Development of a housing over an ultrasound probe used to monitor coagulation during prostate cancer treatment

By

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A thesis submitted in conformity with the requirements for the degree of Masters of Health Sciences
Graduate Department of the Institute of Biomaterials and Biomedical Engineering
University of Toronto

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Abstract

Prostate cancer is one of the leading causes of death by cancer for men. Focal therapy is being tested to target only the dominant cancer lesion in the prostate. However, due to the need to ensure that the laser is targeting only the cancer, a real-time treatment monitoring system is required. A combined optical-ultrasound monitoring system is in development at Princess Margaret Hospital based on different optical properties for coagulated versus normal tissue. In this project, we developed a light delivery and collection device that is compatible for use with an existing trans-rectal ultrasound-imaging probe. Computer-aided design software was used to visualize the prototype in relation to the trans-rectal ultrasound probe. This thesis describes the critical tasks necessary to assemble the final prototype, including listing of specifications, selection of device material based on safety and mechanical properties, method of prototype fabrication, positioning and fixation of optical fibers and testing.
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Glossary of Terms

DOT – Diffuse Optical Tomography
FDM – Fused Deposit Modeling
ISO – International Standards Organization
LITT – Laser Interstitial Thermal Therapy
MRI – Magnetic Resonance Imaging
NIR – Near Infrared
PMH – Princess Margaret Hospital
PSA – Prostate Specific Antigen
SLA – Stereolithography
TRUS – Trans-rectal Ultrasound
UHN – University Health Network
US – Ultrasound
UV – Ultraviolet
1 Introduction

1.1 Thesis Roadmap

This thesis is broken into 5 different segments, each of which outlines the steps taken in this study.

The first chapter discusses the underlying issue associated with this study and why it is relevant to us today.

This leads into the second chapter where the rationale for the study is discussed. Relevant research questions are posed and a hypothesis is developed. This hypothesis leads into an understanding of previous work done pertaining to this study.

The third chapter commences into the meat of the work as several different methods are discussed to indicate how this study will be completed. The third chapter introduces some results also that are critical to understand other aspects that are discussed within the chapter.

The fourth chapter leads into the results and a discussion on the impact of each result. The fourth chapter also discusses next directions and future work.

Lastly, the fifth chapter summarizes the results in a comprehensive conclusion.

1.2 Motivating Problem

Prostate cancer is the leading cause of death amongst the various cancers in men. Furthermore, it is the 3rd most prevalent cause of death due to cancer itself [3]. There were an estimated 186,320 new cases diagnosed in 2008 in the United States [4]. From autopsies, it was found that 35% of men at the age of 60 had cancer cells in their prostate. This number increases to 65% of men at the age of 80. Despite the high number of
incidence, over 90% of cases involving prostate cancer is curable if they are detected early (low risk).

There are several methods that are used to detect and diagnose prostate cancer [1]. A simple digital rectal exam (DRE) can be done where the doctor inserts a finger into the rectum and feels for any abnormalities. This method is not necessarily accurate. Another test is the Prostate-specific antigen (PSA) test where the amount of PSA in the blood is tested. If PSA levels are elevated, this could signify cancer. However, the PSA test is not specific to the presence of cancer. The most conclusive test is a transrectal biopsy where tissue samples from the prostate are extracted and checked for cancerous cells.

Prostate cancer is categorized by different stages. Stage I prostate cancer is characterized by the cancer presenting itself in only one lobe of the prostate. Stage II is where the cancer is more prevalent in the prostate and may have spread to both lobes. Stage III is characterized by the cancer spreading beyond the outer layer of the prostate and possibly to the seminal vesicles. In Stage IV, disease has spread well beyond the prostate onto other organs or tissues.

Currently, there are several standard treatment options for prostate cancer [1]. Active Surveillance (AS) monitors the patient with early stage cancer for changes in symptoms with no actual treatment provided unless a change is observed. For patients with late stage disease, active treatment options include surgery, chemotherapy or radiation therapy. Several surgeries can be performed that can remove the lymph nodes or the prostate tissue [1]. If radiation is chosen, implanted radioactive sources are used in order to stop the cancer from growing with the hopes of entirely removing the cancer. Drug therapy includes providing the patient with drugs that block hormonal production and blocks its action to stop the cancer from growing. This occurs because male sex hormones can allow the cancer to grow. Other drugs are used to kill the cancer cells, which are administered during chemotherapy [1]. All these treatment options target the entire prostate, but given the limited precision of these methods, all can damage normal surrounding tissue, significantly reducing the patient’s quality of life.
The quality of life can be reduced in many ways. First and foremost, incontinence, which is loss of voluntary control of defecation or urination, is a major side effect [2]. Overtreatment of the rectum can lead to bleeding and strictures, both of which an impact on bowel movement [2]. Damage to the nerves surrounding the prostate can lead to erectile dysfunction. In addition, infertility can also present itself due to surgery or radiation [2].
2 Background/Literature Review

2.1 Background

Due to the significant reduction in the quality of life after current prostate cancer treatments, the need for an alternative treatment method was considered. Recently, an alternative approach referred to as focal therapy is being investigated, in which only the dominant cancerous lesion in the prostate is targeted. Magnetic resonance imaging (MRI) is used to determine the cancerous region of the prostate [21], which is then targeted for treatment. Successful focal therapy requires i) an accurate definition of the cancerous zone, ii) a technique that is minimally-invasive, and iii) real-time monitoring that shows the progression of the therapy [3]. Focal therapy minimizes the risk of complications because only the clinically threatening cancer is being treated, reducing the risk of treating normal surrounding tissue. At University Health Network (UHN), one treatment modality under investigation for focal therapy is laser interstitial thermal therapy (LITT), in which NIR light energy is delivered through interstitial optical fibers to the zone of interest. This energy effectively destroys the cancerous portion through thermal coagulation [3]. Through trans-rectal ultrasound (TRUS) guidance and co-registration with a pretreatment MRI scan, the boundaries of the prostate are defined that lead to targeting a specific portion of the prostate. A needle is inserted in that region and a focused laser heats and destroys the cancerous area (Figure 2a). The needle is inserted through the help of image guidance (ultrasound) using a template registered to the ultrasound transducer. The ultrasound helps select which location to insert the needle corresponding to the template (Figure 2b and Figure 2c). Other treatment modalities are also being examined for focal therapy, including focal cryoablation of the prostate and high intensity focused ultrasound focal ablation [6,7].

LITT causes localized heating of the tissue leading to coagulation when the temperature increases above 55°C. Real time monitoring of the treatment is necessary to ensure that coagulation does not extend outside the prostate and into other critical structures, such as the rectum. To date, the UHN group has examined two methods of
real-time monitoring. The use of micro bubble contrast-enhanced ultrasound was investigated [4], however, results were inconsistent from patient to patient. Furthermore, the extent of the damage was difficult to see and volumetric images could not be obtained of the coagulation zones. MR thermometry is also currently used as a monitoring technique. However, this method is expensive, taking up to 5 hours and there are concerns regarding temperature accuracy. Also, MR thermometry is not a direct measure of the coagulation zone, and thus it constitutes a less robust method [4].

The UHN group is now developing an optical method of monitoring the tissue coagulation called diffuse optical tomography (DOT). The overall objective is to develop a combined 3D TRUS-DOT system. Diffuse optical tomography is a non-invasive technique of imaging the body. Through DOT, light travelling through tissue is either scattered or absorbed [17]. Scattering takes place due to the size and concentration of cells and subcellular structures present and absorption occurs based on the concentrations of various chromophores such as hemoglobin, water and lipids. [17]. Multiple sources and multiple detectors are positioned around a region of interest. Light is delivered into the tissue at one position. The detectors then sense the scattered light (Figure 1). Multiple detectors at different spatial configurations will collect different amounts of light. The light transport in the tissue can be modeled using the diffusion equation and finite element methods [17]. Typically, the tissue is modeled as a 3D mesh, with each node of the mesh assigned optical absorption and scattering values. Using iterative reconstruction techniques, the optical properties at each node can be adjusted until the difference between the measured and calculated light transmission is minimized. DOT is potentially useful in monitoring tissue coagulation because optical scattering can be as much as 4 times that of native tissue. Furthermore, scattering coefficients are generally consistent with highly coagulated, similar tissue.
Figure 1: Example of light scatter while traversing through tissue
As the treatment progresses, the treated/coagulated tissue will grow in size. It is important to stop this growth before it reaches the rectal wall as it can potentially create a hole in the rectal wall. It has been determined from several different studies that tissue optical scattering increases about 4 times upon coagulation [22]. Based on these observations and the use of DOT technology, a real-time fiber-optic treatment monitoring system was developed at Princess Margaret Hospital that was combined with 3D transrectal ultrasound.
2.1.1 Design Criteria

This project focuses on the development of a device for trans-rectal delivery and detection of light that is positioned onto an existing ultrasound probe for the purposes of 3D trans-rectal DOT. The requirement of fiber optic cables to be placed in the rectum was critical, as the rectal wall is the closest structure to the prostate. Since the TRUS is inserted into the rectum during LITT, an integration of DOT with the TRUS was explored. A sheath that would be placed over the TRUS with embedded fiber optic cables was researched. The actual positions of the fibers on the sheath are being explored in a separate project. However, the spacing between fibers will be in the range of 1-2 mm with an overall separation of 10-20 mm. The housing/sheath was made of a black biocompatible material and should not affect the ultrasound imaging. A condom will be placed over the sheath. The fiber optics will deliver laser light to the rectal tissue, which will be scattered and absorbed by the surrounding tissue. Other fiber optics in the housing will collect the light for delivery to the detectors. Analysis of the detected light will determine if tissue scattering and absorption properties have changed and hence if there is coagulation.

