was similar to the ultrasound probe sheaths in that it was either a condom or manufactured sheath that fit over the probe. However, a specialised faceplate was designed that could be attached to the tip of the insertion probe. It securely attached the cover to the probe and provided an interface for connecting the camera, light pipes, and nozzle. The faceplate design allowed it to be clipped into position by the operator before the examination, and then post-examination, the operator would pull the sheath to detach the faceplate and discard the entire assembly.

The results of the proof-of-concept testing showed that the usability of the probe cover was poor, but the feedback from the clinicians was that the concept was good and needed to be refined to make it more usable and practical. The design inputs, along with several identified risks, were used to make the following design improvements and create the probe cover used in the final prototype:

1. The faceplate needed to be securely attached to the probe tip so that it could not be accidentally pulled off when pulling the sheath over the probe.
2. The cervix-facing side of the faceplate needed to be flat to prevent water from pooling in and around protruding features (refer to risk A.6 in Appendix G).
3. A visual indication of the faceplate's orientation relative to the probe tip was needed to assist the operator in correctly orienting the faceplate before attachment (refer to risk C.5 in Appendix G).
4. The faceplate should easily release from the probe tip after the screening procedure.

4.4.2 Faceplate Development

The probe cover was designed to have two manufacturing methods, one providing pre-assembled probe covers and another that allows operators to self-assemble the covers in the field using any available condom. For the self-assembly to be possible, the faceplate was designed to be a two-part assembly that is press-fitted over the sheath, with one part on either side of the sheath. This assembly is shown in Figure 30 below, which explains how the sheath is sandwiched between the top and bottom plates. The top faceplate is on the cervix side of the sheath, and the bottom faceplate is on the probe side.

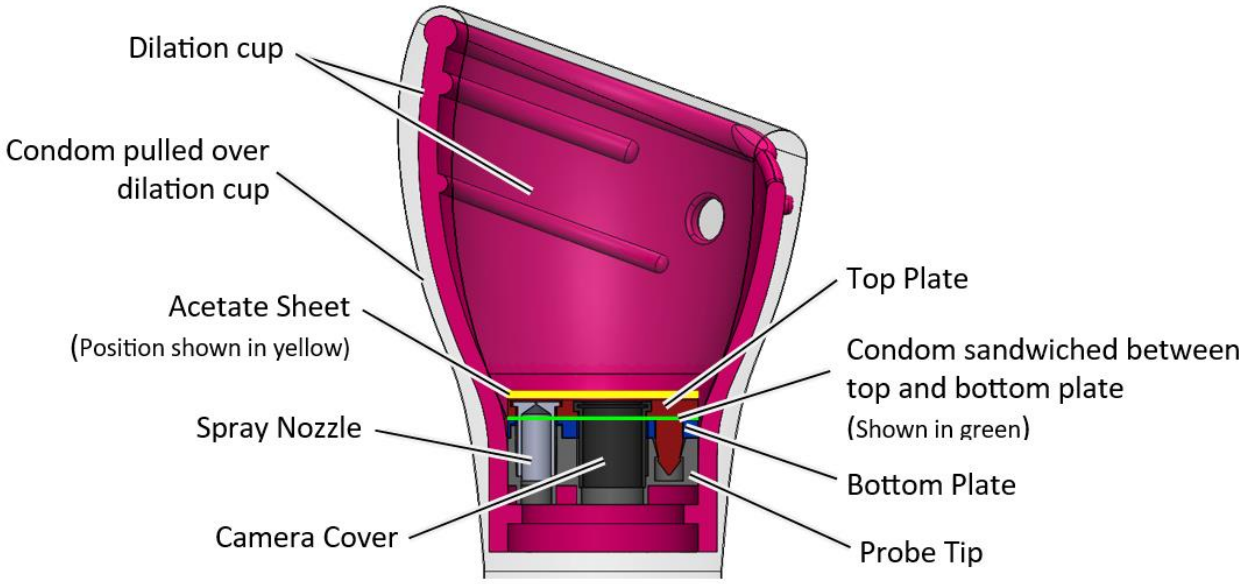

Figure 30: Cross-section view of faceplate assembly and attachment to the sheath (condom).

For the faceplate to be effective, the top and bottom plates were designed to achieve four functions:

I. Connect to the components mounted in the probe tip that must interact with the cervix – the camera, light pipes, and liquid dispenser.
II. Securely attach to the probe tip during screenings, but be able to release when tugged by the operator after screening.
III. Permanently and tightly sandwich the sheath between the two plates such that the plates cannot be separated once assembled.
IV. Pierce the sheath at the locations where the camera, light pipes, and liquid dispenser are to prevent the sheath from interfering with the efficacy with which these components function.

The final top and bottom plate designs are described in more detail in Figure 31 below, showing the essential features that enabled them to achieve the above functions. The diagram shows one of the three connector pins on the faceplate and how it interfaced with the other components to achieve the two connecting functions. Firstly, the pin attached the top plate permanently to the bottom plate with two 90° connecting notches. The fit between the pin and the hole in the bottom plate was a 'press-fit' connection, meaning it could not be released once the bottom plate was pressed past that notch. This was critical to ensure the two plates did not separate during use (refer to risk A.7 in Appendix G).

The angled connecting notch at the end of the connector pin was the second feature that allowed the faceplate to be securely attached to the probe tip while still easily detaching after use. The probe tip (grey part in the diagram) was permanently mounted to the probe and had a pin connector hole to allow the pin to be pressed into the probe tip. The probe tip had a 90° notch that interfaced with the angled notch on the connector pin to create a semi-permanent connection between the two parts. The angled notch on the pin required force to release it from the probe tip (refer to risk C.4 in Appendix G), removing the faceplate and discarding the entire probe cover.

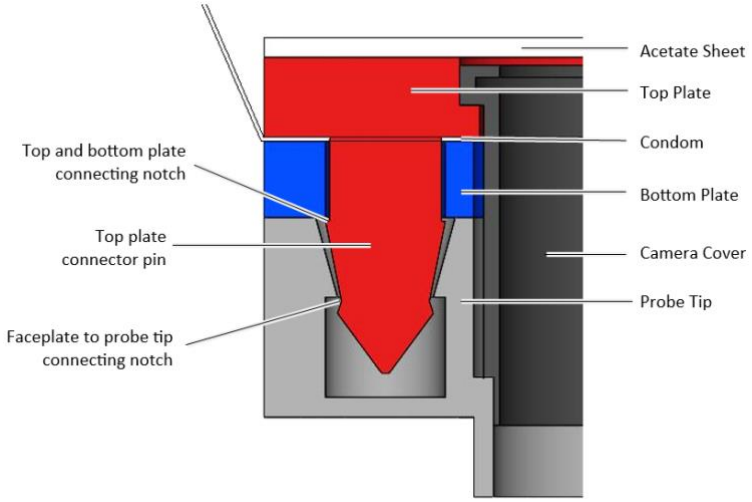

Figure 31: Essential features of the faceplate connecting components.

4.4.3 Probe Cover Assembly

Figure 32 shows how the fully assembled faceplate was attached to a condom and the tip of the probe.

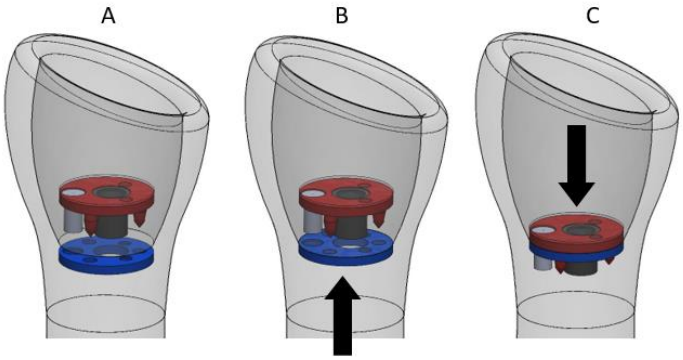

Figure 32: Three-step assembly instructions for the faceplate and probe cover.

The assembly steps of the sheath are as follows:

1. Insert the spray nozzle and camera cover into the top faceplate.
2. Holding the condom open, drop the bottom face plate into the condom and hold onto it at the tip of the condom.
3. Pulling the condom taught over the bottom faceplate, press it hard onto the assembly rig, holding the top faceplate in position until the three fastening pins are securely attached to the bottom plate.

4. Use a sharp scalpel to make small cuts in the condom on the pins that protrude through the bottom faceplate, allowing the taught pieces of the condom to be pulled over the pins, creating a shrink fit (refer to risk A.7 in Appendix G).
5. Remove the entire assembly from the assembly rig.
6. Spread a thin layer of glue onto the top faceplate and press it onto a clean, transparent acetate sheet.
7. When the glue is dry, cut the acetate sheet to the size of the faceplate.
8. Use a sharp scalpel to make a small hole in the acetate sheet around the hole of the nozzle to allow the liquid to pass through.

This assembled sheath could then be attached to the probe's tip and pulled over the probe to create a sterile barrier between the probe, its components, and the patient. This probe cover was pre-assembled for the validation testing since the process was still not optimised for self-assembly by the participant. This probe cover design offered flexibility for the device to either use a pre-assembled sheath or to be self-assembled. In cases where resources are very limited, the operator would be able to use the two-part faceplate with any condom to assemble a sterile sheath for each patient.

4.5 Housing Subsystem Outcomes

4.5.1 Housing Subsystem Overview

The primary function of the housing subsystem was to enclose and support all the other subsystems of the device and to provide an ergonomic and intuitive user interface for the operator. The housing consisted of three main elements: the insertion probe, handle, and display holder. Each element serves a specific purpose, as detailed in Table 14 below.

Table 14: Detailed functions of the housing subsystem elements.

Housing Element	Detailed Functions
Insertion probe	It provides a rigid enclosure for the camera, light pipes, and liquid pipe to be transported to the probe tip, where they interface with the cervix.
	It has a fixation point at the probe tip for the decontamination sheath to be securely attached.
	It provides an attachment point for the dilation cup and transports the actuation string from the cup to the trigger on the housing.
Handle	Houses and securely fastens all the internal subsystems and components.
	Contains the majority of the user interface controls, such as the liquid dispensing button, LED dimmer, colour filter toggle, and dilation cup trigger.
	It provides an ergonomic handle for the user to hold the device and interact with the user controls with either their right or left hand.
Display holder	Securely clamps over the smartphone connected to the device.
	Allows the operator to adjust the orientation and position of the smartphone to suit their preference.
	**It is only required when a smartphone is connected to the device. The display holder can be removed if another smart device is used, such as a tablet, computer, or laptop.*

4.5.2 Final Housing Development

The proof-of-concept prototype was designed with the functions listed in Table 14 in mind for each element. However, the preliminary testing highlighted several problems with the design and layout of the housing elements that needed to be improved, such as:

I. The large size of the device was poorly suited for the limited space available in clinics and screening rooms.
II. The rotation of the display holder helped provide the operator with sufficient freedom of movement to position the display in its desired position.
III. The large freedom of movement offered by the semi-flexible connection between the probe and handle was not required. This connection needed to be reduced and simplified.
IV. The user controls were not optimised for one-handed use and were incompatible with right-handed and left-handed operators.

These design inputs were used to minimise the housing subsystem's size and complexity while preserving each element's functionality. The result of this development process is shown in Figure 33, which labels the five components that comprise the housing subsystem.

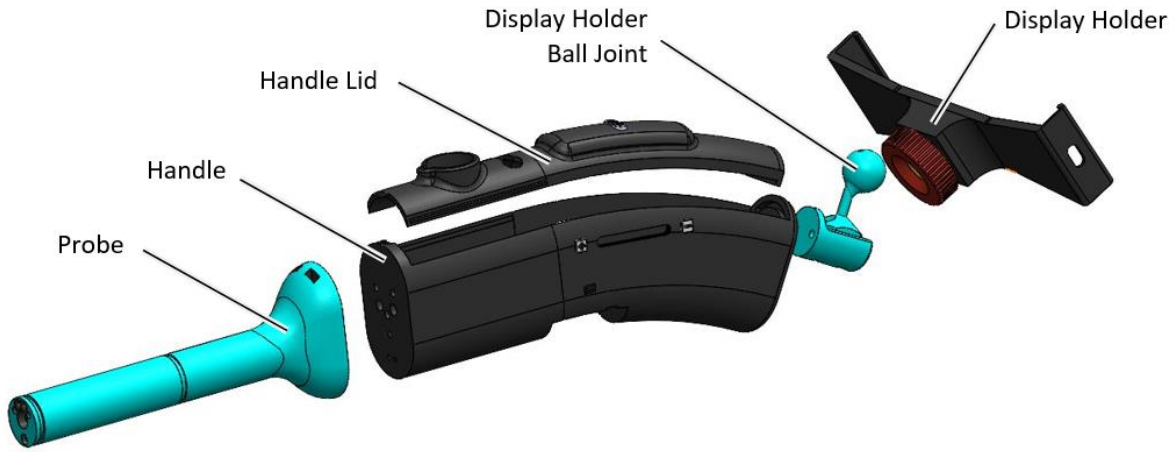

Figure 33: Components constituting the housing subsystem of the final prototype.

4.5.3 System Integration

The final part of the development process was integrating all of the subsystems developed in this chapter into a functional system. Figure 34 illustrates how the different subassemblies were housed in the housing subsystem and what the fully assembled prototype looked like. The physical prototype built and used for verification and validation can be found in Appendix B (Figure 60 on page 101).

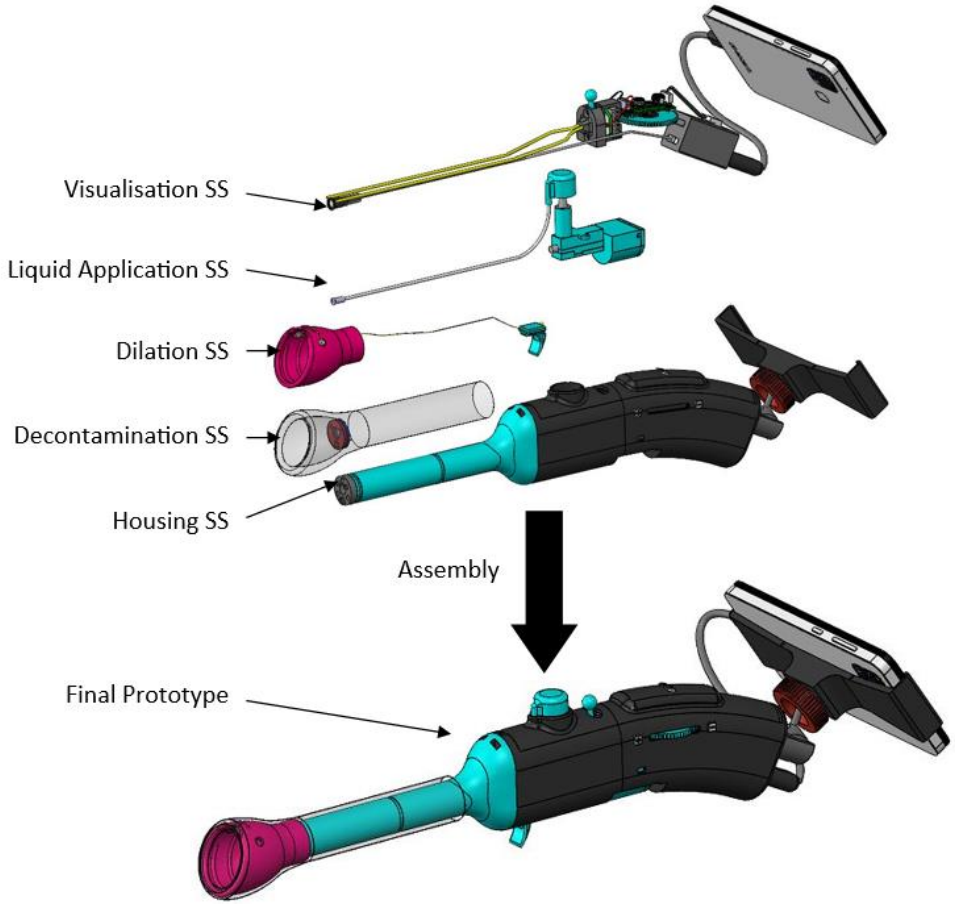

Figure 34: The final prototype and its constituent subsystems (SS) are fully assembled.

5 Design Verification

5.1 Overview

This chapter presents a detailed account of the verification procedures used during the development of the device, which aimed to verify its functionality as a cervical cancer screening device. The verification process encompassed two distinct phases:

1. Verification tests aimed to ensure that the individual components and subsystem of the device met their engineering specifications,
2. Risk identification and mitigation to ensure that the device is safe to use during the validation study and can perform its intended function.

Two sets of verification tests were conducted that had different scopes and aims. The first test focussed solely on the dilation cup and actuation mechanism and aimed to select the most suitable dilation cup design that met the engineering specifications. The qualitative analysis done to design and develop the dilation cup necessitated an in-depth qualitative test to accurately compare the performance of the different cup designs and verify that the designs met the engineering specifications. Based on these test results, the best cup for integration into the complete device was selected.

Subsequently, the second set of tests focused on the fully assembled device and how the various subsystems performed when integrated. These verification tests aimed to assess the various components and subsystems of the developed device to confirm their compliance with the engineering specifications outlined in Chapter 3.2. Literature research and ISO standards were combined to synthesise the functional requirements and engineering specifications the subsystems had to meet. Therefore, the series of verification tests performed on the complete device comprised a combination of standardised ISO tests and supplementary assessments focussing on various aspects of device performance.

The design methodology presented in Figure 8 on page 25 shows that this verification process of testing the prototypes and identifying the risk produced design inputs that fed back into the design and development process. Thus, the design was improved based on these design inputs until the complete device was verified and subsequently validated. This chapter only presents the final prototype's verification tests and risk assessment results. However, since several critical design decisions originated from the preliminary verification tests done on prototype 5, the proof-of-concept device, the detailed test methodology and results can be found in Appendix C for reference.

5.2 Dilation System Test Methodology

5.2.1 Introduction

This chapter presents a detailed analysis of the dilation cup’s performance through experimental testing and force analysis. The primary objectives of these experiments were to validate that the final cup design met the engineering specifications and to select the best-performing cup. The secondary objective was to quantify how the performance of the cups improved as a result of the design optimisations. The two tests performed were a tensile test and a compression test. The tests aimed to analyse the following four key performance parameters:

1. **Actuation Force:** The force required to collapse the cup entirely.
2. **Smallest Collapsed Size:** The minimum size achievable when the cup entirely collapses.
3. **Total Collapsed Percentage:** The extent to which the cup collapses when actuated.
4. **Radial Strength:** The cup's resistance to uniform external pressure.

Eight different cup designs from critical phases in the design process were tested to provide meaningful benchmarks against which to measure the improvements made by the design optimisation. The selected cups consisted of five cup designs that were the outputs of the different phases of the development process and three final designs with some minor design variations. The three final designs result from further physical testing of the second FEA output, with three design variations tested to confirm which practically had the best performance. Table 15 below provides the details of the eight designs tested and images of the cups can be found in Appendix B.

Table 15: A description of the eight dilation cup designs which were tested to quantify the improvements through optimisation and select the best design.

No.	Version	Description of the cup features and design changes made.
1	Baseline	A plain cup with no features represented the starting point for the design process.
2	Initial Collapse Sequence	The first attempt at a collapsing sequence pulled both walls straight down simultaneously, aiming to achieve a symmetrical collapse by pulling the cup at the midline. The cup had sharp front and back lip notches.
3	FEA Round 1 Result	The first optimisation attempt of the collapsing sequence with the wider pull pins used the 'staged collapse'- sequence. The cup had a front and back lip notch and a hole in the back wall to guide the folding point.
4	Physical Prototyping Result	The cup uses a 'staged collapse' sequence optimised by further widening the pull pin positions and increasing the size of the front and back lip notches. The addition of two reinforcement rings aimed to increase the cup's stability and radial strength.
5	FEA Round 2 Result	The internal reinforcement rings were optimised by adding a third ring, moving the rings higher on the cup wall, and positioning them closer to each other. The cup did not have a front lip notch, and the back lip notch was widened.
6	Final Design 1	The cup had a shallower back lip notch and additional features to prevent the actuation string from being pulled over the back lip notch, which compromised the collapse sequence. The overall cup was slightly taller and had more rounded walls.
7	Final Design 2	The cup had the same size and design as cup 5, without the front lip notch, a shallower back lip notch and three internal rings.
8	Final Design 3	The cup had the same size and design as cup 7, but the central ring was removed.

Together, these cups represent the entire evolutionary journey of the dilation cup, culminating in the final design. The objective of these tests was to demonstrate a progressive improvement in performance across these designs, ultimately highlighting the superior performance of the final cup in terms of the critical design parameters.

5.2.2 Tensile Test Setup

The tensile test aimed to quantify the force required to collapse the cup and measure the fully collapsed cup's size. According to engineering specifications ES-4.4 and ES-4.5, the actuation force and collapsed size should be less than 7N and 25mm, respectively. The experimental setup used to perform the test, illustrated in Figure 34, closely mimicked the actual cup mounting and actuation procedures used

in the complete device to get the most accurate results. The cup was connected to an actual insertion probe, as it would in the complete device. The actuation string, routed internally within the mounting probe, was pulled from where it exited the probe base. As shown in Figure 35, both the mounting probe assembly and the force measurement device were securely fastened upside down to a vertical rod using clamps. The bottom clamp which held the insertion probe was fixed in position on the rod while the top clamp that held onto the scale was free to be displaced vertically up or down. Displacing the clamp upward caused the scale to pull on the actuation string, which in turn caused the cup to collapse. This procedure very accurately simulated the actuation motion used in the final prototype when the trigger is used to collapse the cup.

The actuation string was connected to a force measurement device at the probe's base to measure the force required to collapse the cup completely. The force measurement device was a luggage weighing scale capable of measuring weight in kilograms (kg) with a resolution of 50 grams (g). Calibration of the scale was confirmed using a 1kg calibration weight suspended from the scale. Multiplying the weight measurement (in kg) by the gravitational acceleration constant (9.81 m/s^2) converted the weight measurements to Newtons (N). Image processing software analysed images of the cup in the collapsed state to calculate how much the cup collapsed. A smartphone camera captured the cup actuations by taking videos of the cup from three different viewing angles (top, front, side). Screenshots from these videos taken at the timeframes when the cup completely collapsed were analysed using the image processing software. The smartphone position in Figure 35 shows the camera taking a video from the side view.

