

A Design of a Novel Device for Fine Needle Aspiration

A Major Qualifying Project Report

Submitted to the Faculty of Worcester Polytechnic Institute

In Partial Fulfillment of the Requirements for the Degree of Bachelor of Science by:

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WPI

Abstract

This report describes a novel cell collection device for Fine Needle Aspiration (FNA). FNA is a proven yet physically awkward technique to collect cells from suspect tumors located near or at the skin surface. Cell collection using a common disposable syringe and guided by an ultrasound is a complicated physical task and is prone to error. For this project we designed and tested two different devices; a compressive device and a spring-loaded syringe. The novel and single-handed device simplifies cell collection during a FNA. Based on performance and cost, our completed tests and analysis suggests the compressive device with integrated one-way valve is suitable and less awkward for use in FNA.

Acknowledgments

The project group would like to thank Worcester Polytechnic Institute and University of Massachusetts Medical School for providing funding and facilities necessary to compete the Major Qualifying Project. The team would also like to thank Professor Mark Norige and Professor John Sullivan for their guidance throughout the year. In addition, the team would like to extend their thanks to Dr. Adib Karam and Dr. Wannu Asavaroengchai of University Massachusetts Medical School, who provided the group with existing techniques for biopsy procedures and limitations. Also, we would like to thank Tim Baird from Nypro Medical for information regarding injection molding. Finally, the group would like to thank Erica Stults, Lisa Wall, Adriana Hera, Doug White, and Jack Ferraro, Kevin Arruda for their assistance to our project.

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Executive Summary

Biopsies are diagnostic procedures performed to extract tissue samples from a patient for subsequent analysis. The number of biopsies, specifically Fine Needle Aspiration is increasing with the number of cancer cases estimated to be 1.6 million in 2013 in the U.S. [1]. Furthermore, there are approximately 450,000 FNA procedures on thyroid conducted annually in the United States [16]. Fine Needle Aspiration (FNA) is a specific type of biopsy procedure that is minimally invasive, involving aspiration as the method of collecting cells from suspect tumors located near the skin surface and is guided by ultrasound imaging. During a Fine Needle Aspiration, a physician or surgeon uses a standard syringe to create a vacuum with a 22 or 25 gauge needle to penetrate skin and aspirate the target cells.

There are various devices on the market that are used for FNA. Currently, standard 10 mL syringes are primarily used to conduct the aspiration with the guidance of an ultrasound probe for imaging the lesion. There are devices on the market currently including the Tao Aspirator™ and the INRAD® Biopsy Syringe Gun. However, the limitations of these devices are that they are not disposable, difficult to use with one hand, and are expensive. A redesigned device would aim to address these limitations, reduce the dependence of a highly skilled physician or doctor, while considerably improving user comfort and control during the procedure. These devices also must be sterile, accurately gather tissue from target tissue, compatible with a luer lock attachment, and reduce excessive movement by the user during the procedure. The group aimed to accomplish these objectives while adhering to defined constraints of time, the 2012-2013 academic year, and budget, \$450.

To begin the team collected preliminary data using a 10 mL standard syringe to provide groundwork for the alternative new designs. The team measured pressure changes within the 10 mL syringe by pulling the plunger back a distance equal to a volume change of 5 mL in a tissue sample (rat liver). Next, the team created two designs that were prototyped, tested, and evaluated based on objectives and functions provided by the client. The first design consists of a compressible, cylindrical body, attached to a one-way valve. This device is compressed after the needle is inserted into tissue, forcing air out of its one-way valve. It generates a vacuum after its body elastically reforms. The second design is a spring-loaded syringe, which uses a mechanism

similar to a retractable pen. Upon the press of a button, a pre-compressed spring engages and forces a plunger backwards.

In designing the compressive device and the spring-loaded syringe, the team had to determine key engineering parameters. In choosing a plastic compressible body for the compressive device, the team utilized Finite Element Analysis to determine mechanical properties for the compressive cylinder by applying two equal and opposing forces below and above the cylinder. A wall thickness of 0.3 mm, internal diameter of 17 mm, and a material with a low modulus of elasticity and a high yield stress were determined as optimal for the cylinder. After researching different plastic materials, the team chose Thermoplastic Polyurethane Elastomer and Silicone Elastomer. After evaluation of Duckbill Valve and LMS Incorporated SureFlo[®] Valve one-way valve, the team selected the Duckbill Valve over the LMS Incorporated SureFlo[®] Valve, for its pressure performance.

In designing the spring-loaded syringe, the team initially determined the force required to pull the plunger in rat liver using a 20 Newton force gauge and a 10 mL standard syringe. This data was used to select an appropriate spring for the spring-loaded syringe. The spring-loaded syringe is comprised of multiple parts that were designed in SolidWorks and rapid prototyped using the Objet260 Connex Rapid Prototyping Machine, along with parts that were taken from a 25 mL Stylex syringe. All these components were combined together to function like a retractable pen.

After the two designs were prototyped the team verified and validated that these designs met the objectives and functions provided in the client statement. The negative pressure generated in rat liver during an FNA procedure from a 10 mL syringe was compared to the negative pressure generated from the prototypes. Although the prototypes were unable to achieve a vacuum similar to that of a 10 mL syringe, the client, Dr. Karam, informed the team that the acquired tissue was sufficient.

The compressive device with duckbill valve and to the spring-loaded syringe addresses the ease of use, single-handed, and disposable limitations of the existing device. Furthermore, the compressive device is more cost-efficient than the spring-loaded syringe. The compressive device provides better user control for and can be used with one hand so that the physician can use the other hand to maintain a visual with an ultrasound probe throughout the procedure. Validation of each of these design features yielded qualitative and quantitative results proving

most of the design objectives were met. The Thermoplastic Polyurethane Elastomer compressive device attached to a duckbill was chosen as the final design because it provides an efficient, versatile, and user-friendly method for Fine Needle Aspiration.

Chapter 1: Introduction

Biopsies are very common cancer diagnosis procedures utilized worldwide. Biopsies can detect whether abnormal lesions on the body are cancerous. The main purpose of biopsy procedures is to detect cancer. There are approximately 450,000 procedures performed annually in the United States [16]. Fine needle aspiration (FNA) is a widespread technique used to obtain samples from the suspicious lesion. Ultrasound imaging is used to accurately guide the needle placement into the lesion within the surrounding tissue. Ultrasound use is important to locate small lesions below the surface of the skin. FNA is considered a minimally invasive procedure that involves aspiration as a method of collecting tissue samples from the targeted lesion. Fine needle aspiration has various advantages and disadvantages. This procedure is quick, inexpensive and a fairly accurate way to help determine if a lesion is cancerous. However, one of the drawbacks of this procedure is that the accuracy of the cells and tissue collected is based on the experience of the doctor. Currently, a displaced plunger volume of 5 mL in a 10 mL syringe creates enough suction for a doctor to collect enough cells. Often, this procedure is conducted three times to ensure that an adequate sample is collected.

The current devices on the market that assist FNA procedures are inefficient, as they are not user friendly, expensive, and are additive devices that are attached and detached to current standard syringe. These devices are difficult to use with one hand, which can compromise the quality of sample received. There are various devices on the market today that try to improve the efficiency of FNA such as the Tao AspiratorTM, INRAD[®] Aspiration Biopsy Syringe Gun, SuperCoreTM, Reciprocating[®] Procedure Device, and Cameco[®] Syringe Pistol [2, 16, 19, and 21].

The goal of this project was to design and prototype a device for Fine Needle Aspiration procedures that will improve the efficiency of FNA, which can assist doctors in achieving better quality of sample. To complete the Major Qualifying Project, the team designed and prototyped two devices that would be replacements of the current syringes to conduct this procedure. After prototyping the device, the team performed tests on animal tissue.