Several specifications were identified for the device to meet in order to be deemed usable. These specifications were modeled after The Medical Devices Regulations document [36], in particular, sections 10-20. Section 15 states that the material chosen should “…not pose any undue risk to a patient, user or other person.” [36]. Furthermore, section 11 states that the medical device shall not “…adversely affect the health or safety of a patient, user or other person.” [36].

The other specifications were device specific. They were established by the need of the underlying science behind diffusion optical tomography fundamentals. That is to say, fiber optic cables needed to be part of the design; otherwise the design itself would be obsolete. Furthermore, as the US is needed for thermal ablation, it was imperative that the US’s viewing capability was not negatively affected. Otherwise, it would deem the US ineffective, and in extension, the laser therapy ineffective.
In summary, the device must meet the following specifications:

- Needs to be assembled from a strong mechanical material
- Integration of optical fibers
- Integration with TRUS probe; not affecting its imaging capability
- Cleanable, able to be sterilized and usable in the body

2.2 Research Questions and Hypothesis

1. Can a fiber-optic monitoring system be integrated with current ultrasound probes used to image prostate cancer so that we can monitor with thermal therapy?
2. Is there a flexible material that will easily embed fiber-optic cables and be compatible with the human body?

The ultrasound catheter has an oval shape with a groove on the top half. Thus, we postulate that this shape can accompany a flexible material on it. Embedded fiber-optic cables on a sheath of a to-be-determined material, placed on the probe, would allow light to easily shine within the prostate area. We can detect the scatter of the light and get enough information to see if the coagulation front is moving or not.

2.3 Literature Review – Integration of the probe with its housing

While there have had been very limited examples of integrating other measurement systems with TRUS, the following have direct significance to this project. Wan et al integrated a transrectal electrical impedance tomography (TREIT) with a standard TRUS [8]. Standard TRUS is non-specific to hyper and hypo-echoic regions in a benign or malignant tumor. They found that electrical properties of such tumors differ, thus employing an integrated system. To combine the two modalities, Wan et al placed electrodes around the acoustic window of an ultrasound probe. Thirty electrodes were placed along the edge of the acoustic window, four electrodes across the horizontal and
eleven on the vertical. (Figure 3) This was to ensure that the ultrasound field was not blocked [8]. The copper electrodes were placed on a flexible Kapton circuit, which was then fastened to, the TRUS probe.

![Electrodes for the TREIT System.](image1)
![Electrodes for the US](image2)

**Figure 3a: Electrodes for the TREIT System. Figure 3b: Electrodes for the US**

More directly relevant to this project is the work of Piao et al. who integrated a near-infrared (NIR) DOT device with a TRUS probe. The focus of their project is detection of cancer based on contrast differences in hemoglobin concentration and oxygen saturation between cancerous tissue and normal tissue. Piao et al first considered allowing the DOT transducer designed to be a co-centric device. This would allow it to simply slide and fit into the TRUS due to its co-centric probe. They abandoned the idea due to the overall increase in the DOT/US probe diameter. Furthermore, the DOT array and the TRUS would be in loose contact due to their uneven diameters. Thus, a DOT array was placed on top of one side of the TRUS. (Figure 4) The array is divided into the source array and the detector array, which run parallel to the TRUS probe [9]. There are seven source and detector channels. The channels within each array are separated 1cm from each other. The source array is separated from the detector array at a distance of 2 cm [9]. It is connected to the handle by an aluminum brace structure.
Jiang et al continued these developments by incorporating grooves on the polycarbonate material in order to insert the 600 µm-core fibers. These grooves were ~4mm by 4mm. Therefore, in a linear array, they employed 7 packaged fibers [10]. The fibers shine light in the direction along its length. Therefore, in order to bend the light upwards, micro-optic methods were used.

2.4 Literature Review – Material Selection

Paio et al reported that their housing was made from a polycarbonate material [9], which is non-toxic, and thus useful for medical applications [11].

Another biocompatible material that could potentially be used in the construction
of the probe is silicone [12]. Silicones have the added advantage of hydrophobicity, low surface tension and chemical and thermal stability. The latter reasons allow for silicone to be used in the body as implants. Silicone itself is a malleable material, which can “tightly fit” into its surroundings.

To further appreciate the usage of the viability of using silicone, Maggi et al did various studies in the development of ultrasound phantoms. Ultrasound phantoms usually mimic acoustic properties of human tissue. Therefore, they do not attenuate the US signal as much as other materials would. These tissues would need to mimic the US velocity (1435 to 1631 m/s), attenuation (0.22 to 1.47 dB/cm·MHz) and density (916 to 1100 kg/m³) for ideal performance, based on the values for bone, fat and tissue. Silicones presented with higher attenuation and lower velocities. Maggi et al showed that the addition of silicone oil and vaseline actually reduced the attenuation coefficient but had no significant effect on velocities. They concluded that the velocities did not make a huge difference to the final result as the attenuation value has a greater impact. This study rationalizes further investigation of using silicone as a potential material.

The International Standards Organization (ISO) has certain protocols that pertain to the viability of materials that are used inside the body [16]. ISO has set guidelines that materials must meet according to ISO-10993. Therefore, materials chosen should ideally adhere to the requirements under ISO-10993 [16]. Therefore, the materials chosen and the final design would ideally be tested under these standards to provide a good justification for Health Canada to approve the use of the sheath.

2.5 Literature Review – Size

Koprulu et al studied the effect of size of the ultrasound on the pain perceived by patients. They had two ultrasound systems with different circumferences, 58 mm and 74 mm respectively. Three groups, 1 – with injectable anesthesia with the 58 mm probe, 2 – with injectable anesthesia with the 74 mm probe, 3 – without the injectable anesthesia with the 74 mm probe, were examined during this study. Their subsequent pain was
assessed through a 10-point visual analog scale (VAS) test. It was shown that groups 1 and 2 did not experience any pain however more than 60% of patients in group three experienced moderate pain [14].

Patients will be anesthetized in our study; therefore there should be some freedom on the size of the sheath. However, it might be a good indication to limit the overall circumference to 74 mm as that was the largest value of ultrasound probe size that was noted in literature. The diameter of the probe at Princess Margaret Hospital is 20 mm. 74 mm is equal to $\pi d$. Therefore, $d \approx 23.6$ mm. Hence, the housing should add at most approximately 4 mm to the overall diameter of the combined system.

Paio et al referred to size in their paper as they stated that a co-centric circular design would increase the overall diameter to above 25 mm. They stated that any diameter above 25 mm is not desirable in a clinical setting [9].
3 Methods and Materials

3.1 Design Specifications

Based on the information presented in section 2, several design specifications were identified. A comprehensive list is shown in Table 1. The rest of this section explains the necessity of these components to this project, typical values or observations for each specification and the approach taken to meet all the requirements for these specifications.

<table>
<thead>
<tr>
<th>Main Specification</th>
<th>Detailed Specifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Material</td>
<td>Colour</td>
</tr>
<tr>
<td></td>
<td>Sterilization</td>
</tr>
<tr>
<td></td>
<td>Method of Production</td>
</tr>
<tr>
<td>Fiber Placement</td>
<td>Material Biocompatibility</td>
</tr>
<tr>
<td>Design Modifications</td>
<td>Conformity and Positioning relative to TRUS probe</td>
</tr>
<tr>
<td></td>
<td>Robust Fiber Management</td>
</tr>
<tr>
<td>Imaging</td>
<td>Effect of Bridge on Contrast</td>
</tr>
<tr>
<td>Mechanical Stress</td>
<td>Withstand Anal Pressures</td>
</tr>
</tbody>
</table>

Table 1: Specifications of Proposed Design

3.2 Key Equipment

3.2.1 US Probe

The ultrasound transducer used for the purposes of this study is from BK Medical, model number 8848 (Figure 6a). This probe is designed for scanning the anal canal and
has been used clinically. The tip of the ultrasound probe is the basis of the structure of the housing that will be developed. All subsequent designs will have to adhere to the structure of the tip of this probe.