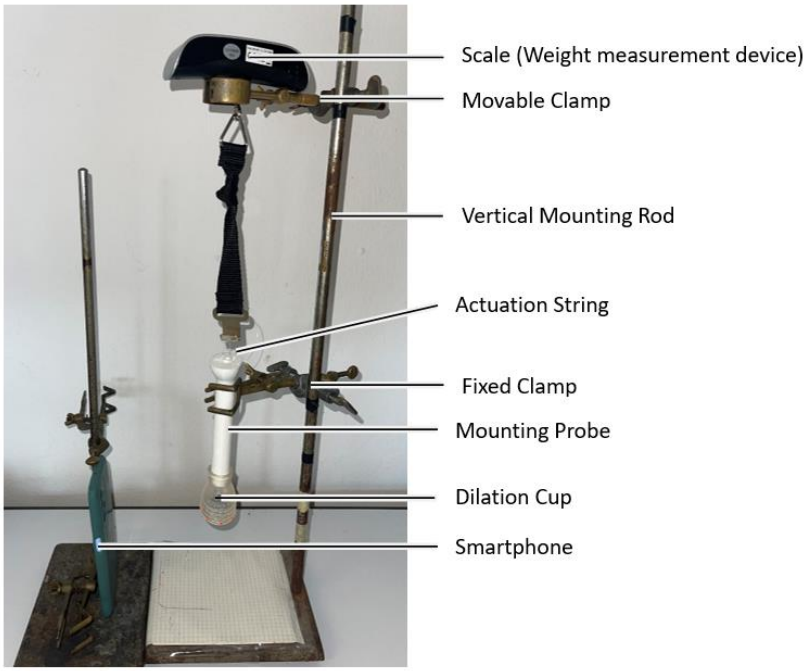

Figure 35: Dilation cup tensile test setup.

The vertical displacement of the force measurement device upward initiated the cup's collapse by causing the actuation string to displace and the cup to collapse. Once the cup reached its fully collapsed position, the upward displacement ceased, and the luggage scale took the force measurement. The maximum force was measured at the upper limit of the displacement. A rigid actuation string was used to minimise the impact of elasticity on the force measurement by ensuring constant displacement

throughout the tests. Each cup underwent a total of nine complete collapses in three collapsing cycles, with each cycle consisting of three complete collapses. This protocol resulted in three force measurements and videos from the three camera positions.

5.2.3 Compression Test Setup

The compression test aimed to evaluate the cup's radial strength against external pressure, simulating the pressure that the vaginal walls would exert during use. The test aimed to validate that the cup could withstand a maximum pressure of 0.5 bar without collapsing more than 25%, according to ES-4.2 and ES-4.3. The setup, as shown in Figure 36, included mounting the cup on a rig that replicated its attachment positioning on the probe and allowed a condom to cover the cup completely. The open end of the condom was tied off before placing the entire assembly inside a pressure chamber. The purpose of pulling the condom over the cup and probe and tying it off was to capture air inside the cup, which initially existed at atmospheric pressure, thereby creating a pressure differential between the inside and outside of the cup walls when the pressure increased inside the chamber. Without this pressure difference, generating a net external pressure would not be possible, and the cup could not collapse inward.

A small compressor attached to the pressure chamber's inlet incrementally increased the pressure in a controlled manner. The *150W Wiltec Airbrush Compressor AF18-2* featured a controllable pressure gauge to control the pressure inside the chamber between 0 and 4 bar. The pressure gauge had increments of 0.2 bar, which increased the pressure to the desired value. Although the desired pressure according to the engineering specifications (ES 4.2) was 0.5 bar, the 0.2 bar increments of the gauge necessitated three 0.2 bar increments from 0.4 bar to a maximum of 0.8 bar. The 0.2 bar pressure level was discarded as it did not cause any noticeable deformation for any of the cups. A smartphone camera positioned in front of the pressure chamber's viewing window, as shown on the left of Figure 36 below, captured images of the cup from a top view at each pressure level.

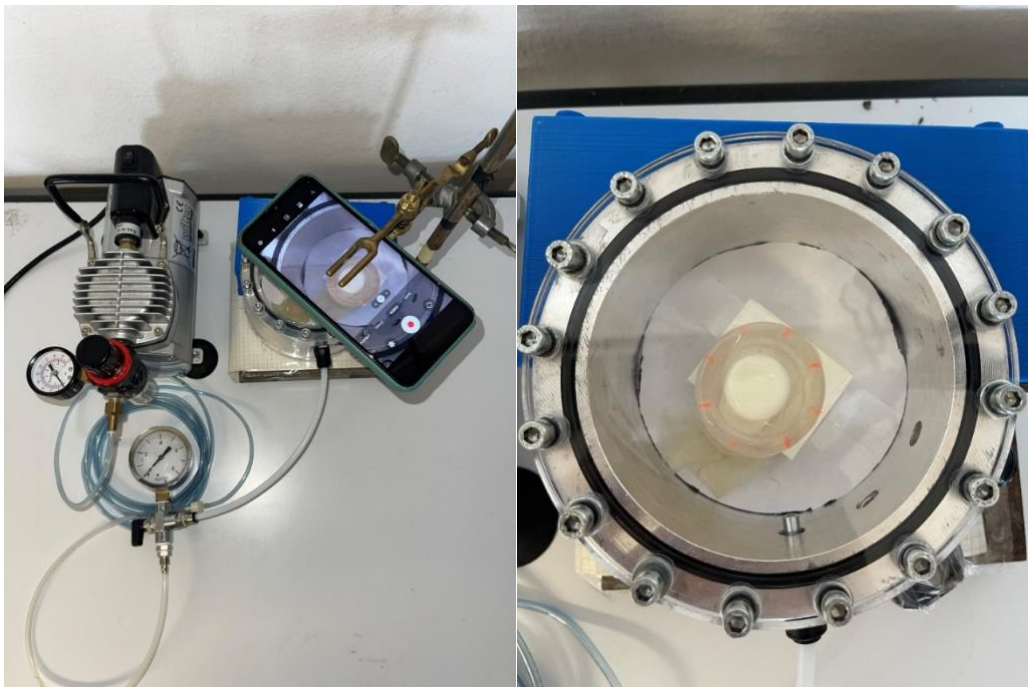

Figure 36: Setup used for the dilation cup compression test.

5.2.4 Data Acquisition and Analysis

MS Excel was used to capture and pre-process the data from the two tests, followed by a detailed descriptive and statistical analysis using *GraphPad Prism 8*. Three types of raw data were collected: the actuation force values from the tensile tests, videos from the tensile test, and images from the compression tests. The tensile test videos captured the entire collapsing sequence of the cup, from which screenshots of the cup in the fully collapsed state were taken to be used for image analysis. The two sets of images from the tensile and compression tests were processed and analysed using open-source *Fiji (ImageJ)* software. This software was employed to analyse cup deformation by measuring specific parameters related to cup shape.

5.2.4.1 Activation Force Calculations

The activation force test used the converted weight measurements from the luggage scale to forces (N) to calculate the activation force. As explained in the test setup, each cup was collapsed three times for each of the three camera angles used to capture the video footage. Thus, a total of nine force measurements were taken for each cup. The final activation force was calculated as the average of these nine measurements.

5.2.4.2 Tensile Test Image Processing Method

The primary purpose of the images captured from the tensile tests was to determine the minimum size of the fully collapsed cup. The cup's collapsing factor (CF) was also calculated using these images. The CF expresses the percentage reduction in the cross-sectional area of the cup when fully actuated and was calculated using the following equation:

$$\boldsymbol{CF = \left(\frac{A_{open} - A_{collapsed}}{A_{open}}\right) x100,} \qquad \mathbf{1}$$

Where A_{open} is the cross-sectional area of the un-collapsed cup, and $A_{collapsed}$ is the cross-sectional area of the collapsed cup. Thus, the CF could be used to compare the different cup designs' collapsing efficacy without the cups' physical dimensions influencing the results. The cross-sectional area calculation of the cup was simplified to be a square instead of an ellipsoid or circle. However, since the cross-sectional area values were used to calculate a percentage, it would not make a significant difference since the ratio between the CFs of the cups would be similar.

The measurements used to calculate the CF were taken from two images of the cup in its collapsed state, one side-view image and one front-view image, as shown in Figure 36 below. The planes along which these measurements were taken, referred to as insertion planes, were positioned perpendicular to the insertion axis of the cup. The angle of this axis was slightly different for each design based on its unique geometry and collapsed shape, but the method of defining the insertion axis remained consistent. For the side-view image (Figure 37a), the pink dashed line shows the line used to determine the angle of the axis, which is between the cup's tip and the cup's base where it meets the probe. The green block and insertion angle line were drawn parallel to this axis. For the front-view image analysis in Figure 37b, the axis was found by drawing the green block parallel to the top edge of the cup and drawing the insertion angle perpendicular to that line down towards the centre of the probe tip. In practice, the cup will be inserted along this axis since it has the smallest cross-section at the tip and would allow for the most

straightforward insertion. Thus, since the cup design was optimised for insertion along this axis, it was used to make the two cross-section measurements.

To accurately determine if the design improvements reduced the insertion size and made the cup more 'streamlined' (to resemble the pushdown fold shape from Figure 7), measurements were taken at three different distances from the tip of the cup. Thus, three insertion planes perpendicular to the insertion axis were placed at three distances from the tip of the cup, expressed as $h_{fold}, h_{10mm}, \text{and } h_{5mm}$ in Figure 37. Insertion planes 1 and 2 were placed 5mm and 10mm from the cup tip (h_{10mm} and h_{5mm}), and insertion plane 3 was placed at the 'fold point' of the collapsed cup, which was the point at which the lip of the cup folded out of view on the side-view image. This point was chosen as a point of interest since it represented the maximum width of the collapsed cup from the side view.

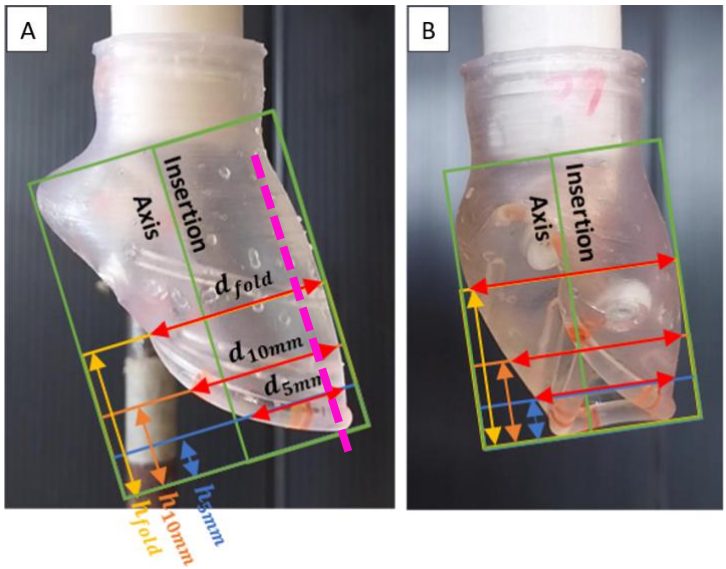

Figure 37: The a) side-view and b) front-view images of the collapsed cup used during image processing, showing the position of the three insertion planes and the insertion axis and the three cross-sectional diameter measurements taken (red arrows).

The three cross-sectional diameter measurements taken on each image are shown by the red arrows and labelled on Figure 37a as $d_{fold}, d_{10mm} \text{ and } d_{5mm}$, respectively. The two corresponding diameter measurements from the front-view and side-view images were multiplied to calculate the cross-sectional area value used in Equation 1. This method of measuring the cup's cross-sectional diameter provided the most accurate and repeatable measurements for the different cup designs. The imaging processing steps used in the *Fiji* software program were as follows, starting with the side-view images:

1. Create a stack of side-view images with one image of the cup in the dilated (open) state and three images of the cup in the collapsed (closed) state.
2. Scale the images using the known diameter of the white probe mount.
3. Draw a large rectangle that aligns with the probe's tip and base to determine the insertion angle, depicted as the green rectangle in Figure 37a.
4. Draw the three smaller rectangles that align with the three insertion planes, depicted as the yellow, orange, and blue lines in Figure 37a.
5. Measure $d_{fold}, d_{10mm}, \text{and } d_{5mm}$ for each image in the stack.
6. Measure h_{fold}.

Then, moving on to processing of the front-view image:

1. Create a stack of front-view images with one image of the cup in the dilated (open) state and three images of the cup in the collapsed (closed) state.
2. Scale the images using the known diameter of the white probe mount.
3. Draw a large rectangle that aligns with the probe's tip and base along the insertion angle, depicted as the green rectangle in Figure 37b.
4. Draw the three smaller rectangles that align with three insertion planes. Insertion plane three was placed at the distance h_{fold} from the tip of the cup. These planes are depicted as the yellow, orange, and blue lines in Figure 37b.
5. Measure $d_{fold}, d_{10mm},$ and d_{5mm} for each image in the stack.

The maximum of the average diameter measurements between the two views were selected at each insertion plane to evaluate whether it met the threshold engineering specification. The average cross-sectional area of the three images was calculated at each insertion plane, and those were used to calculate the CF using Equation 1 above. The average cross-sectional diameter measurements of the three planes were compared to examine the relationship between the side-view and the front-view measurements. This analysis aimed verify that the decrease in size was due to the front-view size decreasing as a result of the improvements to the designed collapsing sequence, and that the size from the side-view stayed fairly constant for all the designs.

5.2.4.3 Compression Test Image Analysis Method

The objective of the compression test was to evaluate the radial strength of the cup by analysing the amount of inward deformation (collapse) of the cup under various external pressures. The images captured during the compression tests were used to calculate the compressed deformation (CD) the cup underwent. The CD expressed the percentage reduction in the cross-sectional diameter of the cup at the various set pressures and was calculated using the following equation:

$$\boldsymbol{CD = \left(\frac{d_{open} - d_{compressed}}{d_{open}}\right) x 100,} \qquad \textbf{2}$$

Where d_{open} is the cross-sectional diameter of the un-compressed cup, and $d_{compressed}$ is the cross-sectional diameter of the compressed cup. Thus, the CD value could determine if the cups met the minimum radial pressure requirements specified by the engineering specifications and compare the radial strength of the different designs.

As previously detailed in the experimental setup in section 5.2.3, each cup was put through a uniform external compression cycle three times, with images taken at the four set pressures (0, 0.4, 0.6, and 0.8 bar). Thus, 12 images were taken and analysed for each cup. The cup's mounting rig ensured that the camera's orientation remained parallel to the lip of the cup to minimise inaccuracies in the measurement taken during the image analysis due to the cup edge being at different heights relative to the camera lens. The diameter measurements were taken between adjacent marked points on the inner edge of the lip, as shown in Figure 38 below. This analysis method produced four measurements per image: A-A, B-B, C-C, and D-D. The method used to make the measurements was as follows:

1. Use a vernier to measure the A-A distance on the physical cup.
2. Create an image stack of all 12 images.
3. Scale the images using the A-A measurement from step 1.
4. Measure the distance between the inner edge of adjacent marked points, maintaining the same order of A-A, B-B, C-C, and D-D for all the images in the stack.

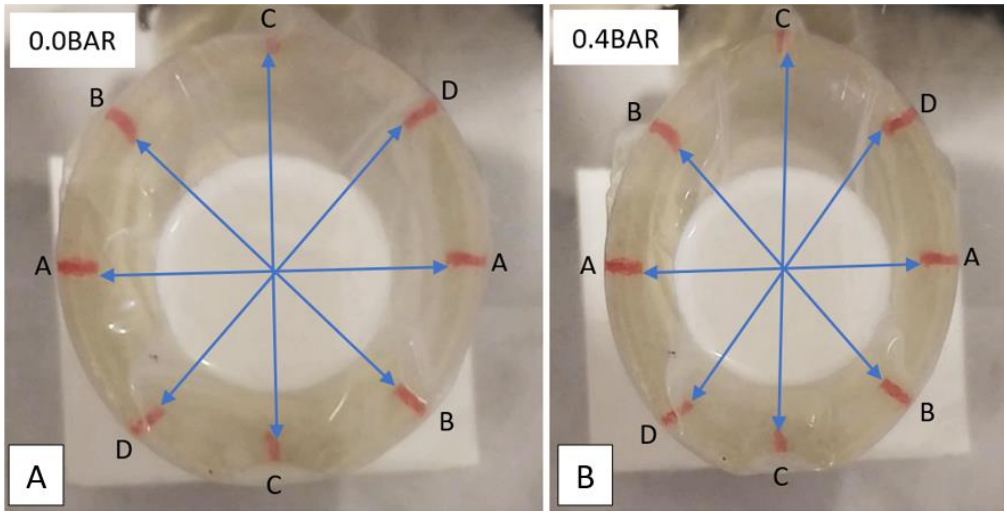

Figure 38: Illustration of the diameter measurements taken from the compression test images at a) 0 bar and b) 0.4 bar.

The average adjacent distances were calculated for each sample at different pressures, and the smallest distance was selected for those. For example, in the case of Figure 38b above, the A-A distance would be selected, and the rest discarded since it is the smallest diameter measurement of the measurement pairs. This minimum distance was used in Equation 2 to calculate the compressed deformation percentage at the various pressures.

5.2.4.4 Data Analysis

The data was first collated using *MS Excel* and then analysed using *GraphPad Prism 8.* The datasets were analysed using an ordinary one-way Analysis of Variance (ANOVA) and descriptive statistics.

5.3 Dilation System Test Results

5.3.1 Actuation Force Results

The average actuation forces for the samples, shown in Figure 39 below, are all below the 6N threshold. Cup 5 had the highest actuation force of 5.4N, and cup 3 had the lowest activation force of 2.21N. There was a significant difference in the actuation forces between all cup designs ($F_{(8,80)}$ = 117.8, P<0.0001). The most significant improvement in design regarding actuation force between two successive cups was a decrease of 2.16N between cups 2 and 3, and the second largest was the decrease of 1.57N between cups 5 and 6.

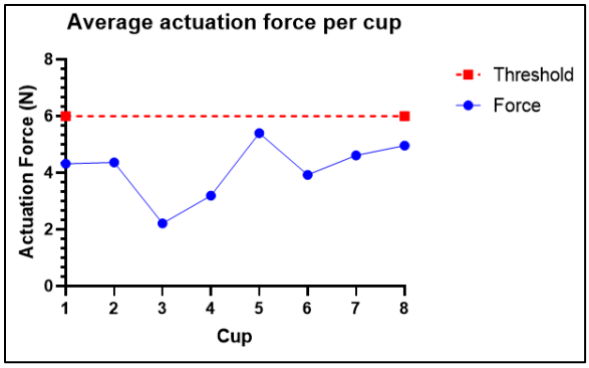

Figure 39: Dilation cup test results - Average actuation force per cup.

5.3.2 Collapsing Factor and Maximum Cross-Sectional Diameter Result

The collapsing factor (CF) measured the percentage decrease in the cross-sectional area of the cup when actuated from the dilated to the collapsed state. Figure 40 below shows the results of the CF measured at three insertion planes for the eight-cup designs tested. The graph shows how the CF at all three insertion planes increases throughout development, meaning that the cup design became more 'streamlined'. The CF at the fold insertion plane was of the most interest (the red line in Figure 39) since that would be the maximum size of the cup during insertion, and it had a minimum and maximum CF of 40.27% and 54.02%. The most significant difference in CF between two successive cup designs was between cups 2 and 3, with a 16.91% increase in CF at the 10mm insertion plane.

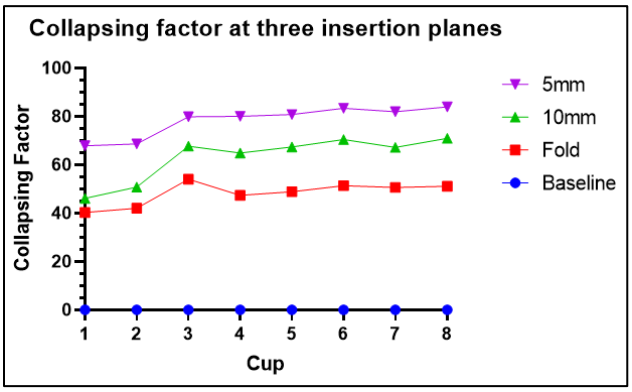

Figure 40: Dilation cup test results - Collapsing factor at three insertion planes.

The maximum cross-sectional diameter results at the three insertion planes are shown in Figure 41 (left) below. The most significant improvement between the diameters of two successive cups is a 15.92mm decrease between cups 2 and 3 at the 5mm insertion plane. Cups 2 and 3 also show the most significant average decrease across all insertion planes of 12mm, with cups 1 and 2 also showing a significant decrease of 3.03mm. Between cups 4 to 8, the maximum diameter does not improve significantly, with the largest difference in maximum cross-sectional diameter between these cups being 0.3mm.

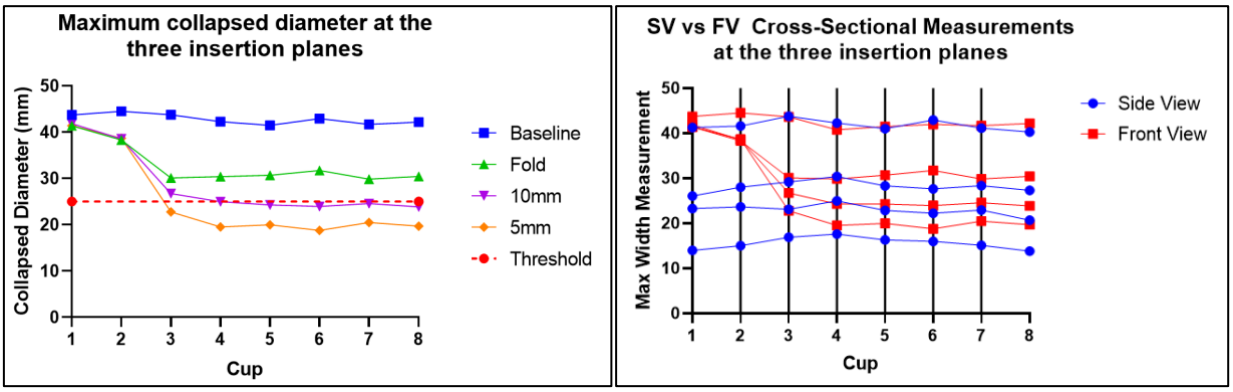

Figure 41: Dilation cup test results - Maximum collapsed diameter at the three insertion planes (left), and the side-view and front-view diameter measurements at the three planes used to select the maximum collapsed diameter (right).

The second graph in Figure 41 (right) shows the maximum cross-sectional diameter measurements taken at the three insertion planes (and at baseline) for the side-view (SV) and front-view (FV) images. The data used in the left graph was the maximum values for each data pair in the right graph, with each data

pair consisting of an SV and FV measurement for each cup at a specific insertion plane. The left graph shows that the maximum collapsed diameter and CF improvements made almost exclusively resulted from the decreasing front-view diameter (the red lines in Figure 41 (left)). At the same time, the side-view measurements stay relatively consistent. This was because the design optimisation aimed to create a narrower, more streamlined collapsed shape with a slimmer tip that gradually increased in size towards the base, similar to the pushdown fold shown in Figure 7.