Chapter 2: Background

2.1 Cancer

Cancer is the second leading cause of death in the United States [2]. Cancer is a class of diseases where abnormal cells divide uncontrollably and invade other tissues. When the abnormal cells compile, a tumor is formed. If the uncontrollable growth is not ceased, it can result in death. Cancer cells spread rapidly through the circulatory and lymphatic system. The American Cancer Society estimates that in the year 2012, there will be approximately 1.6 million new cancer cases, and about 600,000 will result in death [2]. The three most prevalent cancers in men are: prostate, lung and colon. In women, the most widespread cancers are: breast, colon and lung [2]. Various cancers, such as skin and lung cancer can also be reduced risk with lifestyle changes. Some other cancers, such as colon cancer, can be prevented with removal of precancerous tissue. Early detection of cancer is important because the early stages of most cancers are treatable. In addition, cancer diagnosis is critical when trying to detect and remove precancerous tissue. Cancer diagnosis is essential during the cancer is in its early stages, when there is a higher chance of removing the cancer. The cancers that can be detected and diagnosed early comprise about half of all cancer cases.

2.1.1 Diagnosis of Cancer

Various tests are used to detect cancer including; biopsies, blood tests, bone marrow biopsy, chest x-ray, Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI), depending on the locations of the tumor. Biopsy is a common procedure used for detection of various cancers. Biopsy is a procedure where the physician takes a tissue sample from the mass that is thought to be cancerous. Imaging assessments, such as the CT scans, MRI and X-rays are a good way to get a visual representation of the location of the mass and the size, but it is not the best way to confirm cancer because these tests cannot distinguish cancerous cells from noncancerous cells. For most cancers, biopsy is a better way to get a diagnosis because there is examination of the potential cancer cells [9].

Along with the different types of assessments to detect cancer, there are different techniques to perform biopsies. Some examples of different types of biopsies are: Bone marrow, endoscopic and needle. Fine needle aspiration is a type of biopsy that is performed when there is a mass closer to the outer surface of the skin.

2.2 Fine Needle Aspiration

Fine needle aspiration (FNA) biopsy is a minimally invasive procedure used to collect a tissue sample. While this procedure has a wide range of applications, it is most commonly used for diagnostic purposes, specifically to check for malignancy in an abnormal cell growth and monitor the effect of treatment on a known tumor. This procedure is used to screen patients with benign growths, significantly reducing the occurrence of invasive tumor removal. The mechanism for obtaining the cells in fine-needle aspiration is the aspiration, or suction, of cells from a growth into the cannula of the needle. "Fine-needle" refers to the small width of the needle used for the procedure, generally a 22 to 25 gauge needle (0.45-0.65 mm diameter) [15]. Due to the thinness of the needle, it is a low-risk, minimally invasive procedure, and leaves a small cut that is the same size as a standard injection. In the field of pathology, FNA is a highly convenient procedure, as it has reduced the load on both doctor and patient, and has greatly reduced procedure time and costs. Before FNA existed, invasive surgery was required to obtain a tissue sample. This procedure has more risk because it is more invasive. Invasive surgeries are also more costly, and it left a significantly larger wound than FNAs. The ease and convenience of FNA have led it to become very common practice among cancer pathologists [29]. The number of FNAs done yearly across the world is not indicated in the literature, likely due to its wide range of applications and the extent of the frequency with which it is performed. Nearly every patient in developed countries with a suspected tumor or growth that can be accessed by a needle from the surface of the skin will receive one or more fine-needle aspirations. This includes tissue masses in the thyroid, breasts, genitals, liver, lungs, or any growth that can be felt on the surface of the skin. On thyroids alone, over 450,000 FNAs are performed each year in the United States, to put into perspective a commonplace of the procedure [16]. With the extent by which FNAs are performed, it is a heavily researched subject, and therefore there are a large number of papers and technological solutions with respect to FNA. The goal of the team was to improve upon the current state of FNA technology, in accordance with the client's needs.

The step-by-step procedure of fine needle aspiration is as follows. The patient is prepped for procedure on the operating table. The area on the skin where the needle will be inserted is isolated, and the immediate area is sterilized. A cytologist, surgeon, interventional radiologist, or an FNA specialist typically performs the procedure. The operator applies local anesthetic in the skin and subcutaneous tissues to the level of the target/organ. The anesthesia administered to the

patient is called Xylocaine 1% (generic name: Lidocaine HCL) and approximately 1 to 10 mL of it is given with a 25-gauge needle. Concerning release of patient, the patient can be discharged from the hospital soon after the procedure is completed. There will redness and soreness around the area the needle was inserted however, by applying an ointment the soreness and redness can be reduced. There are a variety of tools and syringe holders on the market that are specifically designed for fine needle aspiration, some of which are used commonly for FNA. The most common tool used, however, is the syringe alone.

In earlier years, FNAs were guided only by palpitation, with limited success, but when imaging technologies were introduced to assist the procedure, the accuracy significantly increased. MRI, CT scans; fluoroscopy and ultrasounds can be used to view the cell masses. A client-defined constraint is that the device must be single-handed, applies to ultrasound-guided FNA. Ultrasound-guided is the most common method, and is the focus of this project. During ultrasound-guided FNA, the operator holds the ultrasound probe in one hand, and the syringe in the other hand. Once the doctor or surgeon has an image of the growth, they insert the needle through the skin towards the target. At the beginning of the procedure the syringe needs to be at resting position, which is at the 0-cc mark. Using the ultrasound image as guidance, the needle tip is directed to an area of interest on the mass, such as a lesion. This is because the cells in a lesion have the determinate factors that the pathologist can examine to produce a diagnosis. The growths typically have a certain degree of toughness, and in this case aspiration alone may not be sufficient to separate cells from the mass. The user must move the syringe in a back-and-forth motion, so that the edge of the needle tip can gather the cells from the tissue. While moving back and forth, the user must also aspirate by pulling back on the plunger of the syringe. When the doctor is moving the syringe forwards and backwards, the angle of the needle needs to stay the same to prevent damage to surrounding tissue. There is a negative pressure created with pulling the plunger back, and fluid and cells are forced into the needle [14, 15].

As one might visualize, moving the syringe back and forth, while simultaneously pulling back on the syringe, is a difficult to perform with one hand. For this reason, the validity of the sample acquired during fine needle aspiration is dependent on the experience and skill of the doctors. Inexperienced operators have a difficult time with the maneuver, and studies have shown that they obtain a sample large enough for testing with less frequency than experienced personnel. If the mass is very dense then one may need create suction and apply until the plunger

reached the 10-cc mark [20]. Once the doctor determines adequate samples have been aspirated, they remove the syringe from the patient. The sample is ejected from the syringe either onto a wet slide or into a small sample storage container. The syringe is disposed of. To ensure enough cell samples have been acquired to complete the necessary test, aspiration is repeated twice more. A total of three syringes are used and disposed of during the procedure. Then the needle wound(s) on the patient are cleaned up, and pressure is applied to the area for a few minutes, to prevent bleeding and promote clot formation. The tissue acquired from the biopsy is sent to pathology for testing and analysis [15].

2.2.1 Advantages to Fine Needle Aspiration

Fine needle aspiration is a very useful procedure with many advantages. It is relatively quick and inexpensive, and it is fairly accurate. In addition, this procedure is minimally invasive compared to other diagnostic tests such as an excisional biopsy. It helps doctors to determine if a growth is cancerous, and prevents patients with benign growths from having to receive risky invasive surgeries to remove them. It leaves a very small wound that is quick to heal. Overall fine needle aspiration is a great procedure that has helped in the treatment of millions of people. But there is always room for improvement.

2.2.2. Drawbacks to Fine Needle Aspiration

There are a few disadvantages to fine needle aspiration. For one, studies have indicated varying accuracies of FNA in terms of sufficiently collecting a sample of the target tissue. There will always be a chance that, after three aspirations, there will not be enough cells to perform the pathology tests. In worse cases, FNA can be performed on a malignant tumor, but due to user inexperience, the wrong cells might be aspirated. These cells won't exhibit the characteristics of a malignancy, and a false-negative diagnosis may occur. This delays important treatment for the cancer patient. The inaccuracy rate of FNA can vary greatly as user experience, type of tumor, tumor location, and the aspiration device used, among other things, can affect the aspiration process [11]. The University of Nuevo Leon performed a study from 2003-2005 on the effect of user experience on FNA accuracy. They found that experienced users had an inaccuracy rate of 7.7%, and less experienced users had an inaccuracy rate three times higher at 24.8% [12]. Similar studies have been done with similar results [13, 21]. Also, the difficult maneuver of extending the plunger while aspirating can cause the unwanted movement, decreasing the

accuracy of the procedure. Also, clumsy users might inadvertently cause unnecessary tissue damage or increase wound size. There are a few devices on the market that deal with the single-handed issue, but they are mainly overly expensive or not disposable. With regards to discarding of surgical instruments, doctors prefer devices that are disposable to reduce the risk of infection.