The BK Ultraview (Model 8848, BK Medical, Peabody, MA) is used alongside the probe to provide the US images. This system provides different forms of imaging modes for the purposes of different types of functional imaging, not only focused on the prostate (Figure 6b). A monitor provides to view the images and these images can be saved from the system onto a USB drive.

![BK Ultraview 8848 and BK Medical 8848](http://www.bkmed.com/8848_en.htm)
![BK Ultraview 8848 and BK Medical 8848](http://www.itnonline.com/sites/default/files/imagecache/node_image/photo_article/Analogic_UltraView800%2520ultrasound.jpg)

**Figure 5a (Left): BK Medical 8848. Figure 6b (Right): BK Ultraview 800**

The proposed design needs to fit on the transducer of the US probe, as it is the only part inserted into the rectum.

### 3.2.2 Fiber Optic Cables

FiberTech Optica (Kitcher, ON) manufactured the fiber optic cables[18]. They are side-firing as a prism is attached at the distal end. The core bare fiber is 300 µm with a
low OH (hydroxyl group) and NA (Sodium) of 0.22, which is optimal for use in the near-IR wavelengths.

The proposed design needs to be able to hold up to 20 fibers.

### 3.3 Prototype

#### 3.3.1 Preliminary Designs

Preliminary designs were evaluated primarily on the decision tree shown in Figure 7.

![Figure 6: Decision tree for evaluating preliminary designs](image)

**3.3.1.1 Silicone Based Design**

The first design considered was based on the material consisting of silicone only. Silicone had the advantage of having low failure rates and could withstand any torsional stresses that may present themselves on the design during usage [23]. Secondly, from
literature review, it was determined that silicone should, in theory, have limited impact on the ultrasound functionality.

Silicone was purchased from Wacker (Munich, Germany). It came in liquid form with a part A and part B. Both these parts were mixed together to form the rubbery substance, which was done at the Mechanical lab at PMH.

3.3.1.2 Plastic Based Design

The next design considered was primarily based on a polymer material. The advantages for this design were that it would provide a rigid material that should not deform from the clinical stresses. However, a polymer would disrupt the US’s functionality. Therefore, the material would have to be designed in such a way that it does not cover the US transducer.

3.3.1.3 Combination of Plastic and Silicone

The last design considered was using both the polymer and silicone materials in unison. The added advantage was that the silicone would not disrupt the US’s functionality while providing a rigid structure.

3.3.1.4 Other Materials Categories

Other materials were considered such as a metal-based design and wood-based design. The metal design would not work because metal would not work with the US’s functionality and it would disrupt any imaging during CT scans and MRI scans [24].

Although the wood design would not affect the US, wood has a high chance of failure and any irregularities with the design could cause any adverse affects. An example of this is if the wood design had any sharp edges within the structure, it could catch on to tissue and cause a bleed.
3.3.2 Proposed Final Design

The final design was created in such a way that it would not block the US’s functionality. Therefore, the image from the US should be as clear as possible. Next, the sheath must not cause any adverse effects. Therefore, it cannot contain any sharp points or any edges. A round structure would not catch on to any tissue.

The sheath should be easily placed onto the US probe and also taken off. This is important as the sheath will not be disposable and will be subsequently used on different patients. Therefore, the design should not be complicated, especially when used in a clinical setting. It should have some sort of “cap” that would signal to the clinician that the sheath is in its proper position in order to continue treatment.

Next, the fiber optic cables will be placed on the sheath. Therefore, there should be an easy way for these fibers to be placed onto the US.

Lastly, the material needed to be in the colour black. This was important as black colour absorbs light rather than reflecting it. As light travels through the prostate, the detectors will pick up the scattered light. However, the sheath, due to its non-black colour, could reflect some of this scattered light before the detector senses it. This can cause distortion to the signal and add noise to it.

To summarize, the prototype had four main requirements: i) the material is biocompatible, ii) the device can be easily placed onto the TRUS, iii) the device does not interfere with the functionality of the TRUS (which is discussed further in section 3.6) and iv) the device does not cause any adverse effects to the patient.
With these requirements in mind, a prototype was designed using SolidWorks (Figure 8). To meet biocompatibility requirements, the material PC/ABS was chosen. This material was available in black, is compatible with various sterilization methods [5] and is non-toxic [6], making it suitable for medical applications. For the second requirement, the hollow cavity allows for the sheath to be placed on and taken off the TRUS with ease. For the third requirement, the TRUS’s sagittal and axial scanning windows are left relatively unobstructed by the sheath, which causes minimal interference with the TRUS images. This will be discussed in further detail in the TRUS imaging section. Lastly, for the fourth requirement, the sheath is void of any edges or points. The roundness of the sheath ensures no adverse effects.

3.3.3 Sterilization Methods

Since the sheath will be placed in the body cavity, there needs to be a way to clean and sterilize the sheath without harming the material. Different sterilization techniques were researched to be able to provide the optimal way to clean the sheath multiple times. Some of the main methods are listed below [25]:

**Autoclaving** – The item is exposed to high pressure and temperature (121°C, 132°C). It is non-toxic to the environment, patient and the medical staff.
**Gas sterilization** – At around 60 degrees Celsius, ethylene oxide (ETO) is introduced to the gas chamber, which is microbicidal. It alkalizes protein, DNA and RNA and, therefore, prevents normal cellular metabolism and replication. The main steps include preconditioning and humidification, gas introduction, exposure, evacuation and monitoring. One disadvantage of this method is that it is generally a longer process.

**Hydrogen Peroxide Gas Plasma** – Gas molecules are excited by electromagnetic waves. In doing so, it produces free radicals that interact with cell components, which break them down.

**Gamma Radiation** – Radiation produced by a radioisotope, cobalt-60, which generates radicals, which are able to cleave carbon-to-carbon bonds.

At the hospital, autoclaving and gas sterilization are the most common methods, therefore the sheath was initially designed and materials were selected with the ability to be sterilized under the two techniques mentioned. However, after further investigation and discerning about the sheath in clinical practice, the use of the condom was brought to light. This changed the requirement in how the sheath needed to be “cleaned”, as per Health Canada Standards. From the Spaulding method [26], instruments are classified in the following three categories: critical items, semi-critical and non-critical. In theory, an ultrasound probe would fall under the critical item category as it is penetrating the body cavity. However, since there is a condom covering the sheath, the probe plus the sheath falls under a semi-critical item category [27, 28]. Therefore, simply a high level disinfectant, such as Cidex, would be required to clean the sheath and US probe as long as a condom is placed on top. Therefore, in terms of material selection, the material should withstand the compound Cidex’s chemical components. The sheath should be cleaned with a pH based solution, or a saline solution and a brush. Then the use of Cidex should be performed for cleaning and disinfecting.
3.3.4 Fabrication

A 3D printer allows for the fabrication of a 3D object from digital rendering software. At UHN, there are two such devices that can be utilized. One is at the machine shop at Princess Margaret Hospital. The other, with a better resolution, is at the Toronto Rehabilitation Institute. The one at Princess Margaret will be used to visualize the initial design without going into much detail. However, for fiber placements, the Toronto Rehab one will be used. The final design will be outsourced to a company due to the limited material choices at the mentioned locations.

Several fabrication methods were examined considering ease of fabrication, and the ability of the method to print small parts and channels. Some common printing methods include [29]:

**Stereolithography (SLA)** – The model from the CAD design is cut into horizontal slices and then programmed into the computer. The material is placed as a liquid resin. As laser light touches the material, the material hardens. Then the material is lowered to a depth relating to the smallest thickness and the laser once again contacts the liquid resin. This is repeated to create the entire object.

**Laser Sintering** – Powder material is used where one grain of the powder is 50 microns. The powdered material is spread layer by layer. Then a CO₂ based laser scans the surface and binds together successive cross-sectional areas of the design. This happens because the temperature is so high (past the glass transition temperature) that adjacent particles flow together and form into one.

**Fused Deposit Modeling (FDM)** – A temperature controlled nozzle squirts out the material in a semi-liquid state. With this, the object is built layer by layer (0.2mm).

**PolyJet** – Material is jetted from a nozzle but as soon as it is released, it is UV cured and subsequently solidified. The layer-by-layer process’s resolution is 16 microns.
**Injection Molding** – A master part is produced using SLA or FDM methods. Then different materials are heated and injected to create into the mold to create a part.

Due to the availability of a 3D printer with the FDM method at PMH and one with the SLA method at Toronto Rehab, these two techniques were chosen as the main methods of fabrication. In section 3.3.4, further investigation of material choices shows that final design will be made through the FDM method.

### 3.3.5 Material Selection

Lastly, several materials were examined on account of the requirements in the preceding sections. Physical properties were evaluated to determine a non-toxic material, which could be fabricated and disinfected (Figure 9).