5.3.3 Radial Strength Results

The compressed deformation was calculated using Equation 2 and represented the radial strength of the cup design. The results are shown at the three tested pressures in Figure 42 below, and the threshold value shown in yellow is the 0.5 bar pressure that cup must be able to resist, per ES-4.2. Analysing the data at each pressure showed that there was no significant difference in the compressed percentage between all the cup designs at 0.4 bar ($F_{(8,24)}$ = 0.8166, P=0.5871), but at 0.6 and 0.8 bar, there was a significant difference ($F_{(8,24)}$ = 16.37, P<0.0001; $F_{(8,24)}$ = 5.612, P=0.0021). Only four cup designs (4,6,7,8) fell within the acceptable threshold of 25% CD at the 0.6 bar pressure level, with cup 5 just above the threshold with a CD of 27.1%. At the 0.4 bar pressure level, all the cup designs were significantly below the CD threshold, with an average CD of 2.256 ± 1.101%. For successive cup designs, the most significant differences in CP were between cups 3, 4, 5, and 6, with differences of $CP_{34} = -18.42\%, CP_{45} = +11.13\%, and\ CP_{56} = -21.67\%$.

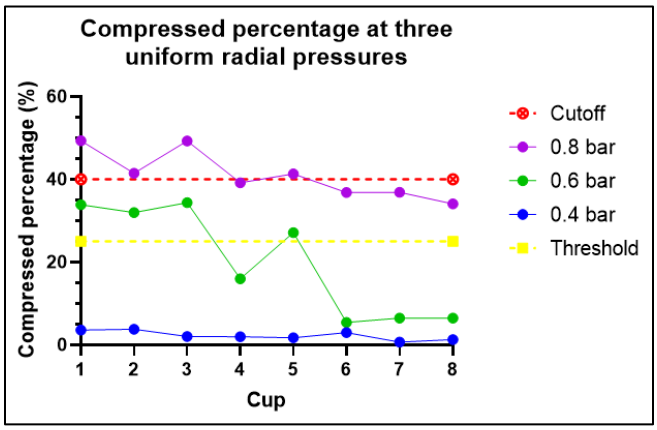

Figure 42: Dilation cup test results - Compressed deformation at three uniform radial pressures.

5.3.4 Dilation System Discussion

The results of the tests showed a general trend of increasing cup performance for the four performance criteria. The final three cup designs (6, 7, and 8) showed very similar performance, and all three met the required engineering specifications to be used on the final device. Based on this, design eight was selected as the cup for further testing.

5.4 Device Testing Methodology and Results

5.4.1 Overview

The objective of the device verification testing was to verify that the final prototype and all its constituent subsystems met the engineering specifications defined at the beginning of the project in Chapter 3. This objective was achieved by performing a series of engineering/benchtop tests based on specific ISO standards and auxiliary tests not covered by the standards. The ISO 8600 standards for

endoscopic medical devices were used to guide the device verification. However, the verification primarily covered design and performance requirements and did not encompass the complete requirements in the ISO 8600 standard that is expected of an endoscopic device, such as safety and biocompatibility.

For this project's scope, the standards used to verify essential device requirements included ISO 8600-3:2019, ISO 8600-4:2023 and ISO 8600-5:2020. These standards delineate the methods and measurement requirements for assessing the field of view and the direction of view of endoscopes, the maximum width of the insertion portion, and the limiting resolution, respectively. A series of auxiliary tests were done on the device to verify other critical performance parameters not covered by the ISO standards. These auxiliary tests were drawn from tests done by the predicate devices that served as reference benchmarks when defining the engineering specifications of the subsystems in Chapter 3.2. Table 16 below summarises the essential tests from the ISO standards and the auxiliary testTable 16s, along with each test's pass-fail criteria.

Table 16: Summary of the verification tests and the pass requirements for each test.

No	Test	Requirement
1	ISO 8600-3:2019 Field-of-View (FOV) and Direction-of-View (DOV)	30mm (70°) FOV and 0°DOV
2	ISO 8600-4:2023 Insertion Width Test	<20mm
3	ISO 8600-5:2020 Limiting Resolution	>11lp/mm
4	Illumination intensity	>1000lux
5	Power consumption	>2hour battery life
6	Acetic acid application efficacy	Target and cover all four quadrants of the cervix
7	Dilation system actuation force of the integrated system	<7N
8	Probe cover integrity	Waterproof seal around faceplate

5.4.2 Testing Apparatus Overview

Several tests utilised the same test rig built based on the testing rig used in the ISO 8600-3:2019 standard, shown in Figure 43, referred to as the optical bench. The rig was simplified slightly from the one detailed in the ISO standard since the device does not have all the features intended to be tested by the original test rig, such as an endoscope with a non-zero degree viewing angle.

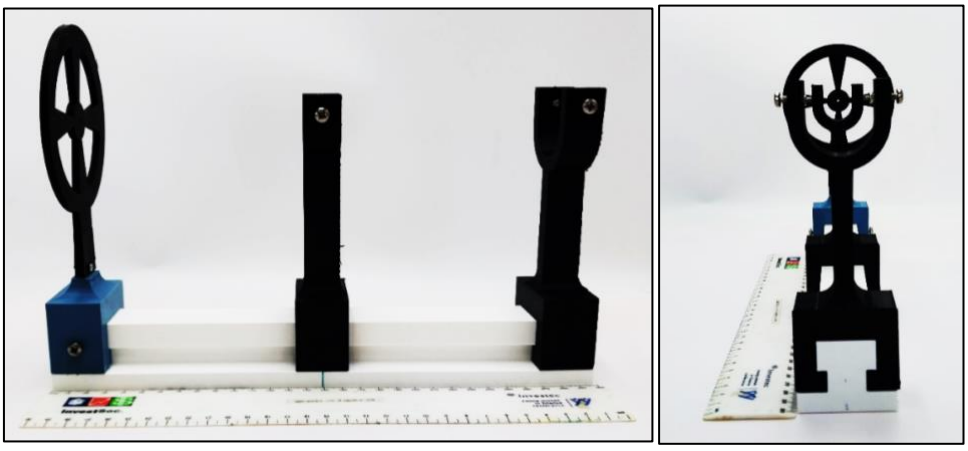

Figure 43: Optical bench used for the device verification testing.

The critical design specifications of this testing rig, per ISO standards, include:

- **Optical bench**: A mounting bench designed per ISO 8600-3 guidelines to support the device while aligning the imaging target perpendicular to the central axis of the imaging window. This bench enables vertical adjustment of the device's central axis and horizontal adjustment and measurement of the distance between the distal window and the imaging target, within a range of 0 to 50 mm ± 0.2 mm. This distance was measured using a fixed ruler positioned next to the linear rail for measurements with a 1mm accuracy and an vernier with a 0.1mm (±0.02mm) resolution for finer distance measurements.
- **Target holder**: The imaging target is positioned on the target holder and mounted at a specified working distance. The target holder sits on a linear rail to position it at various distances from the device.
- **Illumination source**: Standards allow for either endoscope illumination or an external light source. An external white light source was utilised to sufficiently illuminate the imaging target to prevent the custom illumination system from affecting the tests, ensuring visibility throughout the endoscope's field of view.

Figure 43 below shows the targets placed on the target holder for some tests Figure 44. The way the targets were used during each test is elaborated upon in the following protocols.

Figure 44: Verification testing targets used for some verification tests. a) Field-of-View test, b) Limiting resolution test, and c) Liquid applicator efficacy test.

5.4.3 ISO 8600-3:2019 Field-of-View Test

This test aimed to measure the field of view (FOV) and direction of view (DOV) of the device to validate compliance with ES-2.2 and ES-2.4, which specifies a minimum FOV of 30mm (70°) and a DOV of 0°, respectively. The standard outlined two possible methods to measure the FOV, with Method B selected since it was a more robust method that applied to any endoscope. Figure 44 above shows the target used to measure the FOV, as per the ISO standard method. This target was mounted on the centre of the target holder, and the optical bench was used to follow the method described in Appendix C.

The test was replicated with and without the attached probe cover, and the results are shown in Table 17 below. The ES column on the right of the table shows the targeted FOV engineering specification.

Table 17: ISO 8600-3:2019 Field of View Test Results.

Configuration	Field of View (degrees)			
	Vertical	Horizontal	Diagonal	Engineering Specification
Camera only	39.60	64.37	74.67	>70°
Probe cover attached	40.34	63.30	75.14	

Of these three FOV measurements, the one specified by the engineering specification was the diagonal FOV. Based on that, the imaging system met the specifications and passed the test. This result was expected since the camera ordered has a 77° lens. However, it confirmed that the addition of the probe cover did not impact the FOV, passing the test regarding the specification of the probe cover (ES 5.4) not to impact the FOV negatively.

5.4.4 ISO 8600-4:2023 Insertion Width Test

The objective of this test was to measure the maximum insertion portion width of the device and confirm alignment with ES-1.1, which defines the maximum allowable insertion width as less than 20mm. The standard dictates that the maximum diameter measurement of the probe should be taken as "the largest diameter measurement taken in all sections perpendicular to the nominal axis along the length of the insertion portion." Furthermore, if the endoscope had a detachable hood, the maximum diameter measurement needed to be taken with and without the hood. Thus, the measurements were taken with and without the dilation cup and probe cover attached to the probe's tip. A vernier calliper with an accuracy of 0.02mm and a resolution of 0.1mm took the measurements. The test results and engineering specifications that the insertion probe aimed to meet are shown in Table 18 below.

Table 18: ISO 8600-4:2023 Insertion width test results.

Configuration	Maximum diameter (mm)	Engineering Specification
Probe only	20	<20mm
Dilation cup attached	25	

The device met the engineering specification without the dilation cup attached but failed with the cup and probe cover added. The device failed with the cup attached due to the unoptimised attachment mechanism of the base of the cup to the probe tip. The limiting factor resulting in this failure was the probe tip components' layout and the manufacturing method used to make the probe. With a more advanced manufacturing method that could make thinner walls and features, the layout of the components could be optimised, and the diameter reduced to below the engineering specification. However, this was considered an unnecessary improvement at this stage of the development process since it would naturally happen if the device progressed further towards commercialisation.

5.4.5 ISO 8600-5:2020 Limiting Resolution Test

This test aimed to measure the on-axis limiting resolution of the integrated imaging system to verify that the limiting resolution was more than 11lp/mm, per ES-2.5, and that integrating the camera with the probe cover does not degrade the image quality, per ES-5.3. The method detailed in the standard guided the test, which used the 1951 USAF Resolution Target, shown in Figure 44b above. The resolution was measured at both extremes of the device's working distance, 20mm and 50mm, and with and without the probe cover attached. The target was evenly illuminated by an external white light, per the ISO 8600 standard. To calculate the resolution from the 1951 USAF Resolution Target Equation 3 is used:

$$\boldsymbol{Resolution} = \mathbf{2}^{\left(\boldsymbol{Group\ number} + \frac{\boldsymbol{Element\ number} - \mathbf{1}}{\mathbf{6}}\right)}. \qquad \mathbf{3}$$

The group and element numbers are the smallest vertical and horizontal numbers the camera can see. The unit of resolution for this equation is line pairs per millimetre (lp/mm). The results of the test and the engineering specification it aimed to meet are shown in Table 19 below.

Table 19: ISO 8600-5:2020 Limiting resolution test results.

Configuration	Limiting resolution (lp/mm)		
	20mm	50mm	Engineering Specification
Camera only	51	25	>11
Probe cover attached	25	13	

The device passed the test with and without the attached probe cover (refer to risk B.3 in Appendix G). The results show a consistent 50% reduction in the resolution from the minimum to the maximum working distance. It also shows that the probe cover reduced the resolution by 50%, even though the lens cover is an entirely transparent acetate sheet.

5.4.6 Illumination Intensity Test

This test aimed to verify that the illumination system provides a minimum of 1000 lux of illumination to the target, per ES-2.7. The test also aimed to verify that the probe cover does not reduce the illumination below the acceptable threshold, as per ES-5.5. The test evaluated the illumination intensity with and without the colour filter and at the maximum and minimum working distance. The illumination was measured using a UNI-T UT383 Mini Lux Meter, which has a resolution of 1 lux and an accuracy of 4% (0 to 9999 lux). The test was performed in a room with a 0 lux measurement, using the optical bench to hold the device and attaching the lux meter to the target holder. The illumination system was turned on to illuminate the centre of the lux meter's sensor. The results and the engineering requirements that the subsystem aimed to meet are shown in Table 20 below.

Table 20: Illumination intensity test results.

Configuration	Distance (mm)	Illumination Intensity (Lux)		
		No filter	Green Filter	Engineering Specification
No probe cover	20	1950	550	>1000
	50	870	230	
With probe cover	20	1060	340	
	50	530	180	

The results with the probe cover attached show that the device passed the test when placed at the minimum working distance. However, it failed to meet the engineering specification at the maximum working distance and with the green filter engaged. The results clearly show that the probe cover significantly reduces the illumination intensity by approximately 42%, which is consistent with the results from the limiting resolution test. The green filter further reduces the illumination intensity by an average of 69.6%, which is highly inefficient and suggests that the filter method needs to be revised in future designs not to use a mechanical filter.

5.4.7 Power Consumption and Heat Test

This test aimed to verify that the device could be used continuously at full power for 2 hours, according to ES-2.13. This test was performed by connecting the device to a fully charged Samsung A-23 mobile phone with the USB camera app running, displaying the image on the screen, and turning the LED to maximum brightness. The temperature of the LED was continuously monitored to ensure that it did not overheat. The time was recorded using a stopwatch, and the test intended to stop when the phone battery died.

However, the test stopped after 30 minutes due to concerns about the high temperature of the LED and heatsink. Thus, the test failed since the device could not be used continuously for two hours. The phone's battery had reduced by 12% when the test stopped. Thus, although the test only ran for a quarter of the specified time, the results of the shortened test showed that the battery would have lasted the total amount of time. However, the high temperatures generated by the LED when it is left fully ON is a concern that must be addressed to prevent damage to other components or the operator (refer to risk A.5 in Appendix G).

5.4.8 Acetic Acid Application Efficacy Test

This test evaluated the ability of the liquid application system to effectively cover the entire cervix with acetic acid in line with ES-3.2. It consisted of two tests: one to test the coverage and accuracy with a single dispensing actuation and the other to assess overall coverage with multiple dispensing actuations. These tests were performed with the fully assembled probe cover attached to the probe's tip and pulled over the cup.

The single dispensing actuation test was performed using the optical bench to mount the device in position and attach the target shown in Figure 44d to the target holder. The target was positioned at the tip of the cup and in the centre of the field of view before actuating the system to spray a single jet of liquid. The second multiple-spray test used the female pelvic model, which was also used in the validation testing, to evaluate the usability and accuracy of the system in a simulated use case. This test aimed to evaluate whether the device could be manipulated whilst in position inside the vaginal canal to effectively apply the liquid to all four quadrants of the cervix with four dispensing actuations. The same target as the one used in the first test was used for this second test. The device's position was manipulated to 'aim' the spray at the four quadrants of the cervix. The female pelvic model used is explained in detail in the validation section below. The liquid used for the test was water with a colourant added, and the results of these two tests are shown in Figure 45 below.

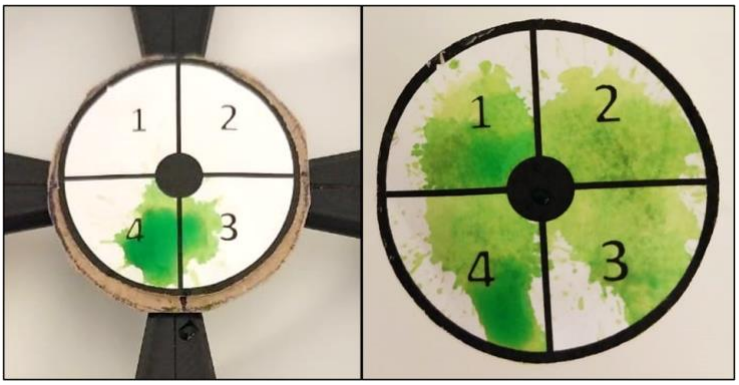

Figure 45: Result of the single spray (left) and multi-spray (right) tests used to verify the acetic acid application system efficacy.

These results showed that the device passed the test and that the system could effectively aim the liquid jet to cover the entire cervix with multiple sprays. The single spray test on the left showed that the spray was directed at the lower centre region of the target. The spray pattern on both images showed that the liquid jet was directed and strong, not diffuse and soft. The result of the multi-spray test on the right showed how four individual liquid jets effectively and accurately hit all four quadrants of the target. The spray-by-spray sequence on the target mounted in the pelvic model is shown in Figure 46 below, which was taken by the final prototype's cameral.

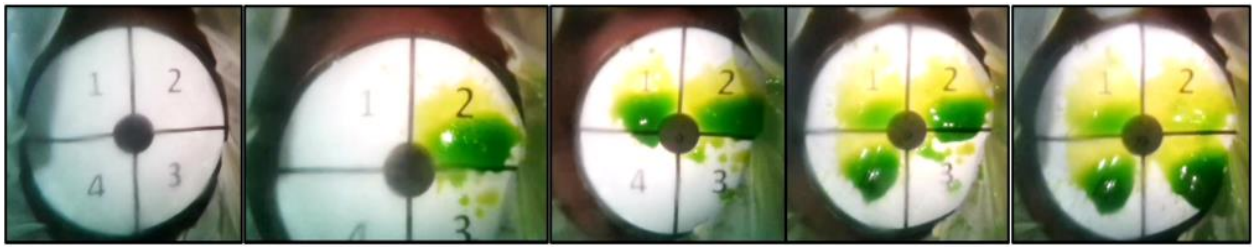

Figure 46: Spray-by-spray sequence of photos from the multi-spray acetic acid efficacy test.

5.4.9 Dilation System Actuation Force Test

The test aimed to verify that the dilation system met the 7 N target actuation force, as per ES-4.5. Although the isolated dilation cup testing done in the previous section showed that the chosen cup (design eight) had an isolated actuation force of 5 N, this test ensured that the fully integrated system did not exceed this specified force due to other factors like friction on the cup trigger. Similar to how the actuation force of the isolated cups was tested in the previous section, a 0.7kg weight was hung from the cup trigger to make it collapse. The 0.7kg weight applied a 7N force to the trigger in the pull direction, which was calculated by multiplying the weight with the gravitational constant to get the applied force. The device passed the test since the hanging weight could successfully collapse the cup.

5.4.10 Probe Cover Integrity Test

The probe cover was tested using a water leak test to verify its integrity and that it creates a waterproof seal around the probe and cup, as specified in ES-5.2. The test procedure filled the fully assembled probe cover with water to asses if micro-tears of leaks were present, especially in the region of the faceplate. The nozzle was closed off for the test since it had a small hole through which the liquid from the spray nozzle (the acetic acid) needed to exit.

The test result was that the probe cover passed the test, with no leaks detected for any of the three covers tested (refer to risk A.6 in Appendix G). This result proved that the wedge mechanism used by the faceplate to pierce the condom and create a shrink-fit around the various protruding elements worked as expected and created a water-tight seal.

5.4.11 Verification Tests Results Summary

At the end of the verification tests, the final prototype passed six tests of the eight tests. Table 21 below summarises these results and indicates whether or not the prototype met the engineering specification for the specific test. The overall design, development, and verification process outlined in Figure 8 on page 25 aimed for the device to pass all the verification tests and mitigate all the identified risks before moving on to validation testing. However, although two of the tests failed, the decision was made to continue with the validation testing since the causes of these failures would not negatively impact the validation test results, and the necessary design improvement to pass the tests was not feasible within this project's scope. These changes are listed as future improvements.

The feasible design improvements that could be made to pass the verification tests were implemented throughout the iterative design process. However, to pass these two failed tests, the requirements to successfully reduce the probe size and improve the illumination system were outside the scope of this research. Implementing these improvements would have required using a different manufacturing process (other than FDM printing) to manufacture the probe and expanding the project

scope to include the development of a software application to create the required colour filters. Thus, the decision was made to continue the validation study since the failure to meet these two engineering specifications does not pose a risk to the operator and will not significantly affect the validation study results.

Table 21: Summary of the verification testing results.

No	Test	Engineering Specification	Result
1	ISO 8600-3:2019 Field-of-View (FOV) and Direction-of-View (DOV)	30mm (70°) FOV and 0°DOV	PASS: 75.14° FOV and 0° DOV
2	ISO 8600-4:2023 Insertion Width Test	<20mm	Fail: 25mm diameter with dilation cup attached
3	ISO 8600-5:2020 Limiting Resolution	>11lp/mm	PASS: 25lp/mm @ 20mm WD and 13lp/mm @ 50mm WD
4	Illumination intensity	>1000lux	FAIL: It only reached the 1000lux requirement without the filter and at 20mm WD. It was under the requirement for the 50mm WD and with the colour filter.
5	Power consumption	>2hour battery life	PASS
6	Acetic acid application efficacy	Target and cover all four quadrants of the cervix	PASS
7	Dilation system actuation force of the integrated system	<7N	PASS
8	Probe cover integrity	Waterproof seal around faceplate	PASS

These verification tests did not explicitly verify that the final prototype met every engineering requirement generated in Chapter 3 for each subsystem. However, the other engineering specifications that were not explicitly tested were still verified, and these results are summarised in Appendix L.

5.5 Risk Assessment Results and Summary

The development process illustrated in Figure 8 on page 25 showed that for the final device to be approved for validation, it also needed to have mitigated all the identified risks to an acceptable level. The various risk mitigation measures that were successfully implemented throughout the design methodology have been highlighted throughout the previous development and testing sections. Table 22 below visually presents the summary of the results of the risk assessment process, which is shown in detail in Appendix G, indicating how many risks that were initially identified were successfully mitigated. The summary of the

risk assessment results illustrates the total number of inherent risks identified initially at each risk level and then the number of residual risks at each risk level after mitigation.

Table 22: Risk assessment results summary.

Risk Level	Inherent Risk		Residual Risk		Change in distribution
	Count	% of total	Count	% of total	
Low Risk	7	28%	19	70%	+42%
Medium Risk	5	20%	5	19%	-1%
High Risk	13	52%	3	11%	-41%
Total Risks Identified	25		27		

The results in this summary show that the design methodology successfully mitigated almost all identified risks to either low or medium risk levels, except for three. Initially, 25 risks were identified, and after mitigation, there were 27 total residual risks, of which 70% were low risk and 19% medium risk. This increase in the total number of risks from 25 to 27 was due to additional risks introduced by the controls implemented to mitigate some of the risks. In this project's scope, the medium-level risks were interpreted as acceptable, but they were to be mitigated if possible. Thus, only three unmitigated risks of an unacceptable level remained after the design methodology was completed.

The reasons for not mitigating these risks as part of this project are discussed individually in the risk assessment register in Appendix G. However, similar to the case of the two failed verification tests, it was outside the project's scope to go through the process of mitigating them to an acceptable level. Nonetheless, the overall risk of the device to the operator's safety and the ability of the device to perform its function was deemed satisfactory for the device to proceed to the validation testing at this point in the development process.

6 Validation Study

This chapter presents a detailed account of the study used to validate the diagnostic performance and usability of the developed device as a cervical cancer screening solution. From this chapter onwards, the developed device will be referred to as the CerviScreen device instead of the final prototype.

6.1 Methodology

This section provides detailed information regarding the experimental procedure and protocols utilised to validate the performance of the CerviScreen device to perform a complete cervical cancer screening procedure in a simulated screening scenario. The methods and protocols described in this section were approved by the University of Cape Town's Human Research Ethics Committee (HREC) (Reference number: HREC REF 570/2023).