2.3 Current Technology

In past decade or so, Fine needle aspiration has allowed doctors to detect cancer without invasive means. Detecting the presence of cancer through fine needle aspiration biopsy by obtaining tissue cells is the best technique. For many years the biopsy of the target tissue involved invasive biopsy methods, which caused pain and serious discomfort for the patients. The fine needle aspiration biopsy has reduced procedure time significantly and is simple. Complications during a FNA biopsy compared to a large biopsy are minimal are rare as the incision to obtain the tissue cells is quite minute [18].

2.3.1 Current Devices on the Market

One of the first devices used for fine needle aspiration biopsy was designed in 1998. This device was held like a pen and it would allow for a comfortable grip in a stable position. Some of the advantages include that it can be operated with one hand. It can provide sensitive and accurate needle placement. Inserting the needle into the lesion and releasing the trigger, which creates the vacuum in the syringe, obtain the tissue cells. However, this device has many drawbacks. This device is made from steel and is designed to fit a 10 ml syringe. Also this device was not disposable and thus required autoclaving after use [19].

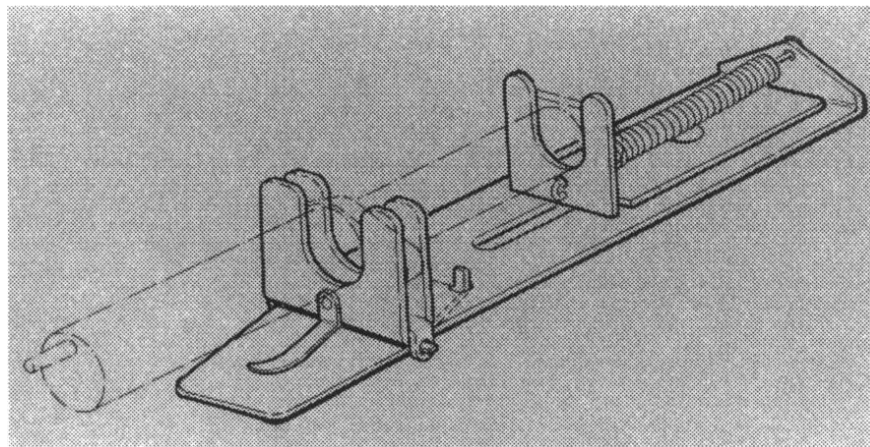


Figure 1: Diagram of the device in resting position [19]

The second device that was used for fine needle aspiration biopsy was the INRAD[®] Aspiration Biopsy Syringe Gun [3]. This device had many advantages from easy, one-handed use, lightweight, and fits into palm for better control during aspiration. Its size and shape increased tactile sensitivity during procedure. The syringe gun was designed to work with a Becton, Dickinson and Company (BD) 10 mL syringe. This device however is reusable and thus would not meet the requirements of this project.

Another device that is currently on the market is the SuperCore[™] made from Angiotech [23]. The Supercore[™] is a semi-automatic, lightweight instrument that can be easily maneuvered during biopsy procedure. It can be operated with one hand. There are numerical centimeter markings on the device to facilitate in the precise depth placement of the needle. This device is disposable as it is only allowed for single use. The specimen is gathered after the needle is positioned in the lesion and the spring-loaded cutting cannula is fired into it. The drawback of this current device is that does not allow for an ideal grip that is comfortable for the user. The motor control of user is significantly reduced since the hand is farther away from the lesion site of the needle.

Another device that is currently on the market and is used for fine needle aspiration is [22]. According to a study that compared the different devices on the market today, the results showed that the highest performance was seen with the Reciprocating Procedure Device[®] (RPD) syringe holder [20]. Some of the advantages of this device are that it is completely one handed, it provides incredible needle control, and it provides an efficient tool for the physician. Also this Reciprocating Procedure Device[®] is superior to conventional syringes that include three ring syringes and syringe pistols and guns. The RPD[®] is a disposable device. To successfully gather the tissue cells using the RPD[®], one plunger is used for aspirating and the second plunger is used for injecting. To optimize needle control, switch between aspirating and injecting to gather the samples. The RPD[®] is available for use with different syringe sizes ranging from 1 mL – 25 mL. The RPD[®] comes in a box of 10 units, which costs, from about \$30.00 to about \$60.00 [22].

The Tao Aspirator[™] device is currently on the market [24]. It has some benefits that include single-handed use, equipped with a release button for automatic drawing of the plunger, and includes a regulating knob that allows for adjusting a predetermined amount of negative pressure during aspiration. Also this device has a pencil-grip, which allows for fine motor control of the hand compared to the pistol-grip holder, which has a large motor control since the

shoulder, and arm muscles are mostly being used. Since the Tao Aspirator™ allows for a fine pencil-grip the distance between the needle tip and the hand are very close allowing the physician to have better sensation of the lesion texture [25]. This device is also user-friendly because it fits all sizes of hands. This device however, is reusable, and costs around \$125.00 to purchase. The device is not disposable and must be sterilized before reuse. It is also limited to a 10 mL BD syringe. Therefore, most physicians refrain from using this device because it would require it to be autoclaved or sterilized through other means [24].

Another device that is currently on the market is the Cameco Syringe Pistol. The Cameco Syringe Pistol has many benefits that include one handed use, enables for the exact position for the aspiration procedure, improves comfort and less traumatic for the patient. The syringe pistol is used for the biopsy of the breast and thyroid and also for the diagnosis of urinary duct infections. Some drawbacks of this device are that it is made of stainless steel, not disposable after one use; it requires more a larger motor control of the arm muscles during aspiration, and cannot be used by physicians that have small hands. Furthermore, this device costs about \$140.00 [5, 15].

	Device of 1998	Biopsy Syringe Gun (INRAD®)	SuperCore™ (Angiotech)	Reciprocating Procedure Device® (RPD)	Tao Aspirator™	Cameco Syringe Pistol
Disposable	NO	NO	YES	YES	NO	NO
Autoclave	NO	YES	YES	YES	YES	
Type of Material	STEEL	PE	_____	PE	PE	STEEL
Single Handed	YES	YES	YES	YES	YES	YES
Designed for:	10 mL syringe Only	10 mL Syringe Only	Not compatible with syringe	All syringes	Only 10 mL Syringe	Only 10 mL syringe

Table 1: Comparison of the Current Devices on the Market

2.4 Clinical Significance

There are millions of Fine Needle Aspiration procedures that are conducted to determine malignant and benign tumors. A device that can meet the functions of the current procedure and be more easily handled by the client will make a successful biopsy procedure. As seen through the current available devices, the idea of establishing an apparatus that is single-handed, inexpensive to purchase, disposable, and gathers tissue cells accurately is difficult. Therefore, our team is challenged to design a device that encompasses all these constraints. As seen above, some devices are more applicable to the FNA biopsy procedure than other devices. However, none of these devices meet all the requirements for a successful device.

Chapter 3: Project Approach

Fine Needle Aspiration is a quick and minimally invasive diagnostic procedure that collects tissue from potentially cancerous lesions [9]. The syringe used for this procedure is cumbersome and hard to operate single-handedly. This procedure is very popular and a new device that could replace the standard syringe used now could make the operation more efficient. The reliability of the procedure is dependent on the quality of the collected samples, the skill of the user and the method used. In order for our team to better understand our project we revised our client statement according to the project's objectives, constraints and functions.