![Decision Tree for material selection](image)

**Figure 8: Decision Tree for material selection**

Furthermore, the material had the added restriction of being black, so it does not absorb any of the scattered light while in practice. [Www.redeye.com](http://www.redeye.com) has a table that
shows the different material properties of the available methods that are used for 3D printing [31]. From these properties, Table 2 was generated summarizing the materials with respect to the restrictions of this project.

<table>
<thead>
<tr>
<th>Material Property</th>
<th>Number of SLA Materials</th>
<th># of FDM Materials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black Colour</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Heat Deflection Temp above 90°C</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Compatible with Cidex</td>
<td>0</td>
<td>Min 8</td>
</tr>
<tr>
<td>Non-toxic</td>
<td>All</td>
<td>All</td>
</tr>
</tbody>
</table>

**Table 2: Summary of Material Properties**

Results from Table 1 state that FDM had more choices for material with the black colour as opposed to SLA. Secondly, none of the SLA materials had the heat deflection temperature less than 90°C. This temperature represents when a polymer would start to deform under a load. This temperature is important as some of the sterilization techniques require a temperature greater than 100°C. Next, compatibility with a high-level disinfectant was necessary. From the Cidex compatibility list [31], it was noted that several of the FDM materials are compatible yet none of the SLA materials are. Lastly, in order to check whether the material was non-toxic, a view of the Materials Safety Data Sheet (MSDS) for each material was examined [30]. Stability and toxic information was examined and showed that each material is stable under normal conditions and non-toxic. The decision tree is summarized in Figure 9. The non-toxic category will be further examined below. Therefore, from these observations and the data summarized in Table 1, FDM was the optimal choice for fabrication.

For the FDM method, 4 materials were further examined to determine the material in which the sheath would be fabricated: PC/ABS, PC-ISO, ABS-M30, ABS-M30i. PC/ABS and ABS-M30 were the only materials, which came in black. However, PC-ISO and ABS-M30i were tested under the ISO-10993 standard and were deemed biocompatible. Therefore, further toxicological information was examined from the
biocompatible materials (PC-ISO and ABS-M30i) and compared to the regular materials (PC/ABS and ABS-M30). Table 3 shows the results.

<table>
<thead>
<tr>
<th>Properties</th>
<th>PC/ABS</th>
<th>PC-ISO</th>
<th>ABS-M₃₀</th>
<th>ABS-M₃₀i</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colour</strong></td>
<td>Black</td>
<td>White, Translucent</td>
<td>Black amongst other colours</td>
<td>Natural Off-White</td>
</tr>
<tr>
<td><strong>Softening Point (°C)</strong></td>
<td>112</td>
<td>139</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td><strong>LD₅₀ Acute Oral (mg/kg)</strong></td>
<td>1800</td>
<td>500</td>
<td>5000</td>
<td>5000</td>
</tr>
<tr>
<td><strong>LD₅₀ Acute Dermal (mg/kg)</strong></td>
<td>2000 (rabbit) and Draize Skin test for 24 h exposure is zero</td>
<td>2000 (rabbit) and Draize Skin test for 24 h exposure is zero</td>
<td>2000 (rabbit) and Draize Skin test for 24 h exposure is zero</td>
<td>2000 (rabbit) and Draize Skin test for 24 h exposure is zero</td>
</tr>
</tbody>
</table>

**Table 3: Toxicological Information for the 4 materials**

LD₅₀ refers to the amount of dose given to a set of test animals (usually rats and mice) that causes death to 50% of the animals [32]. The dose can be administrated dermally (LD₅₀ Acute Dermal) or orally (LD₅₀ Acute Oral). The Draize Skin Test places the substance to-be-tested near the eye of a rabbit and its effects are observed [33]. Therefore, the higher the dose number, the more non-toxic it is. From the table, the LD₅₀ Oral value for PC/ABS is actually higher than PC-ISO. They have similar results for the LD₅₀ Dermal Values. Next, The LD₅₀ values for the ABS-M₃₀ and the ABS-M₃₀i are similar also. Therefore, from these results, it can be said that the 4 materials were similar in toxicological data.

Material PC/ABS was selected for sheath fabrication as it had a higher tensile strength than ABS-M₃₀. However, sometimes ABS-M₃₀ was also used if the fabrication did not have any in stock. Both were interchangeable but PC/ABS was the preferred material. The tensile strength will be further examined in section 3.7.
3.4 Fiber Insertion

3.4.1 Fiber Placement Technique

Two methods were examined for placing the fiber optic cables onto the sheath. The first method examined used holes fabricated into the sheath through which the fibers could be drawn, while the second used grooves on the outside of the sheath.

3.4.1.1 Holes

Holes, with a diameter of approximately 0.6 mm would need to be fabricated onto the sheath. Since the fiber optic cables had a diameter of 0.35mm, a 0.6 mm diameter for the holes was necessary. 0.6 mm was determined to account for any irregularities that the fiber might have and to have freedom in threading the fibers through the holes. However, two main challenges presented themselves with the holes.

1. Since most printing techniques had a resolution of a minimum of 0.3 mm and most techniques suggested a minimum thickness of 0.7 mm, it would be very difficult to fabricate holes that would not fail. After getting these holes printed, the holes either did not even present themselves, or they were not complete. They were irregular throughout their lengths.

2. The second challenge was that the fiber would be need to be bent 90° to allow for the tip of the fiber to protrude out of the sheath (Figure 10). At this time we decided to use side-firing fibers. However, it was nearly impossible to thread the fiber through the hole, as it was very irregular and incomplete. Furthermore, to allow the light to shine out, a clearing of the sheath would be needed where the fiber tip is located. This was once again difficult to do due to the limitations of the printing techniques.

Due to these challenges, the idea of fabricating holes was abandoned.
3.4.1.2 Grooves

Next, grooves were considered to act as a threading template for the fibers. They were considered, as they would not be completely within the sheath, being on the surface. This had the advantage of fabrication with better stability. Therefore, a couple of test sheaths with these grooves were fabricated. The groove diameter was 0.5 mm.

Fibers for light delivery and collection were side-firing, using fibres with a 0.33 mm core and right-angled prisms glued to the end. (FiberTech Optica, Waterloo, ON) In order to embed the fibers into the sheath, grooves were incorporated into the design of the sheath. However, to determine the ideal groove diameter and how much of the groove’s diameter is within sheath, test blocks were made with varying groove diameters and different percentage of diameters which were within the sheath (Figure 11).
To determine the calculations for the percentage of the groove within the sheet, Figure 12 shows an example.

![Figure 11: Example of the specifications of a groove](image)

From Figure 12, it can be noted that the diameter of the groove was 0.65 mm and the distance from the center of the groove to the center of the sheath was 12.2 mm. The distance from the edge (highlighted portion) to the center of the sheath was 12.5 mm. The position of the edge is situated so that half of the groove lies within the sheath and half outside, making it 50% within the sheath. The radius at 50% of the groove is 0.325 mm. However, in this example, the current radius that is not submerged in the sheath would be 0.3 mm (12.5 – 12.2). The difference between this value and the radius of 50% was 0.025. This is the part of the diameter that is not within the sheath.
Therefore,

\[
\frac{[\text{total diameter (0.65) – part not within sheath (0.025)}] \times \text{total diameter (0.65) * 100}}{\text{total diameter (0.65)}} = 96.15\%
\]

This methodology was applied to other holes to determine the first study, as indicated in Table 4.

<table>
<thead>
<tr>
<th>Holes Number</th>
<th>Distance from Centre at 50% mark (mm)</th>
<th>Diameter (mm)</th>
<th>Current Distance from Center (mm)</th>
<th>Radius at 50% (mm)</th>
<th>Diameter Difference from 50% to current (mm)</th>
<th>Diameter that is out % of Hole in</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.5</td>
<td>0.65</td>
<td>12.5</td>
<td>0.325</td>
<td>0</td>
<td>0.325</td>
</tr>
<tr>
<td>2</td>
<td>12.5</td>
<td>0.65</td>
<td>12.2</td>
<td>0.325</td>
<td>0.3</td>
<td>0.025</td>
</tr>
<tr>
<td>3</td>
<td>12.5</td>
<td>0.65</td>
<td>12.25</td>
<td>0.325</td>
<td>0.25</td>
<td>0.075</td>
</tr>
<tr>
<td>4</td>
<td>12.5</td>
<td>0.7</td>
<td>12.2</td>
<td>0.35</td>
<td>0.3</td>
<td>0.05</td>
</tr>
<tr>
<td>5</td>
<td>12.5</td>
<td>0.7</td>
<td>12.25</td>
<td>0.35</td>
<td>0.25</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**Table 4: Methodology applied for different diameters of holes**

Table 5 shows the different variations of diameters and the percentage of the hole within the sheath along with the key observations noted.
From the results in table 4, it was concluded that the depth of the grooves had to be approximately greater than 80%. There were some limitations with this study however. The test blocks did not look into how well the fibers would fit when the fiber path was curved. Secondly, they did not look into grooves with different diameters. They only examined varying depths. Therefore, a more comprehensive study was done with different test blocks.