6.1.1 Study Overview

This pilot study aimed to use the CerviScreen device to perform a simulated cervical cancer screening procedure in a clinical setting. The primary objective was to determine the diagnostic accuracy of the developed device for cervical cancer diagnosis, and the secondary objective was to determine the usability of the device. In the study, the standard of care screening tool was used as a benchmark against which to compare the diagnostic accuracy of the CerviScreen. Thus, the participants used the developed and standard-of-care devices to perform the same screening procedures. The test results identified any technical faults and usability issues with the device which could be improved in future projects.

The flowchart in Figure 46 below shows the experimental methodology followed Figure 47, which should be read from the participant's perspective. The experimental methodology was based on performing a standard colposcopy examination procedure on an anatomically accurate female pelvic model, the *ZOE* by *Guamard Scientific*, using both the CerviScreen and the standard of care devices. The standard-of-care device used in the study was an optical colposcope used in the colposcopy clinic at Groote Schuur Hospital to perform colposcopy examinations. The other elements used in the study (and mentioned in the flowchart) are explained in further detail in the following sections. The methodology consisted of the following three phases:

1. Phase 1: Training the participants with the CerviScreen device and giving them time to familiarise themselves with the device and its features.
2. Phase 2: The CerviScreen and optical colposcope devices perform the complete screening procedures on the *ZOE* model.
3. Phase 3: The participants complete the post-test questionnaires and system usability scores.

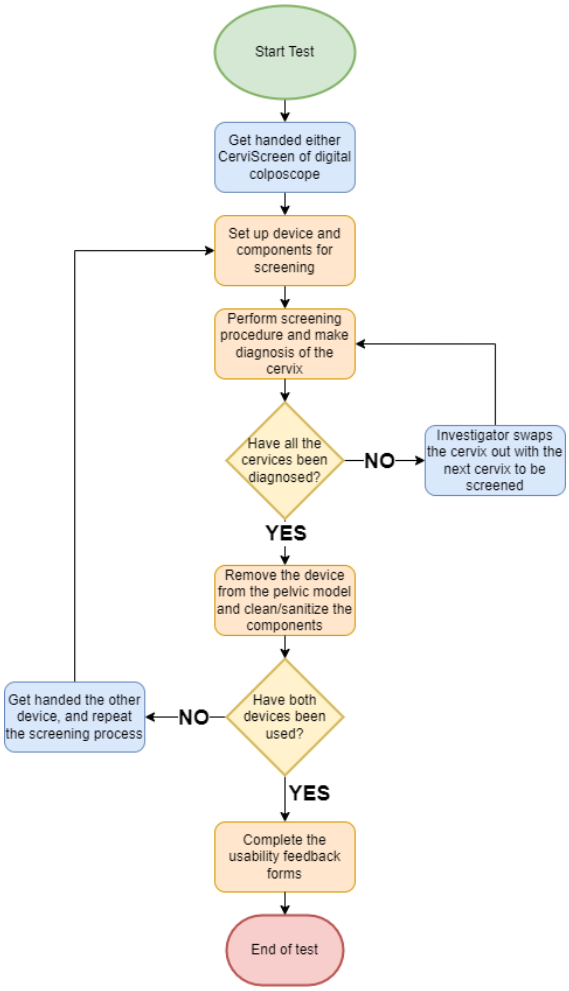

Figure 47: Validation testing flowchart illustrating the tasks the participant performed during phases 2 and 3 of the study.

6.1.2 Hypothesis

The hypothesis of this pilot study was that:

1. The developed CerviScreen device could successfully perform a complete cervical cancer screening procedure.
2. The CerviScreen device had diagnostic accuracy equivalent to the standard-of-care screening device, the colposcope.
3. The CerviScreen device had high usability scores (it was easy to use).

6.1.3 Study Participants

Study participants were selected from two categories of medical professionals: experienced gynaecologists and medical doctors who perform colposcopies at colposcopy clinics. Inexperienced colposcopists (performed <100 examinations) were excluded based on research that highlighted the influence of operator experience on diagnostic accuracy in colposcopy and VIA examinations (Sankaranarayanan et al., 2004). Thus, the inclusion criteria were:

- Had recent experience in performing colposcopies.
- Had conducted more than 100 colposcopies.
- Was a qualified medical professional.

Five participants who met these criteria were recruited to participate in the study (mean colposcopy experience of 14±7.02 years). All five participants were recruited from the colposcopy clinic at Groote Schuur Hospital in Cape Town, South Africa. Four participants had no experience with the CerviScreen device, while one had theoretical knowledge and a single previous interaction with the device. This was considered to be extensive experience, meaning that the results from this participant were analysed in such a way as to evaluate the device's performance and usability from someone with prior experience with using it.

6.1.4 Ethical Considerations

As Appendix H shows, ethics approval (Reference number: HREC REF 570/2023) was obtained before testing commenced. The experimental method conformed to all ethical standards and requirements to ensure ethical responsibility for this study. The participant received an information sheet with detailed information regarding all aspects of the study, which can be seen in Appendix I. Before a participant started using the devices, an informed consent document and a Non-Disclosure Agreement (NDA) form were signed, shown in Appendix J.

6.1.5 Experimental Setup

The entire setup at the colposcopy clinic where the study was done is shown in Figure 48 below, which shows the ZOE model positioned on the examination bed in the lithotomy position, the speculum inserted, and the optical colposcope in position to perform the screening procedure. The ZOE model was in this position while both devices performed the screening procedure.

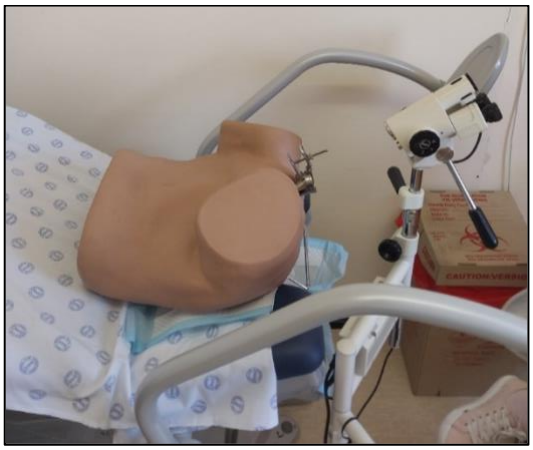

Figure 48: Setup at the colposcopy clinic with the colposcope and speculum in position to perform a screening procedure on the ZOE model.

Some modifications were made to the vaginal canal and cervix of the ZOE model to make the anatomy more realistic and to accommodate the interchangeable cervices required for the study. These modifications came from the *LUCIA* training model developed by Rice University (Parra et al., 2019), a low-cost training model that anyone can manufacture. These modifications included:

1. Lining the inside of the vaginal canal with a pink, waterproof lining to simulate the skin folds that can be naturally found in the vaginal canal and obstruct the view of the cervix, shown in Figure 49a and Figure 49b.

2. 3D-printing a set of hand-painted cervices that represented different pathologies typically encountered during a cervical cancer screening. These cervices could be clipped into the position where the cervix is located on the ZOE model. They are shown at the bottom of Figure 49c and were made to represent the following pathologies (from left to right): acetowhitening, Nabothian cysts, invasive cancer, and coarse vasculature. These cervices were validated by a clinician to represent the target pathologies to a satisfactory level to be used in the study.

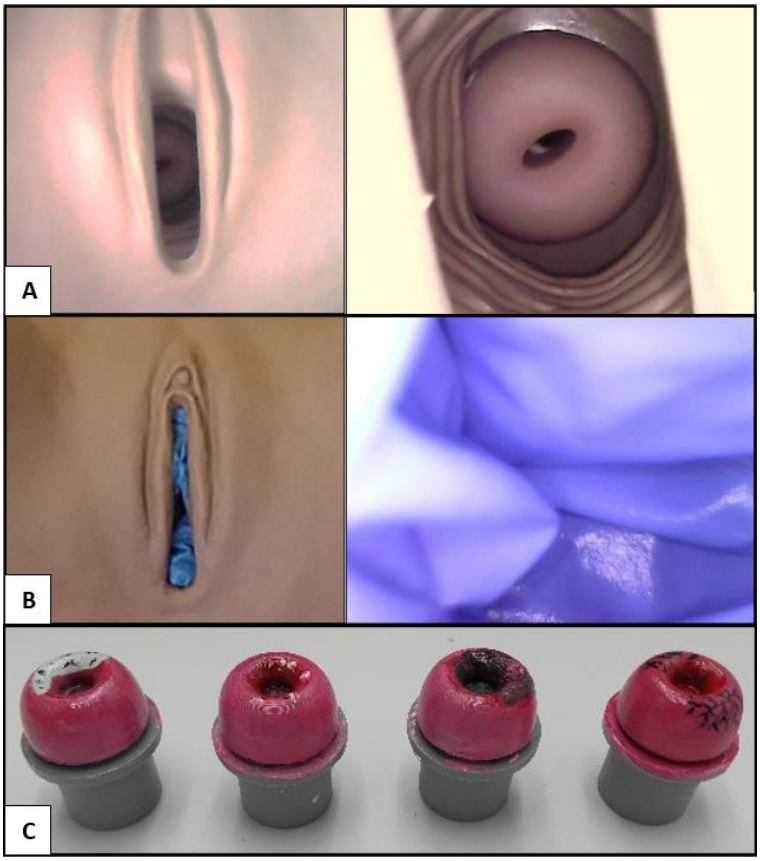

Figure 49: Modifications made to the ZOE model: a) Normal vaginal canal, b) Latex glove added to simulate vaginal folds, and c) interchangeable cervices that represent different pathologies.

The more detailed flowchart in Figure 50 below shows each screening procedure for each device and how the four interchangeable cervices were used. These cervices were designed to allow the investigator to change them without removing the screening device, saving significant time for the participant. Both screening devices used the same set of four cervices, but the order in which they were presented to the participant was randomised to minimise pattern recognition by the participant. Lastly, to make the cervices slightly more realistic, a semi-translucent white cream was applied to the cervices to mimic the presence of naturally occurring mucus on the cervix, which the participants had to wash off with the acetic acid spray as part of the screening procedure. The semi-translucent cream made the pathologies less evident to the participants at first sight and more accurately simulated a screening procedure by forcing them to 'wash' the cervix.

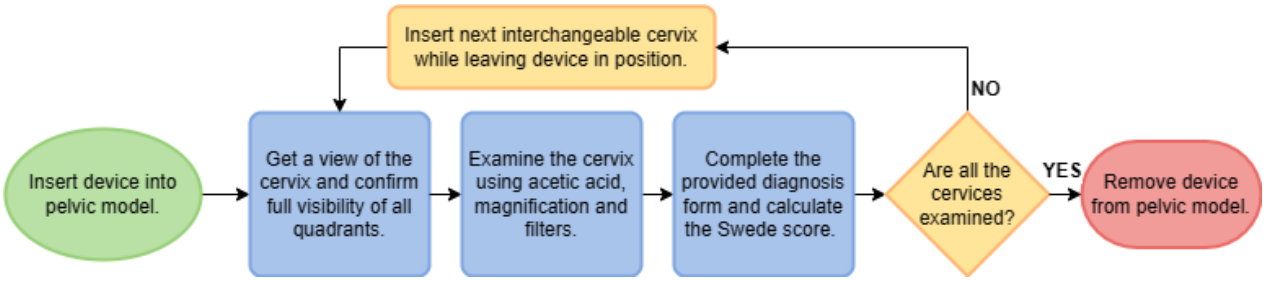

Figure 50: Flowchart detailing the screening procedure followed by each screening device and how the study utilised the interchangeable cervices.

The device that served as the standard of care screening tool was the *Leisegang 1D LED* optical colposcope (more information), which was the colposcope used in the Groote Schuur colposcopy clinic where the study was performed. This colposcope has the CE mark to demonstrate its compliance with the necessary medical device directives, which makes it adequate for use as the benchmark device against which to compare the efficacy of the CerviScreen device. The list of components required for the two screening devices to perform the entire screening procedure is shown in Table 23 below.

Table 23: List of components required for each screening device used in the validation testing.

CerviScreen	Colposcope
CerviScreen device	Colposcope
Pre-assembled probe cover	Speculum
Mobile phone with USB camera app	Cotton swab and forceps for liquid application
Water (substitute for acetic acid)	Water (substitute for acetic acid)
Sterilisation wipes	Sterilisation wipes
Lubrication	Tray to discard speculum after use
	Lubrication

The tasks performed by the participant for both devices were based on the standardised colposcopy examination procedure. While there may be slight differences in the exact sequence and types of tasks due to the design and features of each device, both sets of tasks were derived from the standard procedure outlined by the International Agency for Research on Cancer (IARC) and WHO (Prendiville & Sankaranarayanan, 2017). After both devices performed the screening procedures and diagnosed the cervices, and phase 2 was complete, the participants completed a post-test questionnaire and a system usability scale (SUS).

6.1.6 Data Collection and Analysis

The study aimed to collect data on the diagnostic accuracy of the CerviScreen device and the device's usability while performing a screening procedure. The three types of data that were collected to analyse these performance metrics of the device are:

1. Participant information and diagnosis results.
2. Participant feedback questionnaire and SUS.
3. Investigator observations during the tasks.

The diagnosis results were collected on a standard colposcopy screening report that the participant completed while each cervix was screened. These reports were based on the standard

screening reports used in colposcopy clinics (Prendiville & Sankaranarayanan, 2017), but they were modified slightly to suit the study procedures better. The modified screening reports are shown in Appendix K as part of the 'Participant Data Collection Pack'. Although the appendix only contains one page, the data collection packs handed out to the participants contained eight report pages, one for each cervix screened by each device. The screening reports contained questions regarding transformation zone (TZ) classification, TZ size, colposcopic opinion (diagnosis), Swede score, and two diagrams for illustrating observations and indicating the position of the lesion(s) on the cervix.

After the participant used both devices to perform the screening procedure, they completed the post-test questionnaire and SUS. The questionnaires allowed them to comment on the device's usability and specific features or aspects of the CerviScreen. The SUS focussed solely on the device's usability and was used to attempt to quantify how usable the CerviScreen was. Brooke (1996) developed the system usability score (SUS) framework, a versatile and robust tool for quickly evaluating a system's subjective usability. It consists of a ten-question survey using a 5-point Likert scale to generate a total out of 50, which converts to an eventual score out of 100. In calculating SUS, which is the score out of 100, the point contributions of the questions (out of 5) were adjusted to a point out of 4. The final scores of the odd-numbered questions were calculated by subtracting 1 from the score given by the participant, and scores for the even-numbered questions were calculated by subtracting the participant's score from 5. These new (final) scores were summed and multiplied by 2.5 to obtain the overall SUS score out of 100. (Brooke, 1995).

Furthermore, this single usability score out of 100 should not be interpreted as a percentage value. There are various interpretations of the SUS score, but a large-scale study by Bangor et al. (2008) found that a score of 68 is average, a score above 68 is above average, a score above 73 and 85 are considered ‘good’ and ‘excellent’, respectively, and a score of 100 is ‘best imaginable’ (Bangor et al., 2008). This interpretation scale was used to evaluate the scores given by the participants.

The investigator's observations report was completed while the participants performed the tasks. The report documented the outcome of each task and any additional observations made. All these documents can be found in the Appendix L.

Ensuring Data Accuracy and Reliability

To ensure data integrity and accuracy, only experienced colposcopists were included in the study. Furthermore, the order in which participants used the two screening devices was randomised to minimise carry-over bias. And the order in which the interchangeable cervices were examined was also randomised and single-blinded to minimise pattern recognition between the two sets of cervices and reduce observer bias.

6.2 Results and Discussion

6.2.1 Colposcopy Screening Report

The five participants completed the screening procedure and aimed to make a realistic assessment/diagnosis of each cervix using the standardised screening report template for colposcopy examinations. The entire screening report filled out for each cervix can be seen in Figure 63 in Appendix L. The purpose of collecting this data was to evaluate how accurate the CerviScreen device was in making

the same diagnosis as the standard of care device, the colposcope. The answers used to evaluate if the correct diagnosis of the cervices was made were the 'Colposcopic Opinion' answers. Since each cervix was made to replicate a pathology that fits into one of these categories, it best represents each device's 'diagnostic accuracy'. Moreover, using the 'known' pathologies of the handmade cervices, the 'Colposcopic Opinion' results of the two devices could be compared to a known correct answer. The results are shown in Table 24 below, with a '1' indicating a 'correct' diagnosis and a '0' indicating an incorrect diagnosis. P1 to P5 refer to the five participants of the study, and the CerviScreen device and colposcope are indicated by A and B, respectively.

Table 24: Diagnosis results for the two devices (A = CerviScreen, B = Colposcope).

Services	Answer (0 = Incorrect, 1 = Correct)										A Total	B Total
	P1		P2		P3		P4		P5			
	A	B	A	B	A	B	A	B	A	B		
A	1	1	1	1	0	0	1	1	1	1	**4**	**4**
B	0	0	1	1	1	1	1	1	1	1	**4**	**4**
C	1	0	1	1	0	1	1	1	1	1	**4**	**4**
D	1	1	1	1	0	0	1	1	1	1	**4**	**4**
Totals	**3**	**2**	**4**	**4**	**1**	**2**	**4**	**4**	**4**	**4**		

These results show that both devices made an equal number of correct diagnoses, with the average diagnostic accuracy for each device being 80%. Of the five participants, three made all the correct diagnoses, and 2 made multiple incorrect diagnoses. Although this is not a fair assessment of the ability of the participants to make the correct diagnoses since the cervices used were artificially made, it does highlight the subjective nature of the visual screening methods used in cervical cancer screening.

Another analysis used all the data collected on the screening report to evaluate how well the answers between the two devices compared to each other rather than a known correct answer. This analysis was beneficial since it mitigated the problem created by the artificially made cervices to represent the different pathologies accurately. Thus, the results of the tests, shown in Table 25 below, did not compare the diagnosis of the two devices to a known 'correct' answer but instead assumed that the colposcope made the 'correct' diagnosis and compared the results of the CerviScreen device to those results. The results in the table show the accuracy with which the CerviScreen was used to make the same diagnosis as the colposcope for each question as a percentage.

Table 25: Colposcopy examination report results showing how the CerviScreen results compared with the colposcope results.

Question	Average diagnostic accuracy percentage				
	Cervix A	Cervix B	Cervix C	Cervix D	All Services
TZ Classification	100	80	40	100	80
TZ Type	80	100	80	80	85
Colposcopic Opinion	100	80	60	100	85
Proposed Management	100	80	60	100	85
Raw Swede Score	80	80	80	60	75
Converted Swede Score	100	80	80	80	85
Average Percentages	**93**	**83**	**67**	**87**	**82.5**

The diagnosis results show that, on average, across all the data collected, the CerviScreen made the same diagnosis or got the same result 82.5% of the time. Analysing the results more deeply, the 'Raw Swede Score' has the lowest accuracy with 75%. However, when converted to a category, which converts the raw score to a diagnosis, the accuracy is increased to 85%. The average accuracy for the four cervices was 82.5%, and the standard deviation of the accuracy between the questions was 3.82, and the standard deviation of the accuracy between the cervices was 9.63. This significant variation in the accuracy percentage spread indicates the limitations placed on the test using artificially made cervices that aimed to represent real pathologies and the subjectivity of visual screening methods. All five participants pointed out problems with the various cervices that caused them to doubt their observations and answers, which resulted in 14 questions not being answered due to a lack of certainty by the participants.

The cervix that had the biggest problem was cervix C, which represented invasive cancer, contributing to 7 of the unanswered questions. The unrealistic representation of invasive cancer by the cervix was the primary reason this cervix received an average accuracy score of 67%. The participants had the least confidence in observing the TZ zone, with the 'TZ Classification' and 'TZ Type' questions accounting for 3 and 9 unanswered questions, respectively. Furthermore, between the screening devices, 10 out of the 14 unanswered questions were from the CerviScreen, which indicates that the participants had more confidence in their observations when using the colposcope.

6.2.2 System Usability Assessment

Following the testing procedures, each participant completed a SUS to rate the usability of the CerviScreen device. The SUS questionnaire was only completed for the CerviScreen device and not for the colposcope. The reasoning behind this was that the participants were highly experienced users of the colposcope, with an average of 14 years of colposcopy experience between them, which made the comparison of usability between the two devices inaccurate. Figure 63 in Appendix L shows the SUS questionnaire completed by the participants for the CerviScreen, and the results of the usability assessment are shown in Table 26. The table shows the individual scores after they have been converted to a score out of four, with the totals multiplied by 2.5, as explained in section 6.1.6. As mentioned previously, one of the participants (marked with an asterisk *) had prior experience with the device, so the average SUS scores were calculated with and without their results.

Table 26: System usability scores for the CerviScreen device.

Question No.	**Participants**				
	1	**2**	**3**	**4**	**5***
1	3	3	2	4	3
2	3	4	4	3	4
3	3	4	3	3	4
4	4	4	3	4	4
5	3	4	2	4	4
6	4	4	3	4	4
7	3	4	3	4	3
8	2	3	3	3	4
9	3	4	2	4	4
10	3	3	4	4	4
System usability score	77.5	92.5	72.5	92.5	95
Average SUS without experienced participant	83.75 (Good)				

Average SUS with experienced participant	86 (Excellent)

**User with prior experience with the device.*

The average SUS without and with the experienced user are very similar, with average scores of 84 and 86, respectively. However, without the experienced user, the SUS was categorised as 'good', and with the experienced user, the SUS category increased to 'excellent' according to the rating system discussed in section 6.1.6. These SUS scores are visually represented in Figure 51 below to illustrate the range of acceptability scores (Smyk, 2020). These results demonstrate that the system had a high perceived ease of use and system satisfaction from the operator's perspective.

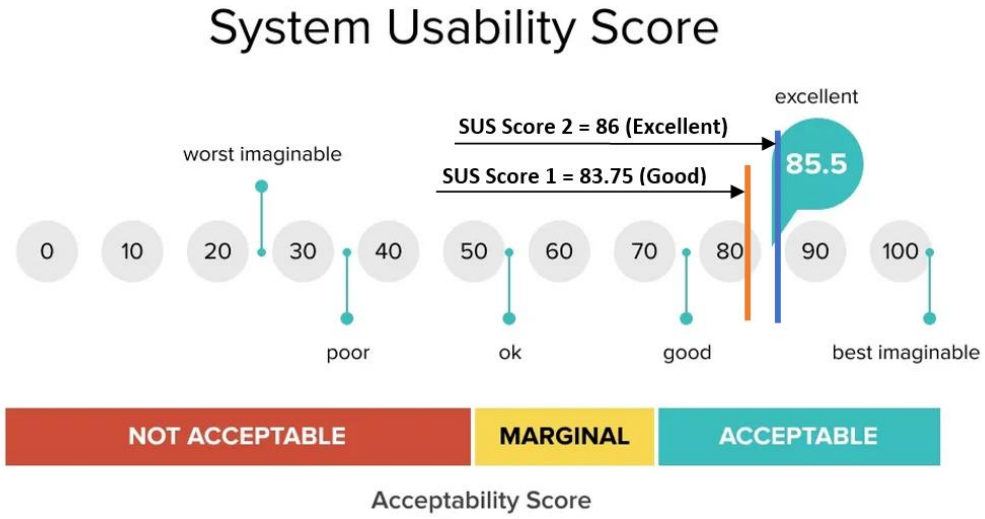

Figure 51: A visual representation of the CerviScreen's average SUS, annotated with the results achieved without (SUS Score 1) and with (SUS Score 2) experienced user (Smyk, 2020).