3.1 Initial Client Statement

Fine Needle Aspiration (FNA) is a procedure used for tissue biopsy. It consists of advancing a fine hollow needle, mounted on a regular syringe, into the target tissue (tumor). Once the tip of the needle is in the tumor, a back and forth movement is performed while applying suction by the syringe. The needle is progressed under imaging guidance, usually ultrasound imaging. The syringe is operated by one hand and with extreme caution to avoid moving the needle tip outside the target tumor. This makes the mechanism of needle operation and suction at the same time very cumbersome. The other hand will be holding the ultrasound probe to visualize in real-time the tumor and needle tip during the procedure. The aim of Fine Needle Aspiration is to provide a simple and handy device with adjusting suctioning mechanism, operated by the thumb and index finger of a single hand, to provide an accurate and gentle mechanism to perform FNA. This new device will potentially replace the standard syringe during FNA procedures.

This initial client statement was given to our group by Dr. Adib Karam and Dr. Wannii Asavaroengchai from UMASS Medical School.

3.2 Objectives

The objectives of the device were determined after discussion the client, Dr. Karam. The physician using the device will ultimately determine if the device is successful. These objectives can be seen in Appendix A, the objectives tree, and their order of importance was determined using a pairwise comparison chart, which can be seen in Appendix B. The four main objectives are safe, effective, marketable in terms of cost, and ergonomic. These objectives are not necessarily the most important; most of them are broadly defined and have multiple sub-objectives.

The device must be safe, for both physician and patient. Safety is always a major concern for invasive medical device. The sub-objectives for safe are sterile, sturdy, and minimize tissue damage. The device must be sterile, to eliminate the risk of contamination and patient infection. The device should be sturdy in that it will not break during the procedure. A fracture, or any other type of failure in the device while inside the patient could be very serious. The device should also minimize tissue damage to the patient.

The next main objective is effectiveness. Concerning efficacy, the biopsy device must obtain a usable tissue sample from the patient, by aspiration or other means. If the device does not function effectively, it will not be marketable or applicable to biopsy procedures. In order to be effective the device should be minimally invasive. It should also reduce procedure time. According to our client, the standard for fine needle aspiration is three passes of a needle, ensuring a minimum of one viable sample. This requires additional procedure time, and three disposable syringes. A disposable, single-handed biopsy device that reduces procedure time, distress of the patient, and procedure costs is ideal.

The biopsy device should also be marketable. Hospitals will have no interest in the device if it is not marketable. The team defined qualities that would make our device marketable: affordable, efficient, disposable, and easy-to-use. These are all important aspects that the design should aim for if it can be considered marketable. Due to the low cost of the current syringe used for this procedure, our device needs to be inexpensive. The price of our device should be equal to or lower than that of the conventional 10 ml syringe. Disposability is an important aspect of the device. According to Dr. Karam, many doctors prefer single-use devices in this situation, so they resort to using a disposable standard syringe. It should also be easy-to-use. Studies have shown that the efficiency of fine needle aspiration is dependent on the experience of the doctor

performing the procedure. If insufficient amount of sample is obtained in a procedure, the procedure must be performed again, greatly increasing the cost of obtaining the sample and the distress on the patient. Using the new device should be easy-to-learn, and the device should be able to obtain a usable sample consistently, independent of user experience.

The final objective is ergonomic, meaning that the device will minimize physical effort of the user and maximize efficiency of the procedure. Studies on fine needle aspiration have shown that a certain degree of tactile dexterity is needed to accurately obtain a sample. Careful manipulation of the needle tip is necessary so that a sample can be obtained from specific lesions on the growth. These objectives were used to direct the team's focus on the most important design aspects.

3.3 Constraints

The team was constrained to a \$450 budget for on the project. And it needed to be completed within our senior undergraduate year. In order to properly prototype and test the design, further project deadlines must be implemented. Ordering parts, manufacturing a prototype, and repeating to optimize the design is timely, so these deadlines must be established accordingly to complete project goals.

Aside from institutional restrictions, the team determined the design constraints due to the nature of the project and the existing technologies for fine needle aspiration solutions. Since the device is an invasive surgical instrument, it must be safe for both user and patient. The current procedure results in a small puncture wound for the patient, so the team's design must not create a wound greater than the current technology would. Also, the device must be sterile upon reaching the operating room. The device will have to be sterilized by FDA-approved methods, in manner that will maintain the device's affordability. The device must also be disposable. Current devices, such as the Tao AspiratorTM, satisfy the need of single-handedness. These devices, however, are for multiple-uses, due to their high cost. Many physicians prefer a single-use, disposable device, to avoid the effort and cost of re-sterilizing. Disposing of such devices also reduce the risk of contamination and infection.

The final constraint is that the device must function with a single hand. A standard syringe is most often used for fine needle aspirations, but this method requires a second hand, or awkward single-handed manipulation of the syringe plunger, which can reduce procedure efficiency and can cause unnecessary tissue damage from doctors who lack a steady hand. If the

team's device is not an easily used, single-handed device, it will not be any different from what currently exists, and the project will be a complete failure. The design of a single-use, single-handed biopsy device is constrained by the variety of parameters listed above, which in addition to limiting design options, also help narrow the scope of the project and provide the design with well-defined parameters.

3.4 Revised Client Statement

The goal of our team is to design, prototype, and test a device that will improve the efficiency of Fine Needle Aspiration procedures. This device must provide mechanical stability and durability to ensure that the device accurately gathers cells from target tissues while reducing the excessive movement by the user during aspiration. The aspirator must also be disposable, sterile, and operated with either hand. The design and development of the aspirator must be completed by April 2013.

The initial client statement that was given to us from our client was lengthy and included background information. Also, it summarizes the procedure and explained that the procedure needs to be more efficient and effective. This initial client statement only mentioned that the device should be single-handed use and it did not include the other objectives such as being disposable, sterile, durable, and inexpensive. The client statement did emphasize that single hand use is essential for the device to perform its function because the other hand will be used for the ultrasound probe to view the real-time images. The initial client statement that had a design possibility incorporated in it; however, designs and design alternatives should not be in the client statement so that part was removed.

3.5 Project Approach

In order to design a device that can be used in Fine Needle Aspiration procedure, there are various goals that our team needs to accomplish. We need to finish this project before April 2013 with a budget provided by the school. The steps to making a successful device for our clients are: researching current devices, brainstorming and creating potential designs, developing target specifications, prototyping, understanding the relevant engineering and technical

considerations, evaluating by creating a 3D model for Finite Element Analysis building and testing, and finalizing a prototype. One type of research that we will specifically be looking for are patents on current devices on the market. Investigating these patents will help us get an idea of what is available to physicians and the advantages and disadvantages of each product. We will examine the limitations of the device, which will give us an idea of what design challenges our team faces. After our team conducts background and patent research, we will create potential designs, whether they are modifications to a current device or an entirely new device. Following finalizing a design, we will prototype and if we think it will meet the objectives and functions of this project, and then we will build and test this device. Next, we will evaluate the effectiveness of this design. We have to consider that this device needs to be disposable and sterilizable. Our final device must be appropriately pre-sterilized and inexpensive to purchase since it will need to be disposable.

Chapter 4: Design

Fine Needle Aspiration (FNA) is a quick and minimally invasive diagnostic procedure that collects tissue from potentially cancerous lesions [9]. The syringe used for this popular procedure can be difficult to operate single-handedly. A new device that could replace the standard syringe used now could make the operation more efficient. The reliability of the procedure is dependent on the quality of samples received. There is existing technology today that helps in this procedure, but they are lacking in some key aspects, which will be discussed later in this chapter. This section includes details of the design alternatives by discussing the Needs Analysis, Functions and Specifications, Description of the design alternatives, Conceptual Final design, Feasibility and Experiments, and Preliminary Data.