**Table 5: Observations taken from initial groove study**

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>% of Hole in</th>
<th>Takeaway Observations</th>
<th>Fibers completely submerged in groove?</th>
<th>Good fit?</th>
<th>Fiber leaves the groove while threading?</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.65</td>
<td>50</td>
<td>Unable to thread the wires</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>0.65</td>
<td>96.154</td>
<td>good fit, fibers were completely submerged in the groove, no part of fiber was sticking out of the surface</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>0.65</td>
<td>88.462</td>
<td>similar observations as above</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>0.7</td>
<td>92.857</td>
<td>similar observations as above</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>0.7</td>
<td>85.714</td>
<td>similar observations as above</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
From the second test, the bending ratios were applied as per the drawing in Figure 13.

![Figure 12: Example of a groove drawing for second groove study](image)

Each groove’s vertical length was 60 mm. However, each fragment was an arc of a specific radius, in this case 160 mm. Similar drawings with different radii were laid side-by-side. These drawings were then projected on to the bisected cylinder shape that was used.
These test blocks (Figure 14) were made with different diameters and different bending ratios but similar depths. The similar depths were necessary to show consistency in the testing. Table 6 shows the results for the second study.

Figure 13: Test block for second study
From these results, it can be concluded that the diameter has to be greater than or equal to 0.55 mm and the bending ratio can go down to approximately 160 mm. However, the bending ratio depends on the path of the groove. During the insertion of the fibers, various methods, discussed later, were utilized to ensure the fibers stay in the groove during threading. Therefore, the bending ratio can go down further to the accepted factory value of 115 mm. The bending ratio is characteristic of the fiber optic cable and is given from the vendor.

To summarize, based on the two studies, it was determined that:

- The percentage of the groove within the sheath had to be greater than 80%
- The diameter of the groove had to be greater than or equal to 0.55 mm
- The bending ratio could go down to at most 115 mm

The final groove specifications chosen were with a diameter of 0.65 mm and the groove within 88% of the sheath. For testing purposes, Figure 15 shows the groove

<table>
<thead>
<tr>
<th>Hole Type</th>
<th>Diameter of groove (mm)</th>
<th>Bending Ratio's Radius (mm)</th>
<th>Fibers completely submerged in groove?</th>
<th>Good fit?</th>
<th>Fiber leaves the groove while threading?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.6</td>
<td>240</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>0.6</td>
<td>160</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>0.6</td>
<td>115</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>0.55</td>
<td>240</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>0.55</td>
<td>160</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>0.55</td>
<td>115</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>240</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>160</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>115</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>0.45</td>
<td>240</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>0.45</td>
<td>160</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>0.45</td>
<td>115</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Table 6: Results of the second groove study
configuration for this project. This configuration can change later on to provide the optimal scatter and detection resolution. One point to note, the following configuration did not employ any bending of the groove path and thus, no bending ratio values were used.

![Groove Configuration](image)

**Figure 14: Groove Configuration**

### 3.4.2 Fiber Insertion Jig

In order for the fibers to be successfully inserted, control of three variables was required: translation of the fibers, rotation of the fibers and rotation of the sheath.
To guide and position the fibers into the grooves, a custom jig was designed and assembled consisting of a translational stage for fiber translation (Model 562-XYZ, Newport, Irvine, CA), a rotating disk (Model BUP-2, Newport, Irvine, CA) for sheath rotation and a fiber rotator (Model HFR007, Thorlabs, Newton, NJ) plus custom parts to hold the sheath in place (Figure 16, 17 and 18).

In order for the sheath to be easily placed and rotated using the item in Figure 14a, a custom model had to be made through SolidWorks. Figure 17 shows the SolidWorks model, which was then fabricated through a 3D printer.
Figure 18 shows the initial setup of the entire jig.

Figure 17: Assembly used to guide the fibers into the sheath

UV cured, optically transparent epoxy (Model OG603, Epotek, Billerica, MA) was used to fix the fibers onto the sheath [7] since this provided flexibility in controlling when and where the epoxy was applied. This epoxy was further compatible with the high-level disinfectant mentioned earlier.

3.4.3 Fiber Insertion Method

The following steps were taken to put the fibers into the groove:

1) Thread fiber into the groove,
2) Clamp the fiber,
3) Adjust the fiber using the translational platform for greater accuracy,
4) Place epoxy onto a Q-tip,
5) With fiber in the groove, carefully apply the epoxy at different spots along the length of the fiber,
6) Place entire setup in under the UV lamp, and finally
7) Repeat steps 1-6 for all the fibers.

Figure 18a (Top Left): Placing epoxy onto Q-tip. Figure 19b (Top Right): Applying epoxy via Q-tip to sheath. Figure 19c (Bottom): Entire Jib was placed under UV lamp

Challenges and Solutions

With this method, certain challenges presented themselves. One main issue was that there was run-over epoxy from the adjacent groove. This delayed the insertion process, as the epoxy had to be cleaned before it was placed under the UV lamp. A second issue was that the fiber would not always stay within the groove when being threaded by the jig. This once again delayed the process, as the fiber had to be manually held while the epoxy hardened. Lastly, the method did not test for the rotation of the fiber.
To address these issues, certain measures were considered. To ensure there was no run-over epoxy, UV spot curing was investigated. UV spot curing would focus the UV lamp to a specific area and only harden that area. Even though there was still run-over epoxy, it could be easily cleaned after being placed under the UV lamp. Unfortunately, this technique was not available within UHN. The microfabrication center had this method however its setup was unable to accommodate the jig. Therefore, this was abandoned. A second solution that was considered was to manually block the UV lamp with a material that would allow a small portion of the UV light to go through. A piece of black plastic and a piece of wood, with UV coating, were placed over the UV lamp that had a small hole in it. However, the UV light that went through was extremely weak and produced a diffraction pattern that was unable to cure the epoxy. The solution proposed was more of a brute-force method. A napkin was used to cover up the adjacent grooves so that it would adsorb any run-over epoxy.

To combat the fiber not staying in place, rubber bands were used to secure the fibers in place. This technique worked flawlessly with the added advantage of also securing the tissue papers.

Lastly, to orient the side-firing fibers in their proper orientation, a marker was placed above the grooves, that would help to guide the fiber to reach its proper orientation. Figure 20 shows the final assembly.
3.5 Modifications

Several modifications and additions were made to the design, considering the end user and shipping and handling of the sheath.

3.5.1 Robust Fiber Management

With the current design and the method described in section 3.4.3, the fiber-optic cables do not have a point where they converge. From a handling point-of-view, that can be a problem as the loose fibers can disrupt regular handing. Furthermore, there could be inadvertent pulling and tugging of the fiber optic-cables, which can cause them to break or come out of their groove. Therefore, it was necessary to converge these fibers into a bundle so they are not free flowing. Figure 21 shows the end cap as it was designed in SolidWorks.

Figure 19: Jig with the markers and rubber bands
One of the advantages of this piece is that it bundles up all the fibers into one location. Another design aspect was that it had an attachment point to which some sort of encapsulation of the fibers can take place. This can be seen in the first viewing of Figure 21.

With the fiber in place and converged at one point, it was necessary to encase the fibers in order to protect them from the outside environment. Since the end cap had a hollow attachment piece, different means of attaching the tubing were examined and the type of tubing required.
Different attachment methods were considered. A simple option, which encompassed a nail and a screw, was examined but it was abandoned due to the small size of the attachment point. A screw in mechanism was considered but was once again abandoned as it was assumed that too much stress would be on the attachment point. The final method chosen was to use glue. Glue is easy to apply and will not cause any physical deformation of the attachment point.

Next, different casings were examined. A casing made out of metal allowed for a sturdy solution to protect the fibers but it would weigh down the entire sheath and cause an unbalance of weight. Moreover, it would shift the center of gravity of the sheath towards the casing, and that could be detrimental during handling. The option that was used was a heat shrink tube (Figure 22). The heat shrink tube was made out of plastic and its weight was not an issue. Secondly, it was very easy to slip on. When exposed to heat, the tube shrinks. Therefore in this case, it would grab onto the attachment point during shrinking. To further reinforce the attachment, the attachment point would have glue applied.

![Figure 21: Examples of heat shrink tubing](image)

### 3.5.2 Positioning relative to TRUS Probe

The current US probe fits into a custom built apparatus for motor-controlled rotation of the probe around its long axis. This allows the US probe to rotate automatically when it is in use (Figure 25a). The sheath is independent of the US,
therefore it needs some sort of attachment to the US, the custom built apparatus or to the robotic holder. An attachment was chosen with the robot. Firstly, since the robotic holder controls the rotation, directly connecting the sheath to the robotic holder would minimize the flex in positioning the sheath. Secondly, since most of the US probe is circular/oval without any edges, there were not any areas on the US probe that could be used for attachment. Figure 23 shows the attachment piece.