The lowest score given was 72.5, which is considered to be 'average' usability, while the highest score of 95 was given by the experienced user. The scores of two inexperienced participants were 92.5, which is close to the score the experienced participant gave and could indicate that the goal of making the device easy to learn and keeping the design and components simple was achieved. One of the strengths of this usability assessment that adds credibility to the results is that all participants were experienced colposcopists since they knew the standard of usability of the equipment typically used for a colposcopy. However, a larger sample size is needed for a more accurate representation of the system's usability.

6.2.3 Post-Test Feedback Questionnaire

The feedback questionnaire, shown in Table 35 in Appendix L, was completed by each participant after the SUS questionnaire. The questionnaire aimed to get feedback on various topics surrounding the CerviScreen regarding its usability, their experience interacting with the device and the different components, and how it compared to the colposcope. The results were grouped and averaged according to the question category, and the average results across the five participants were calculated with and without the experienced user's scores. The questions were either asked as positive or negative, indicated by the question number being either green or red in Table 27 below, according to which the participants had to say if they either agreed or disagreed with the question/statement. The scoring index is shown at the end of the table.

Table 27: Post-test feedback questionnaire results.

Category	Question	Participants					Average without experienced user	Average with experienced user
		1	2	3	4	5		
General Usability	1	4	5	3	5	5	4.25	4.4
	2	4	4	5	4	5	4.25	4.4
	3	4	4	5	5	5	4.5	4.6
	4	4	4	5	5	5	4.5	4.6
	5	4	5	5	5	5	4.75	4.8
							4.45	**4.56**
User Interface	6	3	5	4	4	5	4	4.2
	7	3	4	3	4	5	3.5	3.8
	8	4	5	2	5	5	4	4.2
	9	4	5	3	3	5	3.75	4
							3.81	**4.05**
Specific Features	10	3	3	2	1	5	2.25	2.8
	11	4	5	5	5	5	4.75	4.8
	12	4	4	4	5	5	4.25	4.4
	13	4	4	4	5	5	4.25	4.4
	14	5	4	5	5	5	4.75	4.8
	15	4	4	5	5	5	4.5	4.6
	16	4	4	3	5	5	4	4.2
	17	3	3	1	5	5	3	3.4
	18	1	3	3	5	4	3	3.2
	19	4	5	3	5	5	4.25	4.4
							3.9	**4.1**
Screening Process	20	4	4	3	5	5	4	4.2
	21	4	4	2	5	5	3.75	4
							3.875	**4.1**
Compared to the Standard of Care Device	22	3	4	2	3	4	3	3.2
	23	4	4	3	4	4	3.75	3.8
	25	4	4	5	5	5	4.5	4.6
							3.75	**3.87**
Problems with the CerviScreen	26	3	3	3	1	1	2.5	2.2
	28	2	1	2	3	1	2	1.8
	29	3	1	3	2	1	2.25	2
	30	1	2	4	1	1	2	1.8
							2.19 (3.81*)	**1.95 (4.05*)**
Overall average score*							**3.95**	**4.14**

**The overall average score was calculated with the 'Problem with the CerviScreen' categories scores inversed such that 5 is the highest score and 1 the lowest, similar to the rest of the categories.*

***Scoring index: 1 –Strongly Disagree, 2 – Disagree, 3 – Neutral, 4 – Agree, 5 – Strongly Agree.*

The results of the questionnaire are that the overall average score across all six categories with and without the experienced user was 3.95 and 4.14 out of a possible 5, respectively. The variation in average scores per category was reasonably similar, with the standard deviation being 0.24 and 0.21 for the two groups of participants.

The category that performed the best was 'General Usability', which asked about the participant's comfort and confidence when using the device, how easy it was to learn to use, and how intuitive the design and functionality were. Except for participant 3, who scored the level of comfort and confidence at a 3, all the other scores were 4 or 5. The question that marginally got the best score was number 5, which asked how adequately trained and confident the participants felt after the short introduction and training session they received before the procedure started. This result supports the design's success in making the device simple and effective to facilitate ease of use, which was one of the design requirements identified in Table 2 at the start of the project. The ease of usability and ease of learning to use the device is reinforced by the minor differences in scores between the four inexperienced and experienced participants, with an overall difference in the average scores of just 0.19.

The worst-performing category was comparing the CerviScreen directly to the colposcope, receiving an average score of 3.87 for all five participants. The lowest scoring question was number 22, which asked how the usability of the two devices compared. The average score was neutral, but Participant 3 said that the usability of the CerviScreen was worse than that of the colposcopes. Despite this, question 25 scored very well, with an average score of 4.6, which asked if they would consider using the CerviScreen in regular screening practice as a triage device if it was developed further into a commercial product.

The lowest-scored question overall was number 10, which asked if the probe cover was easy to attach. This question also has the most significant difference in average scores between the inexperienced and experienced users, with none of the inexperienced users giving a score higher than 3 and the experienced users' score being 5. Although attempts were made to improve the ease of attachment of the probe cover by adding visual cues indicating the correct orientation of the faceplate (refer to risk C.5 in Appendix G), the inexperienced participants still took three attempts on average to attach the faceplate to the probe tip successfully. In contrast, the experienced participant who had had the opportunity to attach a probe cover before succeeded on their first attempt. This result highlights the need to improve the ease of attaching the probe cover to the probe tip or to provide more training before use. Another observed factor that made it more complicated to attach the probe cover was the presence of the dilation cup, which limited the space for the user's fingers and the visibility of the connection point between the faceplate and the probe tip. However, the result of the experienced participant shows that although it is not easy at first, the usability improves after a few successful attempts.

Two other questions in the same category also had low scores, namely numbers 17 and 18. These questions focussed on the efficacy of the green filter and the acetic acid application. The problem highlighted by the participants that gave the green filter a low score was that the filtered green light was not sufficiently filtered and that the light needed to be brighter. The comments on the lack of intensity of the illumination system were expected based on the results of the verification testing done in section 5.4.6 showed that the green filter significantly reduces the intensity of the light. The low scores given to the

acetic acid applicator were due to the participants' need for more confidence that the spray would be strong enough to remove mucus effectively on an actual patient. Thus, this needs to be tested further with a better simulation of naturally occurring mucus that is harder to remove or be optimised later when the device is ready to undergo small-scale trials on actual patients.

Focussing on the scores of the individual participants, it is clear that participant 3 had lower scores than the rest of the participants, with only two other participants giving a single negative score each. While using the CerviScreen device, Participant 3 had trouble with the image quality and could not accurately visualise the cervices. The probe cover was replaced with a different one to fix the image quality, suspecting that the lens was dirty from having been used multiple times, but this did not have the desired outcome. A post-inspection of the device found that the camera lens was dirty and slightly fogged. Cleaning the lens restored the image quality and provided insight into why the participant had the lowest diagnostic accuracy scores, the most unanswered diagnosis questions, and the lowest usability scores.

The other feature of the CerviScreen device that received ‘high’ scores was the dilation cup, with participants finding it easy to collapse and making the probe's insertion and removal easy. Relating to this, participants also agreed that the device's speculum-free design would simplify the screening process. However, there was some uncertainty about whether the dilation system would be as effective when used on an actual patient, which needs to be investigated in future projects.

6.2.4 General Discussion

This general discussion section focused on reviewing the results of the entire validation testing and looked for commonalities and trends between the results. One of the main objectives of the project was to develop a device that a user can quickly learn to use and is easy to use during the screening procedure. This point was raised in the in-depth discussions of the SUS and feedback questionnaire results, which showed that the difference between the results of the inexperienced and experienced participants was minor. The experienced participants' usability scores and general feedback scores were the highest. However, the fact that it was not significantly higher than the rest of the participant's scores supports the success of the design being easy to learn and use. Although the colposcopy examination report did not explicitly test for this, the minor differences in the screening results between the participants implicitly further supported this point that the device was easy to use.

The study's primary limitation was the use of the anatomically accurate training ZOE model. Even though attempts were made to make the training model represent the actual anatomy encountered during a cervical cancer screening more realistically, and the interchangeable cervices were made to mimic typical pathologies as closely as possible, these did not perfectly represent human anatomy. Moreover, the simplified anatomy and pathologies may have resulted in better test results than if a human patient had been screened. Thus, although the results of the test and the feedback from the participants were positive in general, it should be noted that further testing on human patients should be done before the CerviScreen can be said to be an effective cervical cancer screening device.

7 Conclusion

The research aimed to develop, verify, and validate a speculum-free cervical cancer screening device with diagnostic accuracy equal to the standard-of-care screening device, with a high usability rating in a clinical setting. Several primary objectives were set at the start of the project to achieve this aim, which included:

1. Develop a device to perform a speculum-free cervical cancer screening procedure.
2. Conduct engineering tests on the developed device, guided by ISO 8600 standards for medical endoscopes and endotherapy devices and identify and mitigate risks relating to usability and device functionality.
3. Validate that the proposed device has diagnostic performance equivalent to the standard care screening tool and high usability ratings in a clinical setting through comparative testing.

The project concluded that all of these objectives were met, thus achieving the research aim. This chapter summarises the outcomes of each objective and how they were achieved.

7.1 Design and Development

The literature review identified the need for a resilient cervical cancer screening device in low-resource settings that could be used as a primary or secondary/triage screening solution. The research identified several design requirements that such a device needed to meet, of which the most noteworthy requirements were to be independent of a speculum, the device being digitally enabled, compactness and portability, and reducing the number of individual components required to perform a screening procedure.

Through a concept generation and selection process, the concept selected to meet these requirements was a speculum-free handheld point-of-care device that makes a diagnosis using the VIA screening method. The device uses digital technology to enhance the efficacy and accuracy of the traditional VIA diagnosis, which is known to have highly variable results due to its subjective nature. This concept was broken down into five independently designed and developed subsystems, then integrated into a final device that could perform a full VIA screening procedure. This final device, the CerviScreen, was theoretically able to perform an entire screening procedure but needed verification through testing and risk assessment.

7.2 Design Verification

The verification methodology evaluated the CerviScreen and its constituent subsystems and components to verify that they met the engineering specifications they were designed for and had a low enough risk level to be safely used in the validation study. These engineering specifications were set at the conceptual design phase for each subsystem, which would ensure that the device ultimately met the design requirements and the project's aim. Thus, verification testing was performed using a combination of ISO 8600 standard testing and auxiliary engineering tests on various components and subsystems to verify that they met the critical engineering specifications for the device to perform as intended.

The first phase of verification testing focused on the dilation system. The objectives were to verify the outcomes of the extensive design optimisation done on the system and to select the best-performing dilation cup for use in the complete device. Two tests were performed, a tensile test and a compression

test, which measured four key performance metrics of the cup: the actuation force required to collapse the cup, the maximum size in the collapsed state, the amount of size reduction from the dilated to the collapsed state, and its radial strength. The tests concluded that the best-performing cup was selected (design 8), which had the following critical performance metrics: actuation force of 4.95N, maximum collapsed size of 30.43mm, maximum reduction in the size of 83.98% at the cup tip and it could resist 0.6 bar of external pressure and only compress by 6.49%. Based on these results, the dilation cup met all the engineering specifications required

The second verification testing phase was performed on the complete device to test the critical performance requirements of the system as a fully integrated device. A series of eight tests were performed, consisting of a combination of ISO 8600 standard tests for medical endoscopes and auxiliary tests that tested features unique to the device and not included in the ISO standards. The device passed six of the eight tests, meeting the engineering specifications for the field of view, maximum insertion width, limiting resolution, acetic acid application efficacy, dilation system actuation force, and probe cover integrity. The tests that the device failed were the illumination intensity test, where the device failed to meet the required intensity threshold at all of the working distances it was designed for, and the power consumption and heat test, where the device got too hot. However, despite the failed tests, the device's performance was verified to a standard that allowed validation testing to commence. Suggestions to solve these problems that resulted in the failed tests are provided in section 7.5 on page 85 below.

The second verification aspect also included the risk assessment of the complete device, which aimed to ensure that the CerviScreen device was safe to use in the validation study and performed as intended. The risk assessment formed part of the iterative design methodology. It successfully mitigated the overall device risk to a satisfactory level for the device to be used in the validation study.

7.3 Design Validation

The validation study evaluated the CerviScreen device's ability to perform a cervical cancer screening procedure in a clinical environment. The study simulated an entire screening procedure using a female pelvic training model with a variety of custom-made cervices with different pathologies and recruited experienced colposcopists to be the participants in the study. The comparative study used the CerviScreen device and a traditional optical colposcope (the Leisegang 1D LED optical colposcope) to perform the same screening procedures to achieve the study's primary objective: to evaluate if the CerviScreen had equivalent diagnostic accuracy to the standard of care screening tool. The study's secondary objective was to evaluate the usability of the CerviScreen device using a system usability score (SUS) questionnaire.

To evaluate the CerviScreen's diagnostic accuracy in comparison to that of the colposcope each device was used to diagnose a set of four distinct cervices using a standard colposcopy screening report, and the results of these diagnoses were compared. The first data analysis method calculated the diagnostic accuracy of both devices based on the premise that the custom-made cervices were made to replicate specific cervical pathologies typically encountered during cervical screenings. This meant that the 'correct' diagnosis was known for each cervix. The data was also analysed to compare the diagnostic results of the CerviScreen to those of the colposcope by assuming that the colposcope made the 'correct' diagnosis and disregarding the pathology the cervices intended to replicate. The reasoning for the second analysis was that the custom-made cervices did not represent the intended cervical pathologies with a high degree of

accuracy, so the analysis assumed that the diagnosis made by the colposcope was correct since it was hypothetically the superior device. Thus, the CerviScreen's diagnoses were compared to these diagnoses to evaluate how accurately it could make the same diagnosis to the standard of care device.

The results using the first method of analysis was that both the CerviScreen and the colposcope had 80% diagnostic accuracy. Thus, the objective that the developed device needed to have equivalent diagnostic accuracy to the standard of care device was met. Based on the second analysis method, the correlation between the answers across all the questions on the screening report was 82.5%. Although this result showed unequal diagnostic results between the two devices, it must be noted that the study was not designed to take all of the questions on the screening report into account and average the results to calculate the diagnostic accuracy. However, these results provided some insight into the participants' confidence when using the two devices, with 10 of the 14 unanswered questions happening when using the CerviScreen device. This data point indicated that participants had more confidence in visualising the cervix when using the colposcope. However, this could be because of a lack of experience with the CerviScreen.

To evaluate the study's second objective, the usability of the CerviScreen device, two questionnaires were completed by each participant after the screening procedures. The first questionnaire was a System Usability Scale (SUS), which is a standardised questionnaire that subjectively scores the usability of a system. The average usability scores for inexperienced and experienced participants of the CerviScreen device were calculated to be 83.75 and 86, respectively. The two SUS are the consequence of one of the five participants having prior experience with the CerviScreen device, which made them an 'experienced' user and required differentiating the usability results gathered from this participant from those with no prior experience with the device. Nonetheless, the SUS without the experienced participant of 83.75 translates to a ‘good’ usability rating, and the SUS with the experienced participant of 86 translates to an 'excellent’ usability rating. Thus, with and without including the experienced users' scores, the CerviScreen device met the objective of achieving a high usability score. The second questionnaire was a more general feedback questionnaire that asked the participants to score the CerviScreen based on different questions regarding various aspects of the device. The questionnaire used a 1-5 scoring system, with 5 being the highest and 1 being the lowest score. Once again, the average scores were calculated without and with the experienced user's scores. The result was that the average scores for all the questions were 3.95 and 4.14 out of 5, respectively. Although the sample size for the study was small and the screening procedure was not completely accurate, the results of the questionnaires indicate that the CerviScreen device has good usability and even improved usability to the colposcope.

7.4 Overall Outcome

The design requirements identified in Chapter 2.5 guided the design and development of the device, which aimed to meet each of these requirements. Table 28 below shows how the CerviScreen device met each of these requirements, which led to the aim of the research successfully being achieved: to develop and experimentally validate a speculum-free cervical cancer screening device that has equal diagnostic accuracy to the standard of care screening device and has a high usability rating.

Table 28: How the design requirements were met.

Requirement	How It Was Met	Value Added
Portable, compact, and robust	Handheld and battery-powered	Increase ease of use in mobile screening settings and clinics that have severe space limitations.
Digital	Smart device-based design for power supply, processing, and image display	Enables the device to capitalise on the benefits of being digitally enables, such as using Telemedicine application and incorporating assistive diagnosis in the future.
Speculum-free	Insertion probe is inserted into the vaginal canal and positioned close to the cervix.	Reduces the need for a speculum and improves patient comfort
Reduced number of components	All of the required components for a full screening are built into a single device.	All the components required for a screening are always together and in a compact form factor.
Easy to use and to learn to use	Good usability scores and correlation between experienced and inexperienced users	Allows inexperienced colposcopists to quickly learn how to use the device and screen patients
Point-of-care/Triage Test	Uses the VIA diagnostic method	Provides immediate screening results and is low-cost
Scalable – can screen many patients in a short amount of time	The decontamination process is simplified and easier	Removes the time loss caused by the extensive decontamination processes required for current equipment
Reduced cost – not only capital cost but also maintenance and running cost	The device uses a small amount of components that are not high cost, and reduced decontamination costs.	Running costs are reduced, and the simple, low-cost components also reduce the maintenance cost
Simplified decontamination procedures	Single-use probe cover instead of speculum and forceps that need to be decontaminated after each patient	Reduces decontamination costs and the infrastructure required around the screening device to perform the decontamination procedures
Low-to-no reliance on grid power	Battery powered	Can be used in mobile clinics and during power outages
Minimal need for consumables	Simplified decontamination process	Reduced running cost and chances of a consumable not being available to perform a screening procedure

The same evaluation used in Chapter 2.4 on the existing cervical cancer screening solutions using the framework proposed by Piaggio et al. was also performed for the CerviScreen device. The results can be seen in Appendix A, with the CerviScreen device being included in the last row of Figure 52. The CerviScreen's results were equivalent to those of the POCKET colposcope, only performing better regarding limiting the number of components. These improvements are mainly attributed to the different decontamination methods that the two solutions use, with the POCKET colposcope using the traditional speculum and forceps for dilation and acetic acid application.

This dissertation demonstrated that the CerviScreen device can perform the functionalities required of a cervical cancer screening device in a simulated screening procedure and has 'good' usability. Thus, based on the verification and validation results and the objectives met, the device and the project

were successful. However, significant improvements can be made in future work on the project to validate the device's success further before it can be used in cervical cancer screening procedures on patients.

7.5 Future Recommendations

The recommendations for future work and development that need to be done on the project for the CerviScreen to be a successful medical device that can perform successful cervical cancer screening procedures are discussed in this section. In order of importance, the required design improvements needed to improve the diagnostic performance and usability of the CerviScreen are:

- **Illumination system:** Replace the current system with small LEDs mounted directly at the probe's tip or around the camera. The current configuration that uses the light pipes to transport the light from the LED in the handle to the target area results in a significant loss in light intensity.
- **Acetic acid application system:** Testing needs to be done with a more realistic representation of naturally occurring mucus, after which the strength of the spray would likely need to be increased. Alternatively, a mechanism could be made that adjusts the strength of the spray according to what is required by the operator at the time.
- **Probe cover attachment method:** Improve and test the visual cues that guide the operator to locate the faceplate in the correct position and give better tactile feedback to the operator in the correct position and when the faceplate has been successfully attached.
- **Handle shape and position:** When the participants were seated, the straight handle's height was uncomfortable for use. Consider adding a larger curve or angle to the handle to improve the holding position.
- **Accompanying software application:** With the recommended changes that will need to be made to the illumination system, an imaging software application that can digitally filter the image to apply the green filter can be included.

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Appendices

A Cervical Cancer Screening Solution Evaluation Matrix

		User Type		
	Medical device	End users' background	Training needs	User's understanding of the technical and clinical impact
Existing solutions	Pap Smear	Any health care professional	High	Medium
	VIA/VILI	Medical doctors only	High	Medium
	HPV-DNA Test (PCR)	Any health care professional	Medium	Medium
	Colposcopy	Medical doctors only	High	Medium
New solutions	Gynocular	Medical doctors only	High	Medium
	MobileODT EVA	Medical doctors only	High	Medium
	Callascope	Medical doctors only	High	Medium
	POCKET Colposcope	Medical doctors only	High	Medium
Developed Solution	Cerviscreen	Medical doctors only	High	Medium

		Design		
	Medical device	Portability, compactness, robustness	Limiting the number of components/spare parts	Reusability
Existing solutions	Pap Smear	Low	High	Yes
	VIA/VILI	High	Low	Yes
	HPV-DNA Test (PCR)	Low	Medium	Yes
	Colposcopy	Medium	Medium	Yes
New solutions	Gynocular	High	Medium	Yes
	MobileODT EVA	High	Medium	Yes
	Callascope	High	Medium	No
	POCKET Colposcope	High	Medium	Yes
Developed Solution	Cerviscreen	High	Low	Yes

		HTM					
	Medical device	Installation requirements	Maintenance frequency	Maintenance complexity	Need for consumables	Need for spare parts	Compatible consumables/spare parts
Existing solutions	Pap Smear	High	Seldom	Requires a trained local person	Frequent	Required specialised	No
	VIA/VILI	Low	No	No	Seldom	None	Yes
	HPV-DNA Test (PCR)	Medium	Seldom	Requires specialised personnel	Frequent	Required specialised	No
	Colposcopy	Low	Seldom	Requires a trained local person	Frequent	Required specialised	No
New solutions	Gynocular	Low	Seldom	Requires specialised personnel	Frequent	Required specialised	No
	MobileODT EVA	Low	Seldom	Requires specialised personnel	Frequent	Required specialised	No
	Callascope	Low	Seldom	Requires specialised personnel	Frequent	Required specialised	No
	POCKET Colposcope	Low	Seldom	Requires specialised personnel	Frequent	Required specialised	No
Developed Solution	Cerviscreen	Low	Seldom	Requires specialised personnel	Frequent	Required specialised	Yes

		Reliance on external factors						
	Medical device	Reliance on power sources	Reliance on water distribution	Reliance on medical location air	Need for sample preparation	Resilience to dusty environments	Resilience to high-temperature environments	Resilience to high-humidity environments
Existing solutions	Pap Smear	High	Low/None	Low/None	Medium	Low	High	High
	VIA/VILI	Low/None	Low/None	Low/None	Minimal	High	High	High
	HPV-DNA Test (PCR)	High	Low/None	Low/None	Medium	Low	High	High
	Colposcopy	High	Low/None	Low/None	Minimal	High	High	High
New solutions	Gynocular	Low/None	Low/None	Low/None	Minimal	High	High	High
	MobileODT EVA	Low/None	Low/None	Low/None	Minimal	High	High	High
	Callascope	Low/None	Low/None	Low/None	Minimal	High	High	High
	POCKET Colposcope	Low/None	Low/None	Low/None	Minimal	High	High	High
Developed Solution	Cerviscreen	Low/None	Low/None	Low/None	Minimal	High	High	High

		Materials		Cost		
	Medical device	Robustness of the material	Durability of the material	Initial cost	Maintenance costs	Running costs
Existing solutions	Pap Smear	High	High	High	High	Medium
	VIA/VILI	High	High	Low	Low	Low
	HPV-DNA Test (PCR)	High	High	High	High	High
	Colposcopy	High	High	High	High	Low
New solutions	Gynocular	High	High	High	High	Low
	MobileODT EVA	High	High	Medium	Medium	Low
	Callascope	High	High	Low	Medium	Medium
	POCKET Colposcope	High	High	Low	Medium	Low
Developed Solution	Cerviscreen	High	High	Low	Medium	Low

Figure 52: Evaluation matrix developed by Piaggio et al. to evaluate the different solutions.