4.1 Needs Analysis

Due to the prevalence of cancer diagnosis nationwide, an effective method for detecting cancer is necessary. FNA is a very common method used to obtain samples to diagnose cancer. Currently a standard syringe is used to collect samples. The syringe is disposable, but operating it with one hand is difficult. While there are various devices on the market that assists the FNA procedure, they are lacking in some aspects that would make the procedure more efficient. Some examples of these devices are the Tao AspiratorTM [25]. The Tao AspiratorTM is a syringe holder that has a pencil grip, but it is bulky and non-disposable. There is also a three-ringed device that can be operated with one hand, but it provides poor control because the grip is so far away from the needle. The ideal device for FNA could be operated with one hand, disposable, have good grip, and give the physician good motor control. The device our team is designing will meet the previously mentioned objectives.

4.2 Functions and Specifications

Our design will be effective because it will meet the design constraints and optimize the functions specified by our client. The functions of our device are:

- Pierce the skin and reaching the target growth
- Aspirate to collect sample
- Maintain the sample until ejection
- Eject sample when needed

Piercing the skin and reaching target growth is a basic function that our device will need to perform. This function can be easily met with the needle and the force of the needle from the physician. All of our design alternatives will perform this function in this manner. Aspirating is the most important function that the device must perform. For each of our designs, a change in volume is used to create vacuum for aspiration. Maintaining the sample in the needle is also important. If the sample is ejected when unintended, the sample will be lost and the procedure will have to be performed again, increasing time and cost. This leads us to the final function the device needs to perform: ejecting sample when required. The sample must be ejected into a container or onto a microscope slide to be sent for pathology testing. If the device cannot eject the sample, then the device fails because the sample cannot be tested.

Some of the specifications that the design must meet are:

- Should produce pressure drop of approximately 50 to 70 kilopascals (kPa)
- Should acquire a minimum of 10 microliters through 3 trials
- Must be compliant with the Luer Lock Needle

These specifications must be met in order for our design to work. Through literature research, it was found that a syringe generates a 50 to 70 kPa pressure drop during a typical FNA procedure [7]. Our device should achieve a similar pressure to ensure sufficient aspiration. The device should also have the capability to obtain at least 10 microliters of the sample [7]. Finally, the device must be compliant with a Luer lock Needle. This type of needle is used for all standard syringes and our device needs to be able to comply with the Luer Lock Needle.

4.3 Alternative Designs

Through discussions among the team and client, a few design alternatives were generating. These designs must accomplish a few functions while staying within constraints and considering objectives. The team originally considered a few "corer" designs. This would constitute a needle with geometry designed to scrape, shear, or core a volume of tissue, and extract this sample upon removal from the body. Such a design would require a larger needle diameter than currently used for FNA, compromising a key advantage of the procedure, its minimal invasion and small wound size. Therefore designs were limited to using standard needles for FNA, typically 22 to 25 gauges. This narrowed the scope of the design space. The team could then focus solely on a syringe body, which must aspirate and have a standard Luer-Lock to form a sealed mate with hypodermic needles. The use of fine needles also accomplishes the function of storing the cells until ejection. Cells, tissue, or other biological material will get clogged within the small inside diameter and adhere to the inner walls. This is observed in current FNA procedures, and the sample will not come out until a positive pressure is applied. Aspiration, or an applied negative pressure, could be attained in a variety of ways. Restrictions on the project, however, such as single-handedness and disposability, prohibit any complicated methods to achieve this. Therefore a simple change in a sealed volume, attached to the needle, was used in each design alternative to create negative pressure. This is accomplished upon input from a single hand of the user, while gripping the device.

4.3.1 Spring-loaded Syringe

The spring-loaded syringe consists of a hard plastic cylinder with an interior plunger driven by a compression spring. Similar to a regular syringe, the plunger forms a seal with the inner wall of the syringe body, preventing air leakage. The syringe attaches to a needle, which has specified length and diameter determined by the user, using a Luer-Lock. The hard plastic exterior allows the user to grip the syringe as close to the needle as desired. This gives the user good maneuverability of the needle tip, and good control for poking the lesion. When the needle tip has reached the target area for aspiration, the physician can press a button on top of the syringe to induce aspiration. This results in a change in plunger position, using a mechanism similar to a retractable pen. Figures 2 & 3 illustrate this mechanism below.

When the user receives the packaged and sterilized device, the syringe plunger is set to the front of the syringe, and the spring is in full compression. The spring exerts a force on the shaft connected to the plunger, as well as a small plastic piece with specific geometry facing the back of the syringe. This plastic piece interlocks with a second piece, which also acts as the "button" on the top of the syringe. There are three small lengthwise extrusions on the inside of the outer syringe. When the plunger is in the initial position, angled notches on the first plastic piece rest on these extrusions. When the user presses the button on top, it pushes the first plastic piece towards the front of the syringe, so that the notches are no longer touching the extrusions on the inner wall. As the compression syringe still exerts a force on this plastic piece, the angled geometry on the button piece caused the plastic piece to rotate slightly. Its notches are no longer aligned with ends of the extrusions; instead the extrusions are aligned with open channels in the plastic piece. When the button is released, this plastic piece can move past the ends of the extrusions, and the spring pushes this piece and the plunger shaft towards the back end of the syringe. It continues back until a width of extended diameter on the plunger shaft meets with the ends of the inner extrusions. This process moves the plunger a total distance of ΔL , as labeled on Figure 2. The change in volume in this design is equal to $\pi * r^2 * \Delta L$, where r is equal to the inside diameter of the outer syringe. Dimensions of the design can be easily manipulated so that the necessary change in volume is achieved to create aspiration. After the needle is removed, the user will let small amounts of air leach into the sealed volume between the plunger and the inner wall of the syringe. This will equalize the pressure inside the syringe to some extent with the pressure in the operating room, so a decrease in volume will increase the pressure. To eject the sample, the user simply has to repress the button. This pushes the plunges back down, decreasing the inner volume and increasing the pressure enough to eject the sample into a container or onto a slide. The user does have to overcome the force of the spring for this step, which will increase as the button gets pushed down farther.

The advantage of this design is that it has a very preferable grip location, giving the user good control to position the needle tip and scrape enough cells off of the growth to be aspirated. It is also fairly easy to induce aspiration; a quick motion of the finger to press the button should not interrupt the procedure. Some downsides of this design are the small custom parts inside the syringe. This will increase the cost of manufacturing, and they have to be able to endure stresses

applied to them during the dynamic motion induced by the spring.

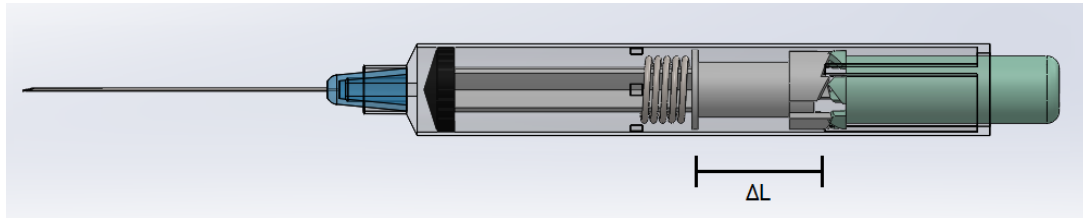


Figure 2: Spring-loaded Syringe Before Aspiration

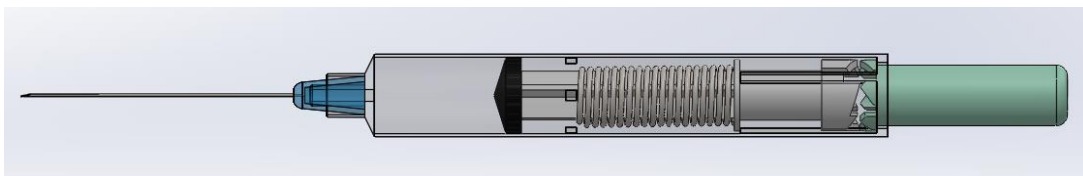


Figure 3: Spring-loaded Syringe During Aspiration

4.3.2 Gear Driven Syringe

A gear and a linear track drive this syringe. This device can be seen below in Figure 4. The gear is partially on the exterior and partially on the interior. When the user rotates the gear with their thumb it engages with a linear track on an extendable volume. This will force an extendable volume backwards to create the negative pressure. There will also be a spring-loaded stopper on the interior of the device, to prevent the volume from closing back in response to negative pressure. To eject the sample, the user must depress a small lever to move the stopper out of the way of the linear track and push the extendable volume back down to increase pressure.