Figure 22: Attachment Piece

The final design added some alterations to the attachment piece where it was made to be adjustable. The adjustability helped to easily slip on the sheath and secure it to the robot holder.
3.6 Evaluation of Impact on Ultrasound Imaging

It was imperative that the sheath does not hinder the clarity of the images from the TRUS. However, two bridges were included in the design of the sheath. Due to the high number of fibers used for this study, some of the fibers ran across the ultrasound window. These bridges were added into the design to provide additional mechanical stability to the fibers. The addition of bridges can compromise the ultrasound’s (US) viewing capability as these bridges are directly over the transducer. Thus, the effects of these bridges were tested. We utilized an Ultrasound Prostate Phantom (Model 053, CIRS, Norfolk, VA) to observe these effects. A phantom mimics actual tissue as viewed from an US and with the required body structures of the prostate region to provide a realistic image (Figure 24).

![Prostate Phantom Diagram](http://www.cirsinc.com/products/all/77/tissue-equivalent-ultrasound-prostate-phantom/?details=specs)

**Figure 23a (Top): Prostate Phantom. Figure 24b (Bottom): Internal View of the phantom consisting of surrounding structures near the prostate**

The sheath was placed onto the TRUS. This entire setup was then placed into the prostate phantom. Figure 25 shows the US probe before the sheath is placed, and after the sheath is placed. Figure 26 shows the resulting image from the US probe, one without the
sheath and one with the sheath. A point worth mentioning is that Figure 22 shows a white sheath. This sheath was fabricated solely for the purposes of this method, and was not tested as a final design.

Figure 24a (Left) Probe without the sheath. Figure 25b (Right): Probe with the sheath

Figure 25a (Left): Image without the sheath. Figure 26b (Right): Image with the sheath
In order to understand the differences with the two images, a custom algorithm was developed through MATLAB, which will be further explained in section 4.3.

### 3.7 Mechanical Stress Testing

A rotation test was simulated to ensure that the sheath would not break in clinical practice. General clinical practice would include the sheath being rotated when in the rectum. The rotational test consisted of a force sensor (Tekscan, Boston, MA) and an arduino board (SmartProjects, Italy). The equipment was calibrated though the methods described in Appendix B. A custom method of applying force was used through the use of a hose clamp. Through this equipment (Figure 27), forces were applied and measured on a specific location of the sheath. These forces were then compared to the typical forces that the sheath might experience in clinical practice. After the force was applied, the sheath was rotated in a counter clockwise direction and a clockwise direction to test for any mechanical deformation that may occur.

![Arduino Board](image1)

![Force Sensor](image2)

![Hose Clamp](image3)

Figure 26a (Top Left): Arduino Board. Figure 27b (Top Right): Force Sensor. Figure 27c (Bottom): Hose Clamp
Patti et al. performed anorectal manometry in patients with Chronic Anal Fissure. They calculated the Maximum Resting Pressure and the Maximum Squeeze Pressure (MSP). The highest recorded MSP was 120 mmHg [20] in the anal cavity. This number was found to give an idea of the pressures that the internal anal sphincter muscle imparts. This muscle is the primary means of contact for the sheath as it is inserted into the rectum. For the purposes of the rotational test, 150 mmHg was used instead of 120 mmHg. A safety factor of 30 mmHg was added to account for any additional pressures the sheath may encounter.

To allow for better comparison, mmHg was converted to kilopascal’s.

\[ 1 \text{ mmHg} = 0.13 \text{ kPa} \]  

Using equation 1, 150 mmHg is equal to approximately **20 kPa**. First, it is worth noting that the 20 kPa is a much smaller value than the respective tensile and flexural strengths of PC/ISO and ABS-M30 [30]. Therefore, theoretically, any deformation is not expected during this test.

Next, it was found that the length of the internal anal sphincter is approximately 4 cm in an adult male [34]. With this, the assumption can be made that the muscle contacts the sheath at only 40 mm portions. A 40 mm segment was isolated within the sheath and its surface area was calculated (Figure 28). This value could be directly calculated from the SolidWorks sketch and was found to be **22 cm²**.
At this time, a pressure value is known (20000 Pa) and an area value is known (0.002225 m$^2$). These values can be combined to find out Force, as stated per equation 2.

$$F = P \times A$$  \hspace{1cm} (2)

Where

- $P$ is pressure (Pa),
- $A$ is area (m$^2$)
- $F$ is force (N)

Therefore, using this equation with the values of pressure and area, a force of 44.5 N.

This force gives us the total force that can be applied to the overall 40 mm segment of the sheath. However, the force sensor is much smaller (Figure 29).
From the technical specifications of the force sensor, its contact point had a diameter of 9.53 mm. The surface area of a circle is calculated as follows:

$$SA_{\text{Circle}} = \pi r^2$$  \hspace{1cm} (3)

From equation 3, the surface area of the contact point came out to be $0.71 \text{ cm}^2$. To understand the relationship between the total surface area and the contact point surface area, the total surface area was divided by the surface area of the circle to get a ratio between the two. This value was 31.2. Since the variables of equation 2 are proportional to each other, this ratio can be used to determine the force that would be present on the force sensor. Dividing this ratio with the total force, a force of 1.43 N is calculated. Therefore, from a theoretical point-of-view, if the sheath can withstand an applied force of 1.43 N then it should not break during clinical practice.
4 Results and Discussion

4.1 Approaching the Final Design

4.1.1 Evaluation of Silicone and Plastic-Based Designs

Initial test to determine the feasibility of using plastic-based designs or silicone-based designs and how they impacted the viewing compatibility of the ultrasound were examined.

After the silicone was mixed and hardened, it was placed over the ultrasound and the resulting image of the prostate phantom was viewed. Similarly, a polycarbonate material was placed on the ultrasound. Furthermore, smaller portions of the two mentioned materials were placed on the US that occluded the transducer only slightly, as most of the window was left free. Figure 30 shows the resulting images.
When the silicone or the polycarbonate material covered the entire US transducer, the image contrast was poor, with the prostate barely visible. It was difficult to view the boundaries of the prostate. The only reason Figure 30b is somewhat clear is because the US transducer was held forcefully against the phantom with a lot of US gel applied, a
practice that is impractical in clinical applications. Image contrast in Figures 30c and d was reasonable, as it was fairly easy to distinguish between the boundaries of the prostate. Therefore, it was concluded that the final design could not completely occlude the US transducer.

4.1.2 Final Design

Figure 30a (Top): Different angles of the final design. Figure 31b (Bottom): Final design on SolidWorks
The final design incorporates the design modifications mentioned in section 3.4. Furthermore, it uses the PC/ABS material and has the US transducer fairly free, aside from the two bridges. Lastly, the largest cross-sectional distance from one end to another of the sheath was 24.68 mm.

The current design went through minor modifications to structurally and aesthetically reinforce the design. The design (Figure 32) had the following modifications:

- The cone shaped hole in the cap is now dome shaped and realigned to allow for full insertion of the probe
- The transducer windows have rounded corners for added strength/stress resistance
- The fiber collector at the back now has a curved opening that matches the profile of the sheath so that it guides the fibers
- The clamp is now in two pieces, the arm opens up to a fork and the clamp extends to a tab, the tab slides into the fork and then twists into position, a peg and slot system holds it in place.
- All edges (wherever possible) have been smoothed, rounded or curved in order to decrease stress concentration and manufacturing defects, minimize the effect of jagged edges scratching up the US probe, and improve the aesthetics.
- The largest diameter is 24.77 mm
Figure 31: Final Design

4.2 Fiber Insertion

Figure 33 shows the fiber optic cables inserted into the sheath as mentioned through the method described in 3.4.3. This method was done manually as each fiber optic cable was inserted individually using the jig. Figure 33 does not show the rotation of the fiber optic cable in its proper orientation.
Figure 32: Sheath with the fibers attached

Figure 34 shows the final product with the recommended changes, mentioned in section 3.3.3.1, made with the fiber insertion method.

Figure 33: Final product showing the orientation of the side-firing fiber as it leaves orthogonal to the surface of the sheath

It can be noted the through the fiber insertion method, the side-firing fiber is oriented orthogonal to the sheath’s surface. Obviously, since this was done manually through the use of the fiber rotator, there was human error involved in evaluating the proper orientation of the fiber. However, this error (approximately +/- 3°) was minimized due to the marker that was placed above the jig. Moreover, each fiber was rotated several times to the same location to show redundancy and limited this error.
4.3 Evaluation of Impact on Ultrasound Imaging

The addition of the bridges added a shadow on the US image. To evaluate the effects of the shadow on the US image, the contrast of the image was considered. If the contrast of the image between hollow space and body structures is high enough within the shadow areas and the non-shadow area, then the addition of the bridges would be justifiable. In order to do this, a shadow region of the US’s image was isolated along with a non-shadow region which essentially depicted similar information as the former image. Figures 35 and 36 show these regions. These regions were isolated in MATLAB with the corresponding code in Appendix A.