	Criteria	Measurement scale		
User Type	End users' background	Medical doctors only	Any health care professional	Lay user
	Training needs	Low	Medium	High
HTM	Installation requirements	High	Medium	Low
	Maintenance frequency	Periodic	Seldom	No
	Maintenance complexity	Requires specialised personnel	Requires a trained local person	No
	Need for consumables	Frequent	Seldom	None
	Need for spare parts	Required specialised	Required easely avaliable	None
	Compatible consumables/spare parts	No		Yes
Design	Portability, compactness, robustness	Low	Medium	High
	Limiting the number of components/spare parts	High	Medium	Low
	Reusability	No		Yes
Reliance on external factors	Reliance on power sources	High	Medium	Low/None
	Reliance on water distribution	High	Medium	Low/None
	Reliance on medical location air	High	Medium	Low/None
	Need for sample preparation	Intensive	Medium	Minimal
	Resilience to dusty environments	Low	Medium	High
	Resilience to high-temperature environments	Low	Medium	High
	Resilience to high-humidity environments	Low	Medium	High
Materials	Robustness of the material	Low	Medium	High
	Durability of the material	Low	Medium	High

Figure 53: Evaluation matrix scoring legend.

		User Type		
	Medical Device	End users' background	Training needs	User's understanding of the technical and clinical impact
Existing solutions	Pap Smear	2	1	2
	VIA/VILI	1	1	2
	HPV-DNA Test (PCR)	2	2	2
	Colposcopy	1	1	2
New solutions	Gynocular	1	1	2
	MobileODT EVA	1	1	2
	Callascope	1	1	2
	POCKET Colposcope	1	1	2
Developed Solution	Cerviscreem	1	1	2

		Design		
	Medical Device	Portability, compactness, robustness	Limiting the number of components/spare parts	Reusability
Existing solutions	Pap Smear	1	1	3
	VIA/VILI	3	3	3
	HPV-DNA Test (PCR)	1	2	3
	Colposcopy	2	2	3
New solutions	Gynocular	3	2	3
	MobileODT EVA	3	2	3
	Callascope	3	2	1
	POCKET Colposcope	3	2	3
Developed Solution	Cerviscreem	3	3	3

		HTM					
	Medical Device	Installation requirements	Maintenance frequency	Maintenance complexity	Need for consumables	Need for spare parts	Compatible consumables/spare parts
Existing solutions	Pap Smear	1	2	2	1	1	1
	VIA/VILI	3	3	3	2	3	3
	HPV-DNA Test (PCR)	2	2	1	1	1	1
	Colposcopy	3	2	2	1	1	1
New solutions	Gynocular	3	2	1	1	1	1
	MobileODT EVA	3	2	1	1	1	1
	Callascope	3	2	1	1	1	1
	POCKET Colposcope	3	2	1	1	1	1
Developed Solution	Cerviscreem	3	2	1	1	1	3

		Reliance on external factors						
	Medical Device	Reliance on power sources	Reliance on water distribution	Reliance on medical location air	Need for sample preparation	Resilience to dusty environments	Resilience to high-temperature environments	Resilience to high-humidity environments
Existing solutions	Pap Smear	1	3	3	2	1	3	3
	VIA/VILI	3	3	3	3	3	3	3
	HPV-DNA Test (PCR)	1	3	3	2	1	3	3
	Colposcopy	1	3	3	3	3	3	3
New solutions	Gynocular	3	3	3	3	3	3	3
	MobileODT EVA	3	3	3	3	3	3	3
	Callascope	3	3	3	3	3	3	3
	POCKET Colposcope	3	3	3	3	3	3	3
Developed Solution	Cerviscreem	3	3	3	3	3	3	3

		Materials		Cost		
	Medical Device	Robustness of the material	Durability of the material	Initial cost	Maintenance costs	Running costs
Existing solutions	Pap Smear	3	3	1	1	2
	VIA/VILI	3	3	3	3	3
	HPV-DNA Test (PCR)	3	3	1	1	1
	Colposcopy	3	3	1	1	3
New solutions	Gynocular	3	3	1	1	3
	MobileODT EVA	3	3	2	2	3
	Callascope	3	3	3	2	2
	POCKET Colposcope	3	3	3	2	3
Developed Solution	Cerviscreem	3	3	3	2	3

Figure 54: Calculation of the total scores by conversion of the scores given in Figure 52 to numerical values using the legend in Figure 53.

List of components/products included as part of each solution:

Solution	List of Components/Products
Pap Smear	1. Speculum 2. Light source 3. Small brush/spatula/swab 4. Glass slides 5. Laboratory with microscope 6. Cytopathologist to make the diagnosis
VIA/VILI	1. Speculum 2. Light source 3. Acetic acid/Lugol's iodine 4. Cotton swab (Acetic Acid Applicator)
HPV-DNA Test (PCR)	1. Laboratory with PCR machine 2. PCR test kit: a. Swab b. Reagents c. Collection chamber (bakkie)
Colposcopy	1. Speculum 2. Colposcope 3. Light source 4. Acetic acid/Lugol's iodine 5. Cotton swab (Acetic Acid Applicator)
Gynocular	1. Speculum 2. Gynocular device 3. Acetic acid/Lugol's iodine 4. Cotton swab (Acetic Acid Applicator)
MobileODT EVA	1. Speculum 2. MobileODT EVA device 3. Acetic acid/Lugol's iodine 4. Cotton swab (Acetic Acid Applicator)
Callascope	1. Callascope device 2. Acetic acid/Lugol's iodine 3. Mobile Phone
Pocket Colposcope	1. Speculum 2. Pocket Colposcope device 3. Acetic acid/Lugol's iodine 4. Cotton swab (Acetic Acid Applicator)

B Evolution of Prototypes

Prototype 1:

Figure 55: Prototype 1 photos.

Prototype 2:

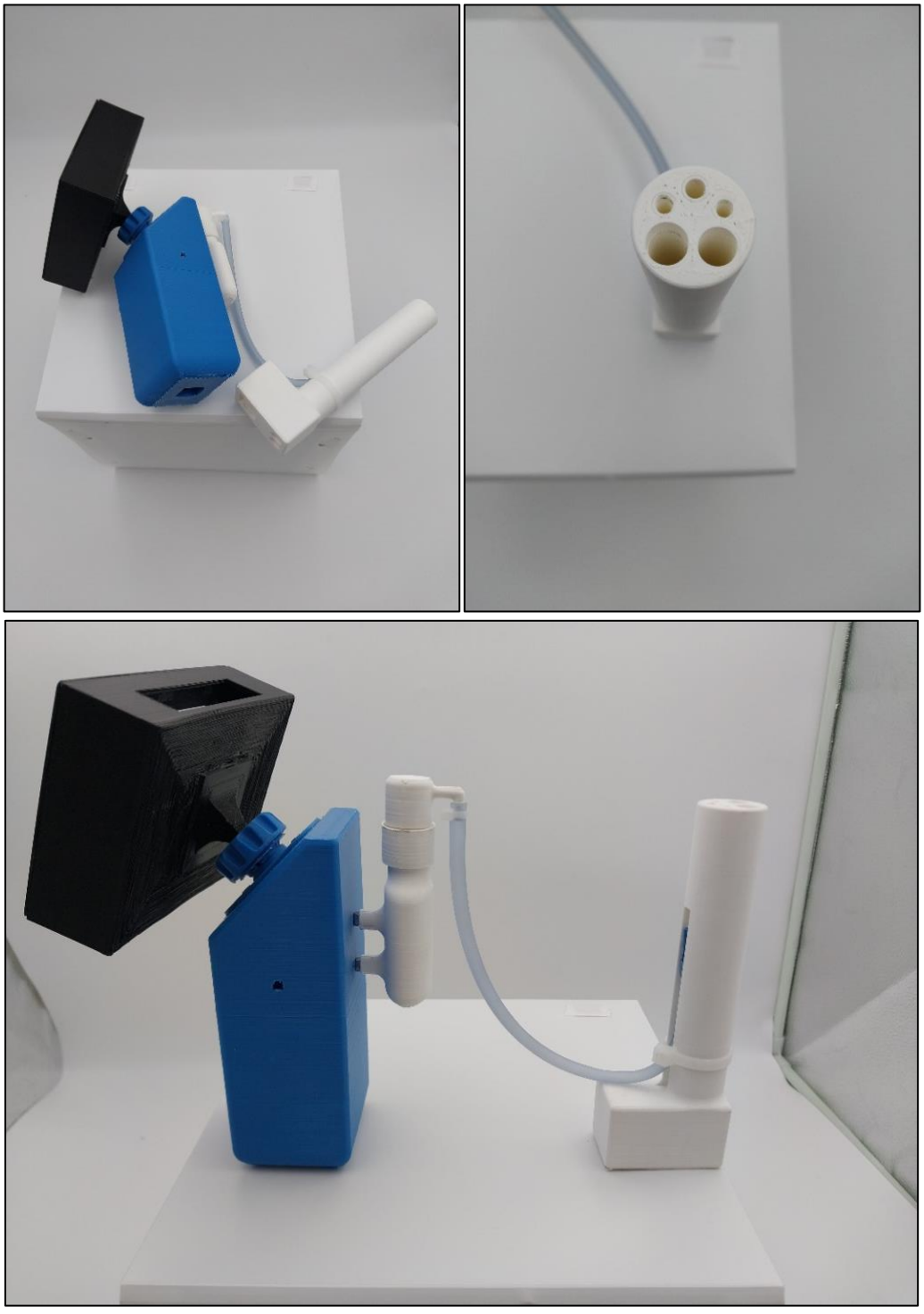


Figure 56: Prototype 2 photos.

Prototype 3:

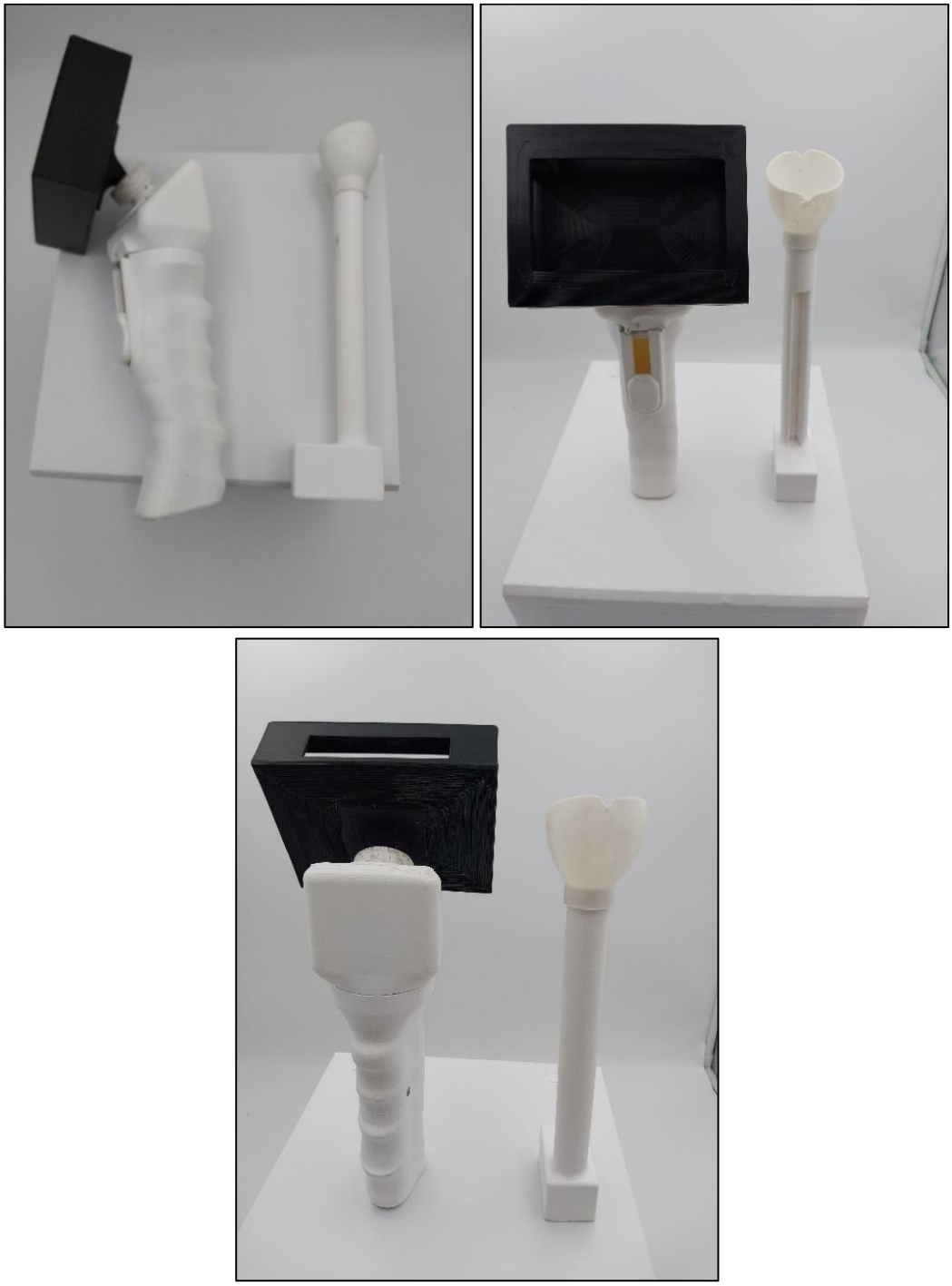


Figure 57: Prototype 3 photos.

Prototype 4:

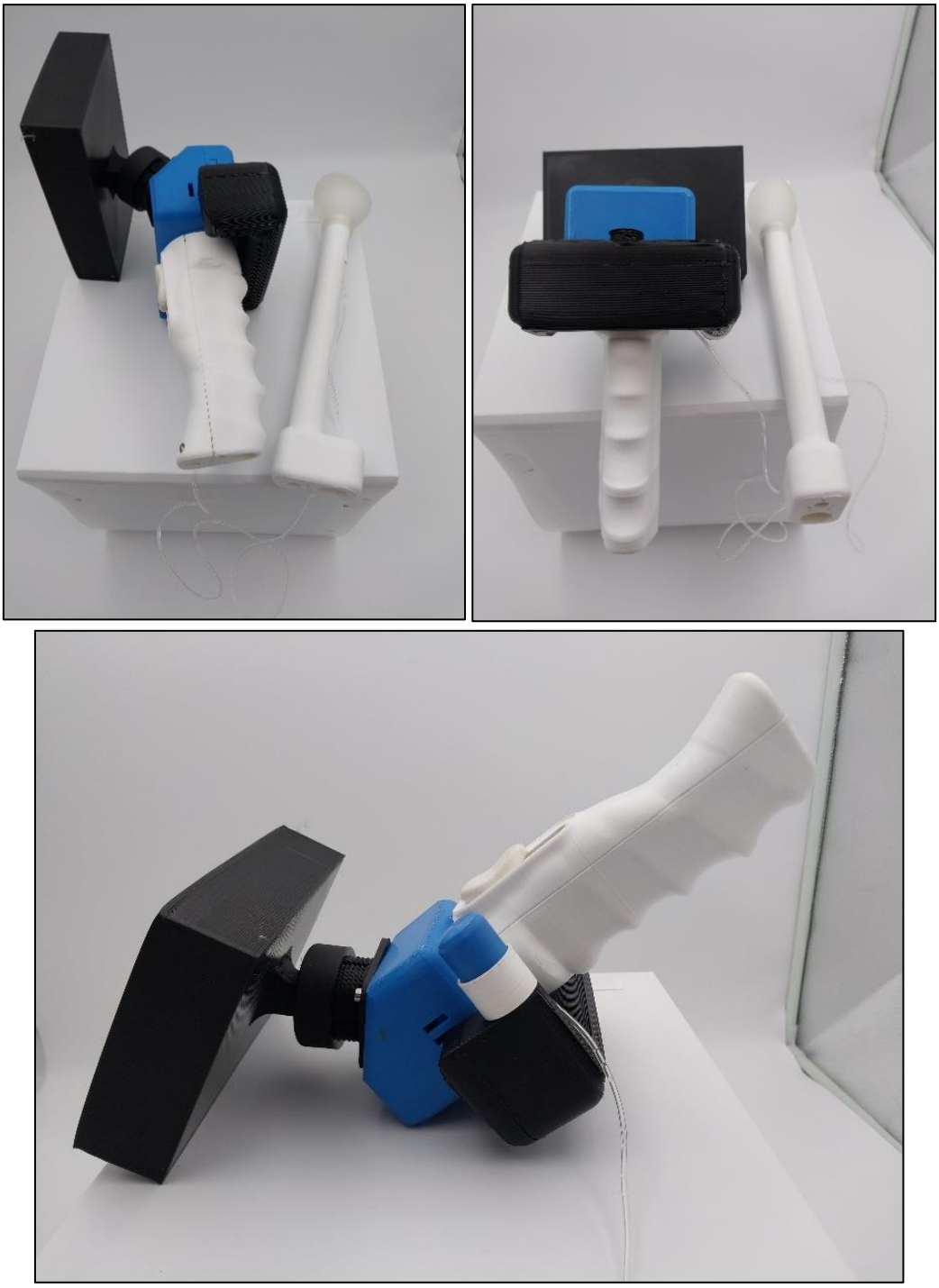


Figure 58: Prototype 4 photos.

Prototype 5:

Figure 59: Prototype 5 (Proof-of-concept) photos.

Figure 60: Final Prototype (CerviScreen Device).

C Proof-of-Concept Preliminary Test Results

Halfway through the project timeline, after 12 months, the proof-of-concept prototype was put through formal testing. The testing aimed to evaluate the performance of some of the key subsystems of the device, and see if the design concepts chosen could work together to perform a full cervical cancer screening procedure. The outcome of the testing was used to highlight the strengths and weaknesses of the device and guide the next phase of development to ensure that the project's objectives are achieved.

The first test focused on performing benchtop tests on various components to evaluate the technical performance of key components to each subsystem and test if they met the engineering specifications. Not all the engineering specifications were tested for since these were preliminary tests aimed at guiding future development and measuring progress thus far in the project. A short summary of the tests done, and the results are shown in Table 29.

Table 29: Proof-of-concept benchtop testing results.

Subsystem	Engineering Specification	Test Procedure Summary	Result
Visualisation	FOV @ working distance = 30mm	Place a circle that is 30mm in diameter in the cup and verify that the entire circle is visible on the display.	**Pass**
	Limiting resolution @ WD = >11lp/mm	Place 1951 USAF resolution target in the cup, which is the working distance of the device, and determine the limiting resolution.	**Fail** Resolution was 1.59lp/mm, which converts to a minimum pixel size of 355µm. Desired pixel size is 100µm.
	Illumination beam diameter @ minimum working distance > 30mm	Place a 30mm diameter target in the cup and place the device in a light-tight container. Verify that the entire target is evenly illuminated.	**Pass**
	Battery life > 2hours	Turned camera, display, and lights on and timed how long the battery lasted.	**Fail**. 800mAh battery lasted 30 minutes
Housing	Probe maximum diameter = 20mm	Measure with vernier	**Pass**
	Weight < 1kg	Weigh on scale	**Pass – 640g**
	Minimum probe length = 200mm	Measure with vernier	**Pass**
	Adjustable display position	Yes/No	**Pass**
Liquid Application	Cover all four quadrants of the cervix with multiple sprays	Place a target of 35mm diameter at the tip of the cup and spray it with liquid dye.	**Pass**

	Can spray 10 patients without refilling container	Calculate liquid container capacity and assume 10ml of liquid is used per patient.	**Pass**
Dilation	Minimum diameter when dilated = 30mm	Measure with vernier	**Pass**
	Maximum size for insertion = 25mm	Measure with vernier	**Fail**
Decontamination	Keeps probe completely dry	Fill probe cover with water and check for leaks	**Fail** Cover plate not sealed.

The initial results revealed that certain key components did not meet the necessary specifications for the device to function at the required standard. Nevertheless, the second testing phase proceeded to assess the overall performance of the device in the context of a cervical cancer screening procedure. This phase aimed to evaluate the integration of various subsystems and their collective functionality and usability during different tasks. This basic usability feedback was instrumental in assessing non-measurable but critical design elements, such as probe insertion and probe cover attachment.

For this evaluation, the final proof-of-concept device, equipped with all integrated subsystems, conducted a simulated colposcopy screening using an anatomically accurate pelvic model (the ZOE from Gaumard Scientific). Specific performance metrics were assessed using a rating scale where higher scores indicate superior performance, ranging from 0 (non-functional) to 5 (excellent). These performance metrics and their respective ratings are provided in Table 8 below.

Table 30: Proof-of-concept simulated colposcopy examination test results.

Performance metric tested	Rating scale	Rating
Ease of probe cover application	0-5	2
Does the cup collapse when the button is moved	Yes/No	Yes
Force required to move the button that collapses the cup	0-5	2
Dilation cup size when collapsed to insert into vaginal opening	0-5	3
Force required to insert the probe into the vaginal canal	0-5	3
Does the cup open once inside the vaginal canal	Yes/No	Yes
Ease with which the cervix was found	0-5	4
Effectiveness of the cup to clear the skin fold around the cervix from the field of view of the camera	0-5	4
Adjustability of the light intensity (brightness) to an optimal level top clearly visualize the cervix	0-5	5
Image quality and how clearly the entire cervix can be seen on the display	0-5	4
Ease with which liquid dispenser button is reached and actuated	0-5	4
Coverage of the cervix with the liquid sprayed out of the nozzle	0-5	2
Can the cup the collapsed to remove the probe from the vaginal canal	Yes/No	Yes
Ease of removal of the probe from the vaginal canal	0-5	4
Ease of removal of the probe cover	0-5	1

The proof-of-concept device demonstrated proficiency in several aspects of colposcopy examination, excelling in visualisation and housing subsystems. The dilation cup effectively cleared skin folds in the vaginal canal, enhancing cervix visibility, aided by a dimmable LED ensuring optimal brightness. However, challenges arose with the probe cover and liquid dispensing system. Attaching and removing the sheath was cumbersome, compromising sterility. Additionally, the sheath's design led to liquid pooling,

hindering camera and light functionality. The liquid dispensing system, hampered by the sheath, couldn't cover the cervix adequately, diminishing its effectiveness. Future iterations aim to address these issues, refining the sheath design and spray pattern for enhanced performance. Overall, the results of the test gave a deeper insight into the performance of the overall device concept and what conceptual changes need to be made during the next development phase.