The advantage of this design is that it gives the user good pressure control. Some drawbacks of this device are that it has poor grip, due to its width; it is difficult to eject the sample, and it requires significant time and force to move the gear.

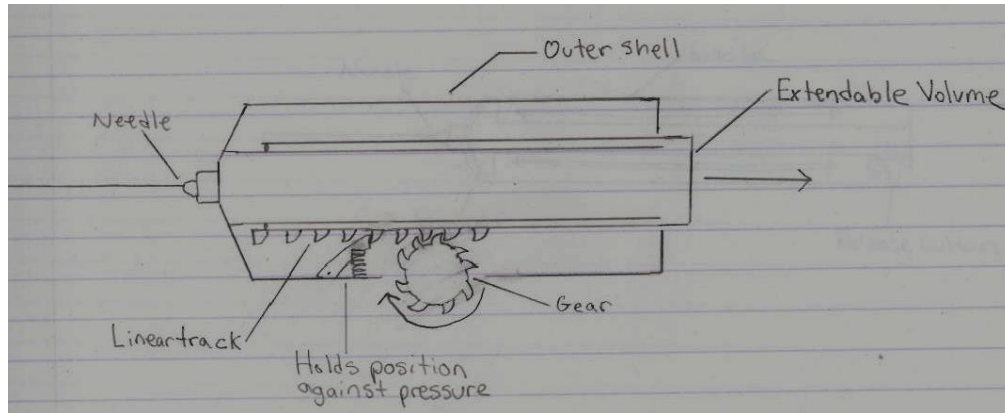


Figure 4: Gear Driven Syringe

4.3.3 Elastic Loaded Syringe

For our third design alternative, we decided on an elastic loaded syringe. The elastic loaded syringe is designed to use two elastic rubber bands in tension. One end of the rubber bands is attached to the plunger shaft and the other end is attached to a hook on the inner part of the syringe. A release button, shown in Figure 5, latches the plunger shaft onto the outer syringe, preventing the contraction of the elastics and movement of the plunger. When the physician presses the button, it moves past the hook on the outer shaft, allowing the tension in the elastic bands to force the plunger back to create aspiration.

The advantages of this design is that this elastic loaded syringe has a good grip due to the strong plastic body, and the physician does not need to make a difficult hand motion to create aspiration. The device is very easy to use for this reason. The elastic loaded syringe, however, has a few disadvantages. First, elastic fatigue can occur over time, reducing the tension in the elastic and possibly rendering the device useless if it is not used for a long period of time. There is also a large inherent stress in the device, which can lead to unintended fracture of the rubber bands or small plastic components of the device.

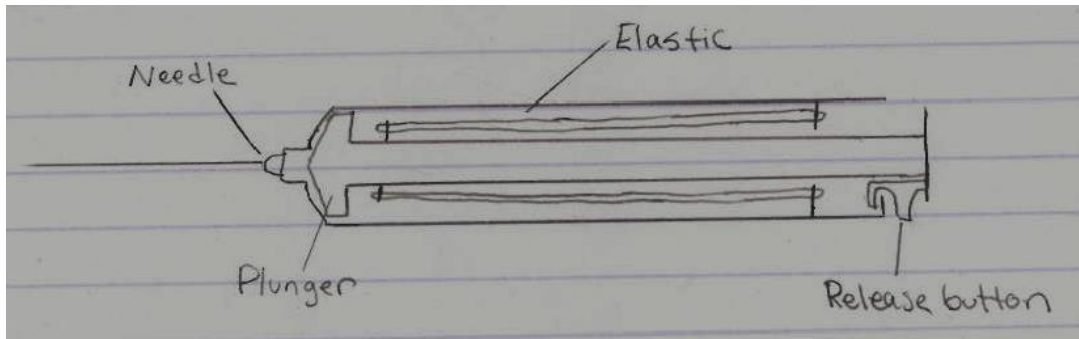


Figure 5: Elastic Loaded Syringe

4.3.4 Compressive Syringe

For our final design alternative we have chosen the compressive syringe. Figure 6 shown below is a SolidWorks model of this design.

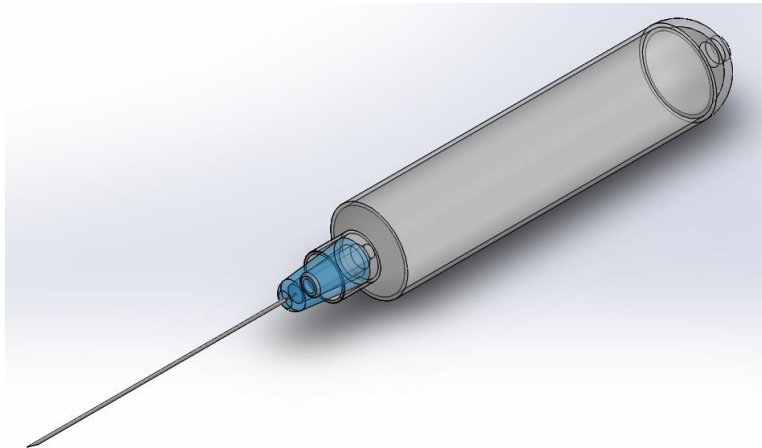


Figure 6: Compressive Syringe

The compressive syringe is a simple design. It consists of a hollowed syringe body made of an elastically deformable plastic. At the back end of the syringe there is one-way back valve, allowing flow out of the syringe, but not in. Like all of the designs, the front is designed to form a sealed mate with most standard needles. Figure 7 illustrates the procedure for fine needle aspiration using the compressive syringe.

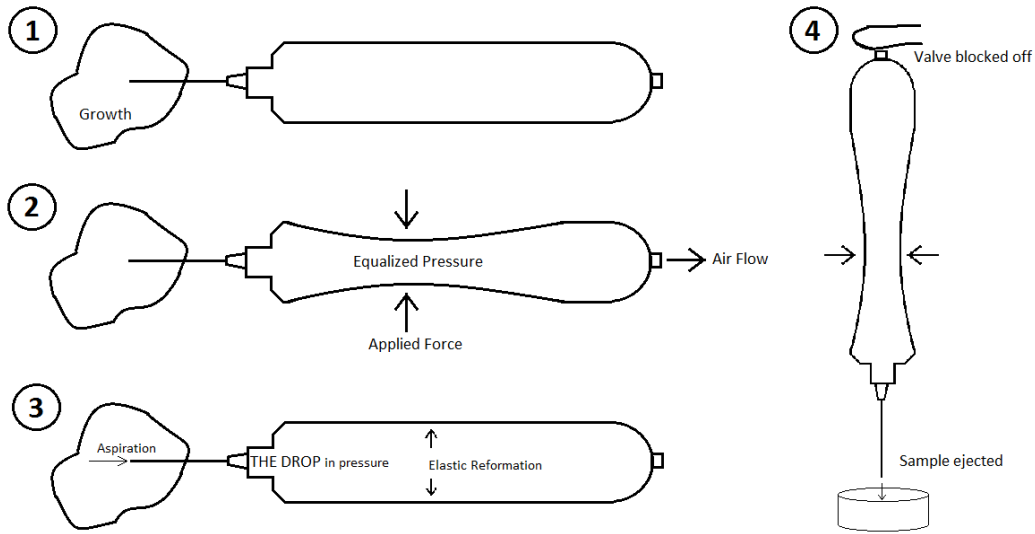


Figure 7: Diagram of Compressive Syringe Procedure

4.4 Conceptual Tentative Final Design

To aspirate using the compressive syringe, the user first directs needle tip into the growth to the target area for aspiration in image 1. After jabbing the tissue to break off cells, the physician applies a force with their grip to compress the syringe body in image 2. The back valve allows air to flow out of it, instead of the needle. At this point, the pressure inside the syringe is equal to the pressure in the operating room. When the user lets go, the back valve closes off, and the syringe body reforms to its original shape. The increase in volume causes a decrease in internal pressure, and aspiration occurs as biological material flows into the needle. The physician removes the needle once enough tissue has entered the needle. To eject the sample, the user places a finger on the back valve, preventing air from flowing out. Upon compression, air is forced out of the needle and the sample is ejected.