Figure 34a (Top): TRUS image with the sheath on. Figure 35b (Bottom): TRUS image indicating the rectangles used
To compare the differences in the contrast, an average contrast value was determined for each horizontal pixelated line in the image. First, two rectangles were segmented; one covered the shadow area on the TRUS image and the other, of similar size, that covered a non-shadow area (Figure 36). Then, within each rectangle, the US contrast in each row was averaged along the vertical extent of the rectangle, starting from the top of the rectangles (Figure 37 shows another explanation of this method). Figure 38 shows the results of the averaging algorithm.
The drop in contrast within the shadow region versus non-shadow region was measured. The TRUS is required primarily to define the borders of the prostate (and to
guide the needle insertion). Therefore, if the drop in contrast is acceptable to the physicians using this device, then the effect of the bridges should not be critical for clinical use.

The change in contrast was measured by comparing the change in signal from the baseline to the shadow. It was observed that the ratio between arrow 1 and arrow 3 was ~6 and the ratio difference between arrow 2 and arrow 3 was ~3. This indicated that in the bridge region there was a 50% contrast drop. However, within Figure 37, the ratio of 3 could still differentiate the prostate boundaries. Furthermore, after discussing these results with the scientists who have experience in the clinical application of this technique, they were satisfied of this 50% drop and its practicality within the clinical practice, especially if it was limited to a small zone along the length of the transducer.

4.4 Mechanical Stress Testing

4.4.1 Rotational Test I

In order to test the whether or not the sheath can withstand 1.43 N of force applied, a simple experimental setup was built. The force sensor was placed onto the sheath near the proximal end (Figure 39). A force was applied at the sensor via the hose clamp. It is worth noting that in order to simulate actual muscle, certain measures were taken:

1. Silicone rubber was placed on top of the sheath. This helped to distribute the force more evenly throughout the sheath. Due to its elastic nature, silicone has the property that it can store and distribute energy [23]. Therefore, by adding silicone to the sheath, it would have the added effect of adding pressure from all sides. This is closer to clinical practice, as the internal anal sphincter surrounds the anal canal [34].

2. In order to further simulate actual clinical practice, US gel was added. The coefficient of friction of muscle is approximately 0.29-0.36 [20]. Although
silicone rubber’s coefficient of friction can range from 0.25 – 0.75 [35], US gel was added to ensure the coefficient of friction was low (under 0.25).

The overall setup including the silicone can be seen in Figure 40.

![Figure 38: Placement of force sensor](image-url)
Next, the entire sheath was attached to ultrasound robot via the attachment piece. This can be seen through the SolidWorks Figures 41 and 42.

Figure 39: Sheath with silicone and US gel

Figure 40: Attachment of the sheath to the robotic holder in SolidWorks
Next, the sheath was rotated in a clockwise and counter clockwise direction to mimic actual practice. The user manually rotated the robot holder to get this result. Due to this rotation, the hose clamp naturally moved with the rotation. Therefore, the hose clamp was fixed with a handle and held in position manually to ensure there was no rotation of the hose clamp (Figure 43).
After each rotation sequence, the hose clamp was tightened and the force acting upon the sheath was measured. This was done 5 times for 5 different forces. Table 7 summarizes the results of this experiment.

<table>
<thead>
<tr>
<th>Rotation Sequence</th>
<th>Lower Force (N)</th>
<th>Higher Force (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.48</td>
<td>3.53</td>
</tr>
<tr>
<td>2</td>
<td>4.01</td>
<td>4.05</td>
</tr>
<tr>
<td>3</td>
<td>5.01</td>
<td>5.35</td>
</tr>
<tr>
<td>4</td>
<td>6.21</td>
<td>6.31</td>
</tr>
<tr>
<td>5</td>
<td>7.3</td>
<td>7.35</td>
</tr>
</tbody>
</table>

Table 7: Results of the rotational test

Initial viewing of these results indicated that the sheath can handle forces up to 7.35N. This is obviously much higher than the 1.43 N theoretical force. Furthermore, during the rotation, no deformation or any mechanical strain occurred to the sheath.
Before the rotation, the force was measured. The code was altered to show the entire range of what was being read on the force sensor throughout the duration of the rotational sequence. This was important to note, since due to the rotation, a constant force was not delivered. Experimental errors such as irregularities of the hose clamp, and minor displacement of the force sensor from its initial location led to these errors. However, in the grand scheme of this experiment, these minor errors did not play a huge role, as the experiment proved the sheath could handle forces greater than 1.43 N. It would be extremely rare that the sheath may experience a force that would reach up to 7 N.

4.4.2 Rotational Test II

However, during one test method, force was applied on the sheath and it broke. It was discovered that the sheath had its weak points, which were the bridges of the cap. Therefore, an additional rotational test was done with a slightly altered design (Figure 44). This design had a covered bottom portion, thus reinforcing the sheath. Furthermore, the bridges were made thicker to give mechanical strength in that region.

The rotational test was done in a similar fashion to the method in 4.4.1. However, a slight modification was made in that the user did not hold the post holder; instead it was mounted onto the platform. Furthermore, a condom was applied. Similar forces in Table 6 were applied without any breakage to the sheath.
4.5 *Light Delivery and Detection*

A final test was completed to show that the fibers are able to act as a detector. The sheath was placed in a dark room. The proximal end of the side-firing fiber was connected to a light detector, which in itself was connected to a computer (Figure 45). Table 8 summarizes the results.
Initially, the sheath picked up other light sources within the room to give the small readings. However, when a laser was moved closer to the sheath, the higher readings were given. This basic test was sufficient enough to prove that the sheath and its fiber optic cables were able to act as a detector.

It is worth noting that, since it could be visually observed that the fiber-optic cables were giving out light in section 4.2, that test indicated that the sheath could also work as a source.

<table>
<thead>
<tr>
<th>Test Number</th>
<th>Reading with only background light – no source fibre (mW)</th>
<th>Reading with light source (mW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.31</td>
<td>2.80</td>
</tr>
<tr>
<td>2</td>
<td>0.22</td>
<td>1.40</td>
</tr>
</tbody>
</table>

Table 8: Summary of light delivery
5 Conclusions

5.1 Summary of Specifications

Through the methods and materials, the design specifications were identified and appropriate values were found. These can be seen summarized in Table 9.

<table>
<thead>
<tr>
<th>Main Specification</th>
<th>Detailed Specifications</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Material</td>
<td>Colour</td>
<td>Black</td>
</tr>
<tr>
<td></td>
<td>Sterilization</td>
<td>Cidex (Disinfectant)</td>
</tr>
<tr>
<td></td>
<td>Method of Production</td>
<td>FDM</td>
</tr>
<tr>
<td></td>
<td>Biocompatibility</td>
<td>LD &gt; 1800</td>
</tr>
<tr>
<td>Fiber Placement</td>
<td>Placement Medium</td>
<td>Custom Designed Method</td>
</tr>
<tr>
<td></td>
<td>Placement Method</td>
<td>Grooves</td>
</tr>
<tr>
<td>Design Modifications</td>
<td>Conformity and Positioning relative to TRUS probe</td>
<td>Custom Attachment Piece</td>
</tr>
<tr>
<td></td>
<td>Robust Fiber Management</td>
<td>End cap and encasing</td>
</tr>
<tr>
<td>Imaging</td>
<td>Effect of Bridge on Contrast</td>
<td>50% reduction</td>
</tr>
<tr>
<td>Mechanical Stress</td>
<td>Withstand Anal Pressures</td>
<td>Yes, up to 7 N</td>
</tr>
</tbody>
</table>

Table 9: Design Specs and Results

The material was deemed biocompatible as long as the LD value of the material was above 1800 mg/kg. The colour needed to be black and it the material did not need to be sterilized, a disinfectant was enough. The method of production was FDM. A custom placement method was derived for placing the fibers onto the sheath and it was done through grooves previously fabricated. Next, the effects of the bridge was tested and found it there was approximately a 50% decrease in contrast. This was acceptable. Lastly,
anal pressures were tested to show that the sheath could withstand up to 7 N of pressure, whereas typical anal pressures are in the 1 N range.

5.2 Contributions

We have shown that it is possible to integrate DOT technology with a standard trans-rectal ultrasound probe with minimal impact on ultrasound image quality. It was essential to investigate different materials for the purposes of this study and complete a comprehensive groove study. After these, we were able to create and fabricate a device that can be used in further practical testing procedures.

The results presented here can help to give a baseline of integrating different imaging modalities, especially ones that are used trans-rectally. The design of the sheath can be altered to fit with other modalities, not only ultrasound.

This thesis also investigates different ways of attaching small fibers onto a sheath. Once again, future projects that need some sort of method of attachment can consider the methods used in this thesis as an example.