D Electrical Circuit Diagrams

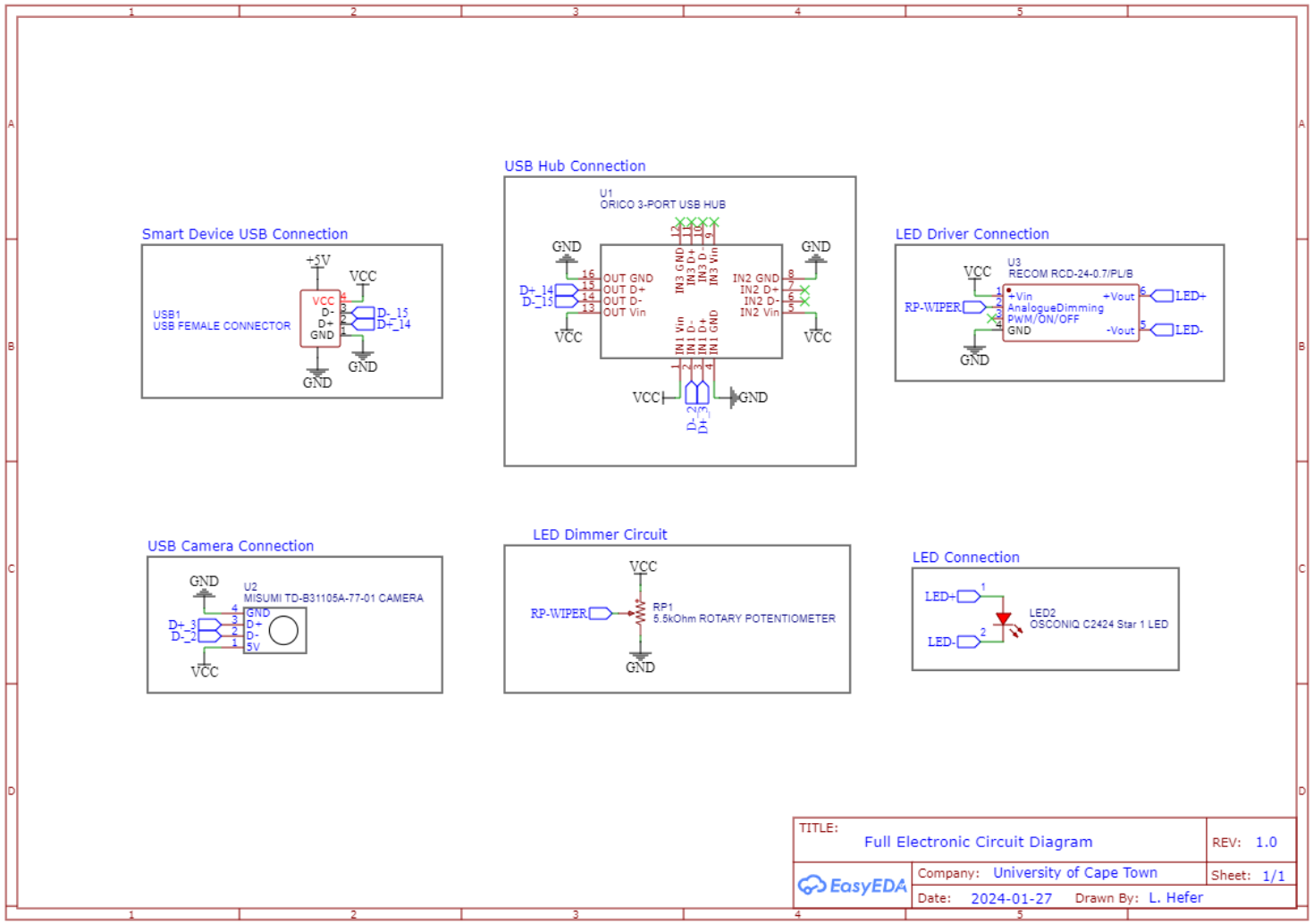
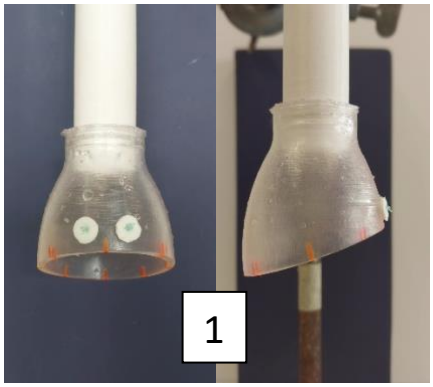
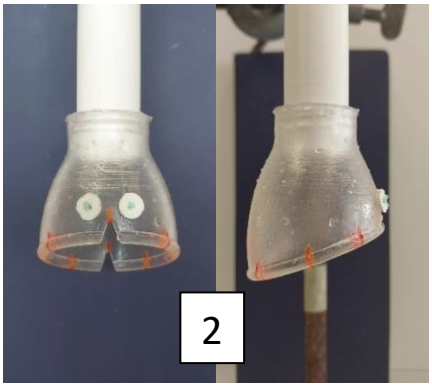
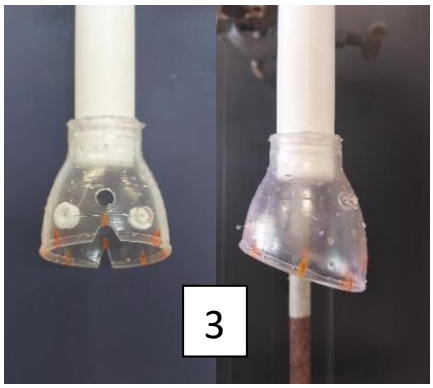


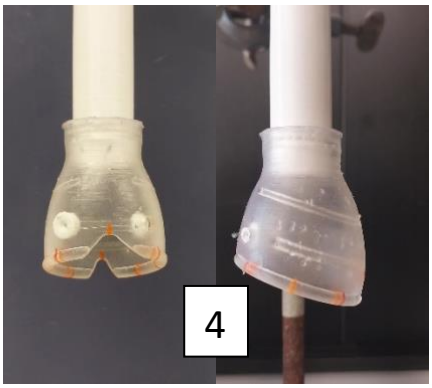
Figure 61: Electronic diagram to produce a PCB for the device.

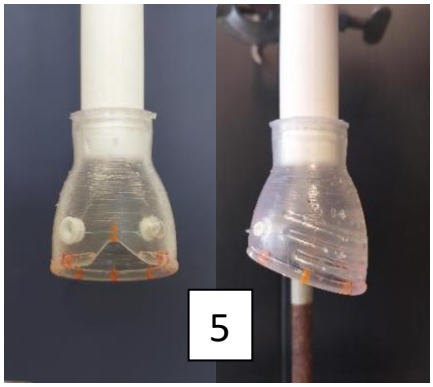
E Verification Testing Dilation Cups

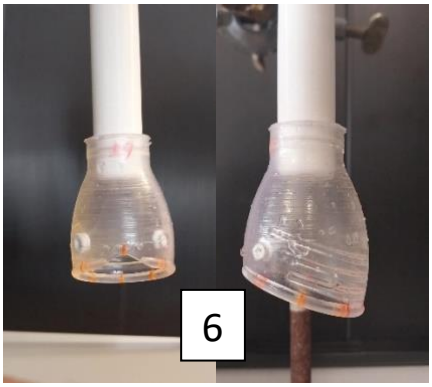


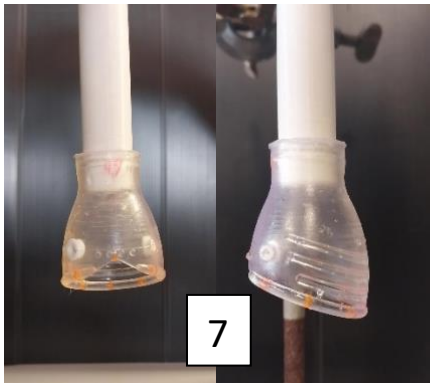


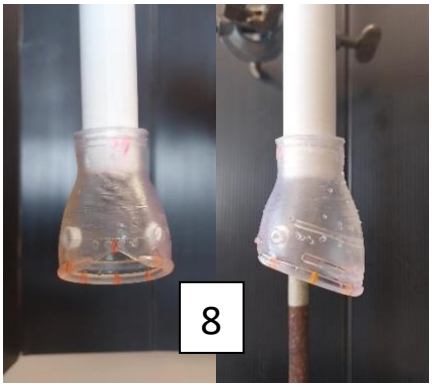












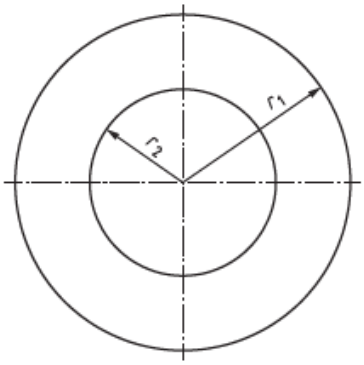
F Verification Test Procedures

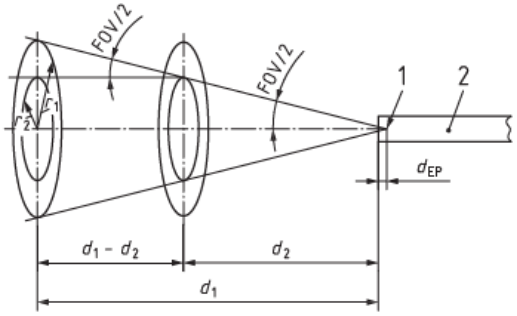
ISO 8600-3:2019 Method B

1. Mount the target into the target holder.
2. Mount the endoscope to be tested in the endoscope holder with the distal window within 0,5 mm of the target. Sharp image focus might not be possible to achieve at this distance. Adjust the endoscope in a way that its entrance pupil (if unknown, distal window) is at the centre of rotation of the rotation stage.
3. Adjust the endoscope holder by looking through the endoscope so that the crosshairs marked on the target and the circumference of the field of view is centred.
4. Move the target away from the endoscope until the outer target circle with radius *r*1 is fully in view. Adjust the viewing direction from the endoscope to the target holder by looking through the endoscope so that the circles marked on the target and the circumference of the field of view is centred.
5. Move the target back to within 0,5 mm of the distal window and confirm that the crosshairs marked on the target and the circumference of the field of view are still centred. If they are not, adjust the viewing direction and repeat steps 6.2 b) through 6.2 e) until both features are centred.
6. Record the distance (*d*1) from the endoscope to the target with the outer target circle (*r*1) coincident with the maximum diagonal field of view.
7. Move the target toward the endoscope until the inner target circle with radius *r*2 is coincident with the maximum diagonal field of view. Record the distance (*d*2) from the endoscope to the target.
8. Calculate and record the field of view (FOV) of the endoscope in degrees according to the formula:

$$FOV = 2xarctan\left(\frac{r_1 - r_2}{d_1 - d_2}\right)$$

9. Read and record as the direction of view the angular position, in degrees, of the protractor relative to the long axis of the insertion portion of the endoscope.





Key

1	entrance pupil
2	optical endoscope
d_{EP}	distance between the entrance pupil and the distal window surface
FOV	field of view

G Risk Assessment

The risk assessment forms part of the design methodology. It is used throughout the development process of the device to assess any risk that could make the device unsafe to use or prevent the device from performing as intended. Thus, the primary goal of the risk assessment process was to ensure that the human operators could use the developed device safely and effectively in the validation study. Risk assessment falls within the broader risk management process for medical device development outlined by ISO 14971:2019, which guided the risk assessment process applied to this project. However, it must be stated that the risk assessment performed in this project did not take the entire lifecycle of the developed device into account, as prescribed by ISO 14971:2019. Since the primary goal of the risk assessment was to get the device ready for the validation study, the device lifecycle phases considered for this project include the design and development, basic manufacturing of the prototype, and basic usability.

The process of risk assessment fundamentally identifies any risks relating to the device and calculates the level of the risk. The calculated risk level is the product of the severity (potential harm) and the occurrence (probability of the risk to occur). The severity and occurrence values allocated to an identified risk are based on the severity and probability scales shown in Table 31 and

Table 32 below. The score given to the risk from each of these scales is multiplied to give the risk score. This risk score is used to determine if intervention is required to mitigate the risk based on specific thresholds. These thresholds are illustrated in the risk matrix shown in

Table 33, which specifies if the risk is either low, medium, or high risk. The interventions required for each risk level are:

I. **Low risk (Green)**: Acceptable - No intervention.
II. **Medium risk (Yellow)**: Reasonable - Intervention required if it is possible.
III. **High risk (Red)**: Unacceptable - Intervention required.

The risks that were identified, evaluated, and mitigated using these tables are shown in the risk assessment register in Table 34 below.

Table 31: Severity rating table.

Severity rating definition		
Severity is defined on a scale of one to five as per the below definitions:		
Severity Rating	**Severity Description (Harm)**	**Severity Description (Failure)**
Catastrophic (5)	Results in patient death	Catastrophic failure
Critical (4)	Results in permanent impairment or life-threatening injury	Partial failure
Serious (3)	Results in injury or impairment requiring professional medical intervention	Temporary intervention required
Minor (2)	Results in temporary injury or impairment not requiring professional medical intervention	Inconvenience
Negligible (1)	Inconvenience or temporary discomfort	Insignificant

Table 32: Probability rating table.

Probability rating definition		
Probability is defined on a scale of one to five as per the below definitions:		
Probability Rating	**Probability Description (prior to verification and validation data)**	**Probability Description with data**
Frequent (5)	81 to 100% probability of occurrence	1 in 100
Probable (4)	41% to 80% probability of occurrence	1 in 1,000
Occasional (3)	11% to 40% probability of occurrence	1 in 10,000
Remote (2)	1% to 10% probability of occurrence	1 in 100,000
Improbable (1)	Less than 1% probability of occurrence	1 in 1,000,000

Table 33: Risk score evaluation matrix.

	Probability				
Severity	**Improbable (1)**	**Remote (2)**	**Occasional (3)**	**Probable (4)**	**Frequent (5)**
Catastrophic (5)	5	10	15	20	25
Critical (4)	4	8	12	16	20
Serious (3)	3	6	9	12	15
Minor (2)	2	4	6	8	10
Negligible (1)	1	2	3	4	5

Table 34: Speculum-free, digital cervical cancer screening device risk assessment register.

Risk Analysis					Risk Evaluation					Risk Control			Residual Risk Evaluation					
Item	Hazard (Potential Source of Harm)	Foreseeable Sequence of Events	Hazardous Situation	Harm	Severity	Probability	Risk Index	Acceptable?	Current Control	Control Implemented (Reference)	New hazard introduced?	Description of the introduced hazard	Severity	Probability	Risk Index	Acceptable?	Residual Risk Justified?	Justification (Reference Documents / Justification)
A	Phase: Design and Development																	
A.1	Electronic faults	The connection between the prototype and the display is faulty, causing a connection error.	The operator cannot make a high quality diagnosis.	Permanent injury or death of the patient due to incorrect diagnosis.	4	2	8	NO	Provide alternative options.	Design the device to be compatible with any smart device that is USB-enabled.	NO		4	1	4	YES	YES	Within acceptable parameters.
A.2		Poor connections between electrical components cause faults that result in time-consuming troubleshooting.	Unnecessary maintenance time.	Minor inconvenience.	2	2	4	YES	Test all connections after soldering.									
A.3		A component of the power subsystem or display subsystem fails unexpectidly.	The device cannot be used to make a diagnosis.	Catastropic failure	5	2	10	NO	Make the design robust to unexpected electronic failures of specialised components	The power and display subsystem design makes use of smart devices to perform the functions of both subsystems.	YES	Compatible smart devices not available	5	1	5	YES	YES	Smart devices are widely accessible, even in low-resource settings.
A.4	Fluid leakage	Liquid dispensing button disconnects from the pump mechanism or the liquid pipe due to repetitive pump cycles or the device being dropped.	Fluid gets pumped into the housing cavity unknowingly while the operator attempts to dispense liquid onto the cervix. The liquid pools inside the housing, contacting electronic components and causing critical damage.	Catastropic failure	5	2	10	NO	Securely connect the liquid dispensing button to the pump mechanism and the liquid pipe.	Secure press-fit connection to the liquid pipe, and a clip-on connection designed to securely attach to the tip of the pump mechanism shaft.	NO		5	1	5	YES	YES	Within acceptable parameters.
A.5	High temperatures	LED is kept fully ON for an extended period of time either intentionally by the operator or unitentionally due to the LED dimmer wheel disconnecting from the dimmer circuit, resulting in a significant increase in temperature.	High surface temperatures causes surrounding components to deform and melt, possibly compromising their functionality.	Partial device failure	4	2	8	NO	Prevent the LED from reaching excessively high temperatures when fully ON.	Add a heatsink and thermal sheet to the back of the LED to help dissipate the heat away from the LED.	YES	Although less concentrated, heat is still trapped inside the housing and could compromise the function of other components.	4	1	4	YES		
A.6	Contamination	The probe cover is not properly sealed around the probe, causing biological material and fluid to come into contact with the probe.	The probe is contaminated with biological material, and does not undergo the required decontamination processes before being used on another patient.	Patient is exposed to a possible life-threatening illness	4	4	16	NO	Improve the quality of the seal created by the probe.	A completely flat acetate sheet is stuck to the top of the faceplate to prevent any pooling of liquid around protruding features.	YES	A small hole needs to be cut in the acetate sheet to still allow liquid to pass through the spray nozzle. However, this leaves the possibility for biological fluid and particles to enter the nozzle through this hole.	4	2	8	YES	YES	Future design improvements will replace the current spray nozzle with a nozzle that includes a one-way valve to prevent any fluid from mixing with the fluid in the liquid pipe
A.7		The two-piece faceplate is not securely attached to each other, causing them to separate when the condom/cover is pulled over the probe and breaking the sterile seal.	The faceplate seperates fully during the screening, resulting in the top plate falling off the device and remaining inside the patient.	Patient is exposed to a possible life-threatening illness (HPV-infection), partial device failure	4	3	12	NO	Improve the design of the faceplate components to create a permanent attachment between the two plates.	The faceplates are redesigned to allow the condom to shrink-fit around the protruding features and the two plates to connect with right-angle corners that cannot separate without destroying the parts	YES	The probe cover self-assembly is harder since the fit between the different components are tigher to ensure a secure fit.	4	1	4	YES	YES	Within acceptable parameters.
A.8	Non-biocompatible materials	The probe cover, which is the only component of the device that comes into contact with the patient, is not made out of biocompatible material.	The device uses materials that is not compatible with the human body.	Infection, impairment requiring professional medcial intervention.	4	3	12	NO	Use materials for the cover that is biocompatible.	Probe cover is designed to be made with any condom, which are biocompatible products.	YES	Some people are still allergic to some types of condoms.	4	1	4	YES	YES	The percentage of people that are allergic to latex condoms is very small, which is why it is the primary type of condom used.

Risk Analysis					Risk Evaluation					Risk Control			Residual Risk Evaluation					
Item	Hazard (Potential Source of Harm)	Foreseeable Sequence of Events	Hazardous Situation	Harm	Severity	Probability	Risk Index	Acceptable?	Current Control	Control Implemented (Reference)	New hazard introduced?	Description of the introduced hazard	Severity	Probability	Risk Index	Acceptable?	Residual Risk Justified?	Justification (Reference Documents / Justification)
A.9	Trouble visualising the cervix	Condensation forms on the camera lens as a result of the hot and wet environment inside the vaginal canal	The operator cannot make a high quality diagnosis.	Permanent injury or death of the patient due to incorrect diagnosis.	5	3	15	NO	Completely seal the camera off from the local environment inside the vaginal canal.	Adjust the faceplate design to create a secure seal between the local environment and the probe components.	NO		5	1	5	YES	YES	Within acceptable parameters.
A.10		Liquid droplet from the spray nozzle forms on the camera and LED lenses reducing the quality of the image of the cervix.	The operator cannot make a high quality diagnosis.	Permanent injury or death of the patient due to incorrect diagnosis.	5	3	15	NO	Make the outermost surface of the faceplate completely smooth and water resistant.	Use the acetate sheet and coat the sheet in a water resistant coating.	YES	The water-resistant coating could be non-biocompatible.	3	3	9	YES	NO	Outstanding risk.
A.11	Permanently dilated cup.	Cup actuation strings fail (snap) when tension is applied to them to collapse the cup.	Cup cannot be collapsed to be inserted into the vaginal canal.	Temporary discomfort for the patient and inconvenience to the operator, Partial device failure.	1	4	4	YES										
A.12			Cup cannot be collapsed to remove the device from the vaginal canal at the end of the procedure. This could prevent the vaccuum that is created by the dilated cup from being released, preventing the cup from being moved.	Injury to patient requiring professional medical intervention.	3	4	12	NO	Use a stronger actuation cable.	Replaced the fishing line with a threaded wire.	NO		3	2	6	YES	YES	Within acceptable parameters.
A.13		Connection points where the actuation string attaches to the cup wall fails due to excessive and repetitive loading from the small diameter string, causing the string to cut through the cup wall.	Cup cannot be collapsed to be inserted into the vaginal canal.	Temporary discomfort for the patient and inconvenience to the operator, Partial device failure.	1	4	4	YES										
A.14			Cup cannot be collapsed to remove the device from the vaginal canal at the end of the procedure. This could prevent the vaccuum that is created by the dilated cup from being released, preventing the cup from being moved.	Injury to patient requiring professional medical intervention.	3	4	12	NO	Reinforce the actuation string attachment points.	Add reinforcement rings to the attachment points that are made out a hard, smooth material.	YES	The hard reinforcement rings could cause minor discomfort or injury to the patient during the screening procedure.	2	3	6	YES	YES	The reinforcement rings are collapsed inward when the cup is actuated, moving them away from the vaginal wall. And they are rounded with a minimalist profile to reduce the amount of hard material protruding from the cup wall.
B	**Phase: Manufacturing**																	
B.1	Electronic shocks	Poor soldering connections.	Wiring loosens and touches parts of the handle, causing the operator and patient to shock.	Injury to patient and operator.	1	2	2	YES	Test all wiring connections and provide adequate slack along cable lengths to prevent forces from being applied directly to the connections									
B.2	Component degradation	Degradation of the probe and handle components due to the decontamination process.	Components become weaker over time, causoing mechanical failures in the structure of the parts.	Partial device failure	3	3	9	NO	Use a different material.	Manufacture the probe and handle components out of materials compatible with th specified decontamination processes.	NO		3	1	3	YES	YES	Not implemented for the prototype, but will need to be implemented in future versions of the device as it is manufactured.