The advantage of this design is that it is simple, easy to manufacture, and easy to use. It eliminates the trick single-handed use of a standard syringe. It also allows for the reintroduction of the vacuum mid-procedure, which is a huge benefit over a standard syringe as well as other devices on the market. One of the disadvantages of the design is that it requires a deformable plastic that has mechanical properties within a very specific range. It needs to be sturdy enough to resist deformation when the syringe is being handled or maneuvered in the skin, yet weak enough to compress during aspiration or ejection.

4.5 Feasibility Study

Understanding the feasibility of our final design, the compressive syringe, is essential for testing purposes and for meeting the requirements of our client. Through the team's research in literature, the team determined that a pressure drop of 50-70 kPa is sufficient for aspiration [7]. In order to obtain this pressure drop; the compressive syringe must have a change in volume of approximately 0.5 mL. The team determined this value from Boyle's Law: $P_1V_1 = P_2V_2$ [3]. The compressive syringe consists of a compressible body, a one-way back valve, and a standard needle. The elasticity of material should allow for compression, followed by an expansion of the syringe body. The reformation of the syringe body will allow sufficient change volume to create aspiration. This design will be easy to manufacture because it has three basic parts rather than multiple tiny parts, which would be harder to manufacture.

To conduct our tests on our final design we have acquired lab space in Goddard Hall. Once a prototype is manufactured we will measure the negative pressure it can produce using a pressure transducer. If the design can produce enough pressure, we will move forward with testing on animal tissues. We would like to test our design on a variety of tissues, preferably tissue types frequently targeted by FNA. On the selected tissues we will perform an FNA using a standard syringe and our prototype, to compare the volumes of sample aspirated. If device shows better or comparable results to a standard syringe, we hope to survey doctors at UMass Medical School to determine if our device would benefit their procedure. However, if any of our tests in the lab are unsuccessful, we will have to make alterations to our device in order to improve function.

4.6 Preliminary Data

Before we move forward with manufacturing a prototype, we need to acquire preliminary data. One value that we need to know is the pressure drop across the needle when the sample is aspirated. While we know the pressure drop in a typical FNA, we will need to calculate, or measure, the minimum pressure required to aspirate biological tissue. To determine a suitable range of pressure, within which the pressure of a typical FNA will fall, the team will use a standard syringe to perform a basic aspiration on water and milk [26]. The viscosity of blood falls between the viscosities of these two substances, so this should give us a better idea of the minimum pressure our device needs [27].

When considering the motion of the alternative designs, it is important to know the force to move the plunger in a standard syringe, to gauge the force that would be needed in these designs. Using a force gauge the team determined that the force required was 10 N. This was done while the needle tip was in air. We would like to repeat this measurement while the needle is in water and other fluids, to give us a better knowledge of the force needed for FNA.

For the compressive syringe, we need to research materials with mechanical properties will allow for elastic deformation and reformation. The material should have elastic properties allowing it to be compressed, yet it should be strong enough to reform its shape and create pressure. We also do not want the material to deform unintentionally, such as when the needle is being inserted or maneuvered. In addition, we will need to research the different back air valves and their pressure resistance. When compressed, air should take the path of least resistance - out of the back valve, instead of through the needle. The valve should also prevent back flow, so fluid will flow up the needle during the volume reformation phase.

The last step before assembling a prototype will be determining an inexpensive and feasible means for manufacturing our device.

Chapter 5: Methodology Chapter

To validate that the compressive syringe and the spring loaded syringe can perform functions of a fine needle aspirator, the group conducted numerous tests and analysis. These include; plunger force analysis, analysis of standard syringe, prototyping, volume analysis of standard syringe, pressure analysis of prototypes, and performing Fine Needle Aspiration.

5.1 Force Testing of Standard 10 mL Syringe

The team conducted some preliminary tests on standard syringes using standard needles in order to determine the required force to pull the plunger in different substances. After discussing and observing a FNA procedure with Dr. Adib Karam, a Radiologist at UMASS Medical School Hospital, we learned that 10 mL syringes attached to a needle of a certain diameter, usually 22 to 25 gauges are most often used in Fine Needle Aspiration. From the free body diagram in Figure 8, the force needed to pull the plunger is equal and opposite to the frictional force of the plunger against the inside of the syringe body. As the vacuum pressure increases, that plunger force becomes equal to the frictional force plus the force exerted on the plunger by the force gauge. Therefore, the team gathered the pullout force required in moving the plunger in water, milk, and rat liver, as seen in Figure 9. Rat Liver was used as a representation for the viscosity of tissue and blood. A stand and a 20 N force gauge were acquired from Physics Department to measure the pullout force. Next, the 10 ml BD syringe along with the needle was attached to the stand via a paper clip and the force was applied to the syringe by pulling it down while the force of the plunger was acting in the opposite. The force was recorded immediately after the plunger started moving. This data was also helpful in determining a suitable spring need to generate this force in the spring-loaded prototype.

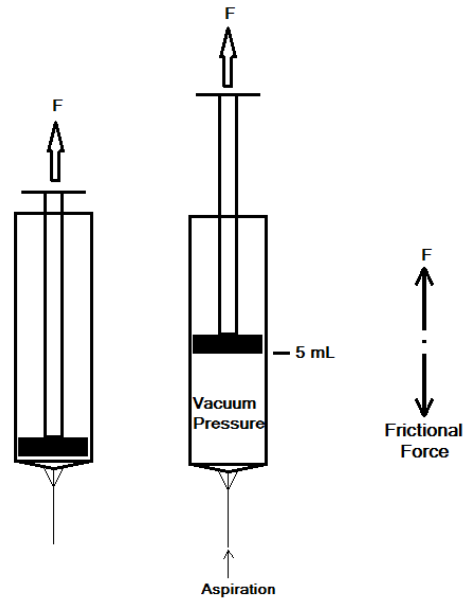


Figure 8: Diagram showing Aspiration through Syringe



Figure 9: Force pullout test performed in rat liver

The force pullout test conducted using rat liver is similar to the test conducted in water and milk. In this test, the rat liver is submerged in 10X Phosphate Buffer Saline (PBS) solution, to prevent the tissue from drying up. Also, the team decided to mimic the fine needle aspiration procedure by aspirating once the needle was inside the tissue. While aspirating the team observed that the

force required moving the plunger was greater than the force required to move the plunger in water or milk.

5.2 Pressure of Standard Syringes

Another important engineering parameter of this system is the pressure within the syringe necessary for the procedure to take place. After observing the procedure done by the physicians, a 5 mL displacement is the standard for acquiring sufficient amount of tissue from a lesion. Therefore, the team used this metric as a design specification for our prototypes. To determine the negative pressure required in order to produce a suction to collect the cells from the target tissue, the team collected pressure data using a VWR pressure transducer connected to the 10 mL syringe. The team initially collected pressure data without a needle attached to the syringes and then collected pressure data during an FNA using a three-way connector and either 22 to 25 gauge needles. To confirm the pressure data of a 5 mL displacement the team used different syringes sizes that included a 10 mL BD syringe, 25 mL Exelint syringe, and 60 mL Monoject syringe. However, the metric that the team used for designing the prototypes was the negative pressure created during an FNA using a standard 10 mL syringe. This average pressure from two runs using two different syringes and needles was 6.07 psi. Next, the team acquired pressure readings from an actual FNA using rat Liver. To do so the team connected a three-way valve to a 22 to 25 gauge needle, a 10 mL syringe, and the pressure transducer. A setup of the procedure is shown in Figure 10.