This thesis investigates biocompatible materials and gives justification on what sorts of materials can be used with the human body. Thus, for testing purposes, the materials researched in this thesis can be used for future studies involving the human body.

5.3 Limitations

There are several limitations on the sheath as it stands right now. First and foremost, the sheath has not been tested under live tissue. All of the tests have only
mimicked actual practice. Actual contractions of muscle applying stresses to the sheath may result in a complex pattern of applied stresses, something that was not tested during the course of this project.

Another limitation arises from the perceived clarity of the ultrasound images. When testing with the prostate phantom with the sheath on the US, it was in a controlled environment. Furthermore, to get a clearer image, the prostate probe was held forcefully against the phantom. This practice is not commonly practiced in clinical practice. The phantom had the added benefit of reproducibility of the images. However, in clinical practice, everyone’s anatomy is different. Therefore, this can potentially cloud the US images.

A fundamental limitation of the device right now is related to its biocompatibility. Certain measures were taken place to ensure the material chosen is non-toxic. However, all this work was done theoretically. Even though it is very unlikely, the biocompatibility might not pass any Health Canada regulations. Furthermore, it could adversely affect the patient during practice. The latter limitation is something that is possible for any medical device however the former limitation can be huge roadblock for getting the sheath approved during prostate cancer treatment.

5.4 Future Directions

Different modifications can be made with the sheath to make it more mechanically sound. Some proposed ideas that were completed but not tested are presented in Figure 47.
The no cap design takes away the stresses on the cap, and limits the chances of failure on the cap’s handles.

Further design alterations can include adjustability with the attachment to the robot. The sheath might not fit securely if the attachment piece is rigid, so some sort of flexibility or adjustability, perhaps in the form of a plunger, should be added to the attachment piece so it is easy for a clinician to slip on the sheath while in practice. This would be in addition to the attachment design right now.

The rotational test was very preliminary just to prove that it can handle stresses acting upon the sheath. A more realistic test would include the sheath being inserted into the anal canal of animals. This would give a realistic scenario of how well the sheath reacts to tissue and rotational forces, mimicking the actual clinical practice.

Different packaging techniques need to be examined. As this sheath will be produced in large numbers, it will need to be packaged in a way that is feasible and practical.

The fiber insertion method is a manual process for the purposes of this thesis. However, in mass production it is impractical to keep it manual. Therefore, some sort of automation with inserting the fibers into the groove will need to be done.
References

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   http://www.cancer.net/patient/All+About+Cancer/Cancer.Net+Feature+Articles/After+Treatment+and+Survivorship/After+Treatment+for+Prostate+Cancer%3A+Managing+Side+Effects


   http://www.prostatecancer.ca/Prostate-Cancer/Prostate-Cancer/Statistics


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   http://www.pacificbiolabs.com/testing_biocompatibility.asp

http://www.solidworks.com/sw/support/software-training-certification.htm


http://www.ccohs.ca/oshanswers/chemicals/ld50.html

http://animalrights.about.com/od/vivisection/f/DraizeTest.htm

http://www.dartmouth.edu/~humananatomy/part_6/chapter_36.html


Appendix A – MATLAB code for Ultrasound Contrast Study

Code for Ultrasound

clc;
clear all;

%% reading the image

baseLinePic = imread('image.bmp');
response = 'n';
while response == 'n' % choosing the other picture
    filename = uigetfile;
    % brdg1Pic = imread('20121017_122107_NoID_0000.bmp');
    brdg1Pic = imread(filename);
    imshow(brdg1Pic);
    response = input('Is this the right file (y/n)', 's');
end

baseLinePic = baseLinePic(40:480, 200:640);
brdg1Pic = brdg1Pic(40:480, 100:640);

figure(1);
imshow(baseLinePic);
title('Baseline Picture');
axis equal;

figure(2);
imshow(brdg1Pic);
title('One bridge');
axis equal;

pause on;
pause(3);
close all;

%% Selecting using summation method – using ginput

brdgMap1 = fndIntensityMap(brdg1Pic);
baseMap = fndIntensityMap(baseLinePic);

plot(intMap1);
hold all;
plot(intMap);
xlabel('Distance from initial click to final click (in pixel)');
ylabel('Average Intensity Values');

function [ intensity ] = fndIntensityMap( picture )
% This function looks at a specific user selected region of interest and finds its
% intensity map

% This part uses the improfile method to find the intensity
% imshow(picture);
% intensity = improfile;

imshow(picture);
axis image;

[x,y] = ginput(2);

% p = ginput(2); %user selects a region
% sp(1) = min(floor(p(1)), floor(p(2))); %xmin
% sp(2) = min(floor(p(3)), floor(p(4))); %ymin
% sp(3) = max(ceil(p(1)), ceil(p(2))); %xmax
% sp(4) = max(ceil(p(1)), ceil(p(2))); %xmin

ROI = picture(y(1):y(2),x(1)-10:x(1)+10); %all of the x coordinates and part of the y are chosen
%ROI = picture(sp(2):sp(4), sp(1):sp(3));
figure;
imagesc(ROI);
axis image;
colormap(gray);
title('Section of US image');
ylabel('Distance from initial click to final click (pixel)');

pause(10);

intensity = sum(ROI,2); %summation of those pictures indicate an intensity
Summary of Code:

Main Code:

The code takes a predetermined baseline picture, one that has no shadows. Then it asks the user to select an image with a shadow. The images are then adjusted to show the relevant information. Then the image is passed onto the function “fndIntensityMap”.

Function fndIntensityMap:

The function asks the user to select a region of interest that will used to find the contrast within the image from top to bottom. After the user selects a point, the code creates a rectangle based on the location of the user and isolates that rectangle and the corresponding image information. Then each row of the rectangle is average to calculate an overall contrast value. These values are then plotted in a bar graph.
Appendix B – Rotational Test Equipment Calibration

Force Sensor Calibration

The force sensor needed to be calibrated before use. 4 items found in the lab were used to calibrate the sensor. These items had a diameter small enough to fit the sensor and they had different weights associated with them. These items were: a rod, a big piece, a large drill bit and a smaller drill bit (Figure 48).

Figure 46: Different pieces used for calibration of force sensor

First, the exact mass was measured out in grams using a weight scale. The weight was converted into Newtons by multiplying it by 9.8, the acceleration of gravity according to the equation:

$$F = mgh$$  \hspace{1cm} (4)

Where

- $F$ is the force or weight in Newtons,
- $m$ is the mass,
- $h$ is the height and
- $g$ is the gravity.
In this case, the \( m \) and \( h \) are considered a weight value and multiplying by \( g \) gives the weight in Newtons.

After that, each piece was individually placed onto the force sensor and its analog output was read. This will be further explained in the next section, Setup of the Force Sensor. Table 10 summarizes these results.

<table>
<thead>
<tr>
<th>Piece</th>
<th>Weight (grams)</th>
<th>analogRead (resister 2)</th>
<th>Weight (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rod</td>
<td>378.73</td>
<td>320</td>
<td>3.14</td>
</tr>
<tr>
<td>Big Piece</td>
<td>239.45</td>
<td>220</td>
<td>2.16</td>
</tr>
<tr>
<td>Drill Bit</td>
<td>106.43</td>
<td>143</td>
<td>1.40</td>
</tr>
<tr>
<td>Smaller Drill Bit</td>
<td>58.88</td>
<td>78</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Table 10: Summary of the calibration results

The analogRead (as the dependent variable) and the Weight (N), as the independent variable, were plotted against each other on a graph. A line of best fit was found to determine the relationship between the two variables (Figure 49). This was done in Microsoft Excel.
This equation was then used in the program code to determine the force applied to the sensor during the rotation test.

Setup of the Force Sensor

The force sensor was combined with the Arduino microprocessor board. The entire set up is shown in Figures 50 and 51.
Figure 48: Schematic of the proposed setup

http://bildr.org/2012/11/flexiforce-arduino/
The force sensor was connected to the Arduino board with a 1M resistor in the middle. This resistor’s purpose was to create a voltage divider so that the Arduino could actually sense a voltage drop. If the resistor was not there, all the voltage would have been used on the force sensor and the analog input pin would read a voltage of zero. However, since there is a big resistor, most of the voltage will be dropped on that resistance, therefore enabling tracking of any voltage changes due to the force sensor itself. The 1M was chosen to match the sensitivity required for our test. Higher resistance leads to lower sensitivity.

The Arduino was then connected to a computer. The Arduino software was downloaded from Arduino.cc and installed. The following code was used to obtain the force values:

```
int flexiForcePin = A0; //analog pin 0
```
void setup()
{
  Serial.begin(9600);
}

void loop()
{
  int flexiForceReading = analogRead(flexiForcePin);
  double newtonReading = flexiForceReading * 0.0134 - 0.6368;

  Serial.println(newtonReading);
  delay(250); // just here to slow down the output for easier reading
}