Risk Analysis					Risk Evaluation					Risk Control			Residual Risk Evaluation					
Item	Hazard (Potential Source of Harm)	Foreseeable Sequence of Events	Hazardous Situation	Harm	Severity	Probability	Risk Index	Acceptable?	Current Control	Control Implemented (Reference)	New hazard introduced?	Description of the introduced hazard	Severity	Probability	Risk Index	Acceptable?	Residual Risk Justified?	Justification (Reference Documents / Justification)
B.3	Low image quality	The manufacturing process used to make the lenses for the faceplate that cover the camera and lights causes image distortion and overall reduction in image quality	The operator cannot make a high quality diagnosis.	Incorrect diagnosis could lead to permanent injury or death.	5	3	15	NO	Improve the manufacturing process used to make the acetate lenses.	The small diameter acetate lenses that were intended to just cover the camera and lightpipe holes in the faceplate was replaced with one large acetate sheet that covers the entire faceplate.	NO		5	1	5	YES	YES	Within acceptable parameters.
B.4	Structural flaws in the dilation cup.	The repetitive loading cycle of the dilation cup and the large deformation that the material has to undergo places stress on structural weak points in the cup, causing it to break.	Cup does not actuate (dilate and collapse) as required, making insertion and removal difficuilt.	Temporary discomfort for the patient and inconvenience to the operator, Partial device failure.	1	4	4	YES	For prototyping purposes the material provides a lifecycle of >50 full actuations, whish is sufficient.									
B.5			Compromised cup wall leads to obstruction of the cervix due to radial forces from the vaginal walls.	Incorrect diagnosis could lead to death.	5	4	20	NO	Improve the manufacturing method.	SLA printing used (FormLabs) which produces a more homogenous product with minimal structural flaws.	YES	Non-biocompatible materials are used to manufacture the dilation cup.	5	2	10	NO	YES	Biocompatibility is not a requirement at this stage of the project.
C	**Phase: Usability**																	
C.1	Acetic acid apllicator not functioning	The reservoir is not fully connected to the pump mechanism after refilling. This prevents acetic acid from being pumped through the system and dispensed onto the cervix.	Acetowhiteing reaction does not occur, which could result in the operator making the incorrect diagnosis.	Incorrect diagnosis could lead to death.	5	3	15	NO	Visually and audibly notify the operator that the reservoir is fully connected.	Tabs on the side of the reservoir clip into positioning holes in the handle when the reservoir is fully connected.	NO		5	1	5	YES	YES	Within acceptable parameters.
C.2		The operator is not aware that the reservior is empty and does not refill it before screening a new patient.	The device needs to be removed, refilled, and re-inserted for the screening procedure to continue.	Inconvenience to the operator and additional discomfort to the patient.	1	4	4	YES	No current control in place, but risk is not high enough at thtis stage of the project.									
C.3	Compromised sterility of the probe cover.	Operator contaminates the probe cover with their hands while attaching it to the tip of the device and pulling the cover over the device.	Probe cover is not sterile when inserted into patient.	Patient is exposed to illness that requires medical intervention	3	2	6	NO	Operator must wear surgical gloves to perform the screening procedure. And the attachment procedure is design such that the operator only touches the probe-side (unsterile) side of the cover.									
C.4		When pulling the probe cover sheath over the probe the operator pulls to hard on the sheath, causing it to tear.	Unsterile probe comes into contact with the patient, possibly causing cross-contamination.	Patient is exposed to illness that requires medical intervention	3	3	9	NO	Improve the connection between the faceplate and the probe tip, and add a visual indication to let the operator know when to the probe cover is in the correct position.	Optimised the design of the connecting pins to be more secure.	YES	The new pin design has a sharp tip which could damage other components when used incorrectly.	3	1	3	YES	YES	Primary harm mitigated. User experience with the device and other design features will reduce the changes of incorrect use and damage to other components.
										Added a line on the probe to indicate up to where the probe cover needs to be pulled.	YES	If a short sheath (condom) is used that does not reach this line the operator will again pull to hard on the cover to reach the line.	3	2	6	YES	YES	The chances of using such a short sheath is small, and with a limited amount of experience with the device the operator will understand when the cover is in the correct position.

Risk Analysis					Risk Evaluation					Risk Control			Residual Risk Evaluation					
Item	Hazard (Potential Source of Harm)	Foreseeable Sequence of Events	Hazardous Situation	Harm	Severity	Probability	Risk Index	Acceptable?	Current Control	Control Implemented (Reference)	New hazard introduced?	Description of the introduced hazard	Severity	Probability	Risk Index	Acceptable?	Residual Risk Justified?	Justification (Reference Documents / Justification)
C.5	Damage to the visualization subsystem.	While the operator attaches the probe cover to the tip of the probe, the protruding elements of the faceplate that interface with the probe tip damage the camera lens when the operator does not align the faceplate correctly.	The damaged camera lens causes a low-quality image to be displayed to the operator to make a diagnosis with.	Temporary discomfort for the patient and inconvenience to the operator, Partial device failure.	5	5	25	NO	Improve the alignment of the elements to make it obvious that the faceplate orientation is not correct, and add visual indications.	The size of the connecting holes and protruding elements for the various elements differ significantly to make it clearer how the element align.	NO		5	3	15	NO	YES	Further usability studies required
										The halves of the faceplate and probe tip that need to align were clearly marked with colour	NO		5	2	10	NO	YES	Further usability studies required
C.6	High temperatures	LED is kept fully ON for an extended period of time either intentionally by the operator or unintentionally due to the LED dimmer wheel disconnecting from the dimmer circuit, resulting in a significant increase in temperature.	The housing temperature increases in the area where the operator holds onto the device.	Temporary discomfort to the operator	1	4	4	YES	None									

H Ethics Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
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08 September 2023

HREC REF: 570/2023

Prof S Sivarasu
Division of Biomedical Engineering
Room 7.17 Anatomy Building-FHS
Email: Sudesh.sivarasu@uct.ac.za
Student: hfrleh001@myuct.ac.za

Dear Prof Sivarasu

PROJECT TITLE: PILOT STUDY TO VALIDATE THE EFFICACY AND USABILITY OF A NEWLY DEVELOPED SPECULUM-FREE DIGITAL CERVICAL CANCER SCREENING DEVICE (MASTERs 'CANDIDATE- MR LEHAN HAYDEN HEFER)

Thank you for your response letter dated 31 August 2023, addressing the issues raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 September 2024.

Please submit a progress form, using the standardised Annual Report Form (FHS016) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Mr Lehan Hefer will also be involved in this study.

Please quote HREC REF 570/2023 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

Signed by candidate

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC registration number: REC-210208-007
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of

Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC/ref 570.2023

I Participant Information Sheet

Participant Information Sheet

In contribution towards the completion of Lehan Hefer's Master's Degree

Participant Information Sheet for Experienced Colposcopists

HREC REF: 570/2023

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET AND THE CONSENT FORM

Title of Study:
Design and Development of a Speculum-Free Digital Cervical Cancer Screening Device

Department:
Faculty of Health Sciences, Department of Human Biology, Division of Biomedical Engineering

Name and Contact Details of the Investigators(s):
Lehan Hefer - hfrleh001@myuct.ac.za
Dr Rakiya Saidu - rakiya.saidu@myuct.ac.za

Name and Contact Details of the Principal Investigator:
Prof Sudesh Sivarasu - sudesh.sivarasu@myuct.ac.za

Name and Contact Details of the Ethics Committee:
UCT Faculty of Health Sciences Human Research Ethics Committee (HREC)
***Address*:** Room 45, E-52 Old Main Building, Groote Schuur Hospital, Observatory, 7925
Tel: 021 406 6492
Email: hrec-enquiries@uct.ac.za

1. Invitation Paragraph

You have been invited to participate in a research project. Before making your decision, it is crucial for you to fully comprehend the purpose of this research and what your involvement entails. Please take the time to carefully read the following information and feel free to discuss it with others if you wish. If any aspect is unclear or if you require more information, please don't hesitate to ask. Take the time you need to decide whether or not you wish to be part of this study. Thank you for taking the time to review this.

2. What is the study's purpose?

This pilot study is designed to assess the diagnostic performance of a newly developed speculum-free cervical cancer screening device by comparing it to the standard-of-care tool. The primary goal is to ascertain the diagnostic accuracy of the device when used by experienced colposcopists. Additionally, the study aims to collect usability data from experienced colposcopists in a simulated clinical setting. The insights gained will be instrumental in refining and improving the device's design and functionality, making it more effective and user-friendly. By evaluating this innovative screening device, the study strives to contribute to the enhancement of cervical cancer screening methods.

3. Why have I been chosen?

A minimum of five participants will be selected from two categories of medical professionals: experienced gynecologists and nurses working at colposcopy clinics. Inexperienced colposcopists (those with fewer than 100 examinations) have been excluded based on research that underscores the impact of operator experience on diagnostic accuracy in colposcopy and VIA examinations. The inclusion criteria are as follows:

- Recent experience in performing colposcopies.
- Conducted more than 100 colposcopies.
- Qualified medical professionals.

4. Do I have to take part?

The decision to participate is entirely yours. If you choose to participate, you will receive this information sheet to keep, and you will be requested to sign a consent form and a non-disclosure agreement (which you will also retain as a copy). You are free to withdraw from the study at any time without providing a reason, and we will inquire about your preferences regarding the data you have provided up to that point.

5. What will happen if I take part?

As a participant, you will be tasked with conducting a cervical cancer screening procedure on a female pelvic model (training dummy) using both the developed device (speculum-free cervical cancer screening device) and the standard-of-care screening tool (speculum and colposcope). You will follow the standardised colposcopy examination procedure used for diagnosing cervical cancer. After completing both screening procedures, you will be asked to fill out post-test questionnaires. The tasks associated with both devices can be grouped into four phases:

1. Setting up the device and ensuring proper functioning.
2. Inserting the device into the model and visualizing the cervix.
3. Performing the screening of the different cervices.
4. Removing the device from the model.

Your participation will involve a single session that will last between 30 minutes and an hour. This time slot encompasses introductions and explanations of the study and devices, the performance of procedures on the training dummy, and the completion of post-test questionnaires. No travel expenses are associated with participating in the study, as all testing equipment will be conveniently set up at your chosen location.

6. Will I be recorded, and how will record media be used?

We will collect personal information related to your experience with colposcopy examinations and existing technologies to compare screening results with your familiarity and experience. However, no other personal details will be collected from you. All participants will be randomly assigned a number, which will be used to refer to them in study results when discussing their screening outcomes.

Photographic and video footage will solely focus on the use of the device and will not include any identifying features of participants, such as your face. Only the investigators involved in this study will have access to the data obtained, which will be entered from the hard copies used during testing and stored on the investigators' computers and university drives. The data will be securely stored throughout the project's duration and may only be accessed by the investigators. No other use of the data will occur without your written permission.

7. What are the possible disadvantages and risks of taking part?

There are no foreseeable risks or disadvantages associated with participating in this study, as the procedures are conducted on a training model, and participants are expert colposcopists who are already well-acquainted with the procedure.

8. What are the possible benefits of taking part?

While there are no immediate benefits for you as the participant, we hope that this pilot study will validate that the developed device matches the diagnostic accuracy of the standard-of-care device. This validation will encourage and facilitate further research and development to enhance the device's features and incorporate more advanced capabilities. In the future, this device could play a pivotal role in improving access to quality cervical cancer screening services in low-resource settings.

9. What if something goes wrong?

You are encouraged to express any complaints or concerns at any point before, during, or after the study. If a complaint needs to be raised before or after the study, it can be directed to the principal investigator. During the study complaints may be directed to the investigator conducting the study. If you feel that your complaints have not been adequately addressed, you can contact the UCT Human Research Ethics Committee at hrec-enquiries@uct.ac.za.

10. Will my participation in this project be kept confidential?

All information collected about you during the research will be held in strict confidence. You will not be identifiable in any subsequent reports or publications.

11. What will happen to the results of the research project?

The study's results will be used to further research and develop the device, aiming to create a final working prototype with superior efficacy and usability to existing screening devices. A future version of this device may contribute to reducing the burden of cervical cancer. This study forms part of a master's research project and will be disseminated to the public through scientific channels. There is also a possibility of producing intellectual property (IP) in this research that may be eligible for a patent through UCT's RCI department.

Thank you for taking the time to review this information sheet and for considering participation in this research study.

J User Consent Form and Non-Disclosure Agreement (NDA)

I agree to participate in the study conducted by the University of Cape Town's Medical Devices Laboratory.

I understand that participation in this usability study is voluntary, and I agree to immediately raise any concerns or areas of discomfort during the session with the study administrator.

I agree to honour the confidential nature of this trial. I acknowledge and confirm that I will not divulge to any party any confidential information including and not limited to the workings of the device used in this trial and the results obtained within the trial. I agree to keep confidential information confidential and to protect the confidentiality of such confidential information with the same degree of care with which I protect the confidentiality of my own information.

I consent to be photographed/video and further authorise that the photographs/videos may be used or published for any project-related purpose. I acknowledge that these photographs/videos will be focused on the device and training dummy and will not contain identifying features of myself, the participant, including but not limited to my face.

By signing below, I indicate that I have read and understand the information on this form and that any questions I might have about the session have been answered.

	Participant	**Witness**	**Investigator**
Date:			
Printed Name:			
Signature:			

Thank you!

We appreciate your participation.

K Participant Data Collection Tools

Participant Information & Data Collection Pack

In contribution towards the completion of Lehan Hefer's Master's Degree

We extend our heartfelt gratitude for your invaluable participation in our trial of the newly developed device. Your time, feedback, and insights are instrumental in advancing our work. Your contribution will greatly enhance the usability and effectiveness of this innovative device, and we sincerely thank you for your collaboration.

This document contains the NDA that you need to sign before starting the test, diagnosis reports that you will use to diagnose each cervix, as well as the feedback forms that need to be completed after the test is complete.

Please ensure that the investigators explained the testing process and device functionality to you before starting the test. Ensure that you are comfortable with the new device, that you understand all of the features and safety aspects of the device, and that any questions that you have are answered before starting the test.

Please complete the table below with your information. This information will be used to help analyse the efficacy and usability of the device and will not be used to comment on the work of the participants.

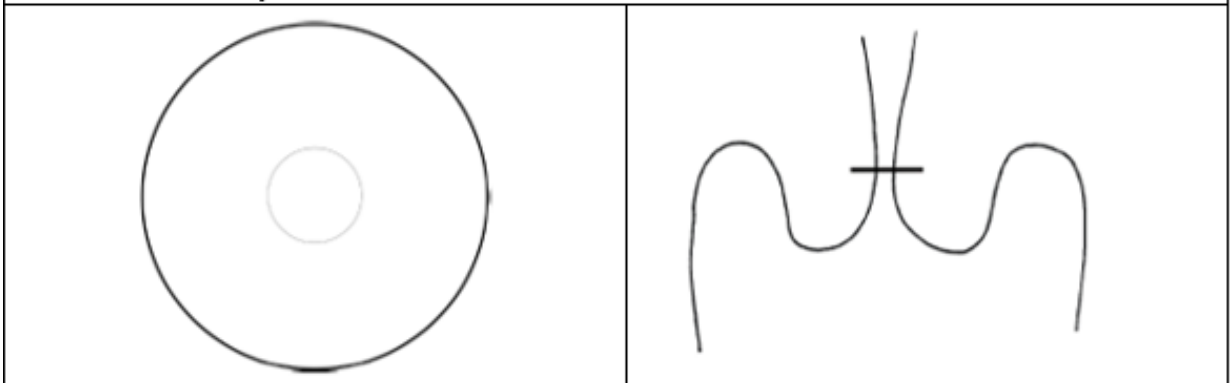
Participant Details	
Participation number	
Profession & Qualifications	
Colposcopy experience (Years)	

Participant No.	
Device	1
Cervix No.	1

Colposcopy examination report

TZ classification: (1. Type 1; 2. Type 2; 3. Type 3)	
TZ size: (1. Large; 2. Small)	
Colposcopic opinion: (0. No cervix; 1. Normal; 2. HPV/Inflammation/Benign; 3. C IN/Low grade; 4. CIN/High grade; 5. Invasive; 6. Other; 7. Not performed)	

Draw the TZ and any the location of identified lesions



Proposed management plan:

Swede score result	

Swede score matrix

The Swede score assigns a score of 0, 1, or 2 to each of the four different characteristics. The total score ranges from 0 to a maximum of 8.

Characteristic	**Score**		
	0	**1**	**2**
Uptake of acetic acid	Zero or transparent	Shady, milky (not transparent, not opaque)	Distinct, opaque white
Margins and surface	Diffuse	Sharp but irregular, jagged, 'geographical', satellites	Sharp and even, difference in surface level, including 'cuffing'
Vessels	Fine, regular	Absent	Coarse or atypical
Lesion size	<5mm	1-15mm or spanning 2 quadrants	>15mm or spanning 3-4 quadrants, or endocervical undefined

Figure 62: Colposcopy examination report and Swede score matrix.

Post-Test Usability Feedback

After completing the testing protocols for both devices and having filled in the diagnosis reports, we would appreciate your feedback regarding the usability of the developed device. The usability of the developed device is in comparison to the standard of care device that was also used in the tests, so please complete the following questionnaires based on that. There are two sets of multiple-choice questionnaires to complete, with the first being a standardised questionnaire to assess the general usability of a device, and the second more focussed on the specific aspects of the developed device to get more detailed feedback about the specific aspects that worked well and other that need to be improved. **Please take your time to complete the questionnaires, as your feedback on this is extremely valuable to this research.**

System Usability Scale

	Strongly Disagree				Strongly Agree
	1	2	3	4	5
1. I think that I would like to use this system frequently.	○	○	○	○	○
2. I found the system unnecessarily complex.	○	○	○	○	○
3. I thought the system was easy to use.	○	○	○	○	○
4. I think that I would need the support of a technical person to be able to use this system.	○	○	○	○	○
5. I found the various functions in this system were well integrated.	○	○	○	○	○
6. I thought there was too much inconsistency in this system.	○	○	○	○	○
7. I would imagine that most people would learn to use this system very quickly.	○	○	○	○	○
8. I found the system very cumbersome to use.	○	○	○	○	○
9. I felt very confident using the system.	○	○	○	○	○
10. I needed to learn a lot before I could get going with this system.	○	○	○	○	○

Figure 63: System Usability Scale questionnaire (Brooke, 1995) completed by each participant after completing the screening procedures.

User Feedback Questionnaire

Table 35: User feedback questionnaire completed by each participant after the screening procedures.

Strongly Disagree (1) – Disagree (2) – Neutral (3) – Agree (4) – Strongly Agree (5)						
General Usability	1	2	3	4	5	N/A
1. I felt comfortable and confident using the CerviScreen to perform the required procedures.						
2. The CerviScreen was quick and easy to set up and start the screening process.						
3. I found it easy to insert the probe and visualise the cervix.						
4. The CerviScreen's design and functionality was intuitive and easy to understand.						
5. I felt adequately trained and comfortable to use the device after the short training and introduction session.						
sDo you have any other comments regarding the general usability of the device?						
User Interface	1	2	3	4	5	N/A
6. The CerviScreen was comfortable to hold and handle during the screening procedure.						
7. The buttons and controls are easily accessible and well-placed.						
8. The digital display made it easy to visualise the cervix and take pictures.						
9. The layout of the various controls is suited for both left- and right-hand dominant users.						
Do you have any other comments regarding the user interface?						
Specific Features	1	2	3	4	5	N/A
10. The probe cover was easy to attach.						
11. The probe cover was easy to remove.						
12. The speculum-free design simplified the screening process.						
13. I could easily locate the cervix and position the cup over the cervix.						
14. The cup was easy to collapse.						

15. The cup was quick and easy to insert and remove.						
16. The LED dimmer was easy to use and provided adequate control over the brightness to see the cervix with minimal glare.						
17. The green filter worked to help identify any abnormal lesions and the TZ on the cervix.						
18. The acetic acid spray was sufficient to clear any mucus of the cervix.						
19. I could easily zoom in on specific areas using the mobile phone.						
Do you have any other comments regarding specific features?						
Screening Process	1	2	3	4	5	N/A
20. The CerviScreen can be used as a triage device to identify patients that need to go for further screening or treatment.						
21. I am confident in the accuracy of the screening/diagnostic results made with the CerviScreen.						
Do you have any other comments regarding the screening process?						
Compared to standard of care device	1	2	3	4	5	N/A
22. How does the usability of the Cerviscreen compare to the colposcope? (>3 is better, <3 is worse)						
23. The developed device offers advantages or improvements over the standard-of-care device in terms of ease of use.						
24. Were there any specific areas where the standard-of-care device outperformed the Cerviscreen in terms of usability?						
25. If the CerviScreen is further developed and perfected into a commercial product, I would consider using the CerviScreen in my regular cervical screening practice.						
Problems with the CerviScreen device	1	2	3	4	5	N/A
26. I prefer to still use a speculum over a device like the CerviScreen that has speculum-free design.						
27. If you agree with the above statement, please explain why you feel like that.						

28. The probe cover is impractical for use in public healthcare settings and will not provide as much benefit as expected over current decontamination methods.						
29. The dilation cup is not robust enough to be effective in the wide variety of scenarios and conditions that a speculum is used in.						
30. The view and interaction provided by the probe design and camera made it hard to be confident with my diagnosis.						

Other General Comments
Are there any specific features, functionalities, or improvements that you would like to see in future iterations of the device?
Overall Impression & Additional Comments:

L Engineering Specification Verification Results

ES No	Specification	Value	Pass/Fail
1.1	Maximum insertion width/diameter	<=20mm	Fail
1.2	Maximum weight	<1kg	Pass
1.3	Minimum probe insertion depth	100mm	Pass
1.4	Adjustable display holder	Yes/No	Pass
2.1	Working distance (WD)	20-50mm	Pass
2.2	Minimum Field of View @ minimum working distance	30mm (70°)	Pass
2.3	Direction of view	0degrees	Pass
2.4	Limiting resolution @ maximum working distance	>11lp/mm	Pass
2.5	Image distortion	<3%	Pass
2.6	Illumination intensity @ maximum working distance	>1000Lux	Fail
2.7	Has a green filter	Yes/No	Pass
2.8	Magnification	>5x	Pass
2.9	Illumination colour	White light	Pass
2.10	Illumination beam diameter @ minimum working distance	30mm	Pass
2.11	Minimum frame rate	30fps	Pass
2.12	Adjustable illumination intensity	Yes/No	Pass
2.13	Minimum battery life	2 hours	Fail
3.1	Liquid capacity	Enough for 10 screenings	Pass
3.2	Covering efficacy	Cover all four quadrants of cervix	Pass
3.3	Able to remove mucus on cervix	Yes/No	Pass
4.1	Minimum dilated diameter	30mm	Pass
4.2	Maximum insertion diameter	25mm	Pass
4.3	Maximum radial compression to withstand in dilated state	50kPa (0.5bar)	Pass
4.4	Maximum allowable compression under maximum compression in dilated state	25%	Pass
4.5	Maximum actuation force to collapse cup and hold it in the collapsed state	7N	Pass
5.1	Creates a watertight barrier over the probe and cup.	Yes/No	Pass
5.2	Does not degrade the camera resolution to below the allowable threshold.	Yes/No	Pass
5.3	Does not increase the image distortion to below the allowable threshold.	Yes/No	Pass
5.4	Does not reduce the illumination intensity to below the allowable threshold.	Yes/No	Pass