Figure 10: FNA procedure using a three-way valve

5.3 Material selection

The two prototypes, spring-loaded design and compressive design include different materials for its function. The compressive design has two components: a compressible body and a one-way valve to create the negative pressure. We decided to utilize finite element analysis, using ANSYS 14.0 software, to help us model this deformation better and help determine a suitable material for this application. Based on the FEA model, the team decided that plastics with low elastic modulus would be considered for the compressible tubing. The materials yield stress must be less than maximum equivalent stress during compression, with some degree of safety. The deformation of a non-Newtonian, non-linear plastic is complex, and the stresses within the cylinder depend on the 3D geometry of the model. The team acquired flexible plastic tubing from Home Depot and McMaster. These plastic tubing include Poly-Vinyl Chloride, Silicone, Tygon, and Polyethylene, and Polyurethane. An important design consideration was that these materials needed to reform back to its original shape after being compressed. Also, these materials had to be able to create a suction that was similar to a 10 mL BD syringe. Therefore, the team explored multiple tubings with changing inner diameters because the inner diameter determines the displaced volume during compression. Figure 11, shown is of the team's initial prototype made of Poly-Vinyl Chloride (PVC) tubing and the dimensions are 5/8 inch (outer diameter) and 1/2 inch (inner diameter).



Figure 11: PVC tubing (5/8 inch x 1/2 inch)

The team obtained different tubing of various materials in order to compare their differences. In addition to the PVC tubing with the current dimensions of (5/8'' OD x 4/8'' ID) the team also conducted testing using Masterkleer PVC tubing (7/8'' OD x 5/8'' ID) and Water-Resistant Clear Polyurethane (PU) tubing (3/4'' OD x 1/2'' ID). Both the PVC and the Polyurethane tubing are clear and flexible tubing. Though these materials were listed as flexible their hardness of Shore A67 (PVC) and Shore A84 (PU), did not allow them to be easily compressible by an individual. Due to the design requirement of being easy to use in collecting tissue samples, the team needed to reduce the wall thickness. Therefore, the team decided to reduce the wall thickness by passing the tubing over the length of a mandrel, attaching the mandrel to a lathe and removing the material from the outside diameter. A mandrel is prepared from stainless steel with a diameter that is slightly bigger than the inner diameter of the material that is being cut in order to maintain the material on the mandrel without slipping. The inner diameter of the mandrel is approximately 0.5 inches. To reduce the outer diameter of the tubing, a technique called turning was performed on the Lathe at the Higgins Laboratory Machine Shop. The turning process is completed at a 30-degree angle parallel to the axis of rotation. As seen in Figure 12, the tubing is passed through on a mandrel and fitted on to the spindle of the headstock and attached to the tailstock. The process of turning used to cut the outer diameter was at 0.030 inch and at 0.040 inch. Figure 12 displays the trimming of the tubing.



Figure 12: Lathe Machine at WPI

After cutting the material from the outside diameter, these tubings were more flexible and were able to be attached to the one-way valves. The one-way valves were obtained from Toys-R-Us, shown in Figure 13 and SureFlo[®] Valves from LMS Incorporated, shown in Figure 14. The SureFlo[®] valves were designed for applications that require different amounts of pressures to be opened. The green valve, a thicker silicone valve requires 6.08 psi to open, while the blue valve requires 0.38 psi to open the valve. The team tested both valves to determine which valve would be best suited for this application. Both these materials are silicone however these materials have different mechanical properties due to their processing techniques.



Figure 13: Breast Pump Duckbill Valve [1]

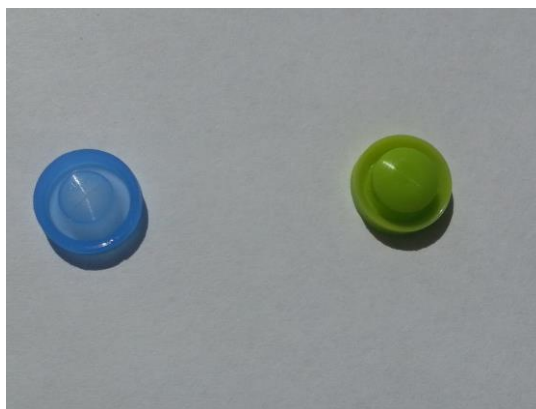


Figure 14: SureFlo[®] Valves

The team also collected pressure data required to push air through a 22 & 25 gauge needle in rat liver. Through this experiment, the data would tell us how much pressure is required for a valve to open. To do so, the plunger started at the 25 mL position and slowly pushed inwards toward the needle inside the rat liver tissue. The point at which bubbles were created by pushing the plunger inwards was recorded as the opening pressure for a valve.

5.4 Prototyping

In order to conduct human testing, the team would need to sterilize these prototypes and acquire an Institutional Review Board (IRB) approval. Due to the limitations at WPI, means of sterilization are not available and are costly to conduct. Therefore, these compressive designs and spring-loaded design were developed are to provide proof of concept that it improves on the current methods of acquiring cells. In order to develop a syringe that would be bulk manufactured the means of doing so requires the assistance of injection molding. Injection molding would assist in mass-producing these syringes and thus would be cost effective. In this manufacturing process produces parts by injecting materials into a mold. These molds are very expensive to create and thus cannot be applied to this project. However the alternative to injection molding is making a prototype with parts made via the prototyping machine located at WPI. To develop the spring-loaded syringe, some of the components were made from the Objet260 Connex Rapid Prototype Machine.

5.4.1 Compressive Syringe

For prototyping compressive syringe the team attached a luer-lock to the plastic tubing and a duckbill valve or a SureFlo[®] Valve. The duckbill valve purchased from Toys-R-Us and the SureFlo[®] Valve was provided to us by LMS Valves Incorporated. After using Finite Element Analysis the team determined that the plastic tubing should have a modulus of approximately 28 MPa upon applying a force of 40 N from the top and the bottom and a thickness of about 1 mm with an inner diameter of 1.4 cm. Furthermore, the client specified that the device had to be attached to a luer lock attachment in order to simplify the complexity of the design. Keeping these specifications in mind the team explored plastics options that not met these requirements but also met the specifications of the client. These being autoclavable, disposable, serve its function of acquiring tissue cells, easy to use.

The explored different plastics from Low density Polyethylene, Thermoplastic Polyurethane Elastomer, Silicone Elastomer, Poly-Vinyl Chloride, and Polypropylene. Through conducting pressure testing with these acquired tubing, the team determined that Silicone Elastomer and Thermoplastic Polyurethane Elastomer were materials that would satisfy the design parameters.

The next step in prototype process is to attach a luer lock to our device. The team decided to cut the luer lock, of the standard 10 mL syringe with the assistance of a vice. To cut the syringe the team used a metal saw and to remove the excess material from the cut a file was utilized. The file also smoothed the edges of the sawed luer lock attachment to allow an easier placement in the tubing.

Next, the luer lock component has to be attached to the tubing to allow for the needle to be connected. The team purchased Loctite Epoxy Plastic Bonder to glue the luer lock component to the tubing. Figure 15, shows the materials that were used to connect the tubing and the Epoxy. The epoxy was squeezed on the surgical paper and then mixed thoroughly with a metal paper clip. Next, it was gently applied to the surface of the luer lock attachment and on the inside of the tubing and both were combined. After applying the plastic epoxy, the recommended wait time for the liquid to harden is about 20 minutes.



Figure 15: Luer lock attachment, Polyurethane tubing & plastic epoxy

To attach the Duckbill valve and the SureFlo Valves the team cut approximately six millimeter (mm) of the standard syringe using the saw to attach to the end of the tubing to provide support for the attachment of the valve. The epoxy was applied on the cut syringe with a paper clip. The six mm pieces of the standard syringe are attached to each of the compressive prototypes, which are seen in Figure 16 and Figure 17.



Figure 16: Silicone tubing with attachment



Figure 17: Polyurethane tubing with attachment

The duckbill one-way valve was glued over the cut standard syringe for the compressive designs for the negative pressure to be created. In another prototype the SureFlo[®] Valve was glued to the end of the compressible tubing. In doing so, a SureFlo[®] Valve was placed on the inside of the upper fitment as shown in the cross section view in Figure 18. In order for the SureFlo[®] Valve to function, an upper fitment and lower, shown in Figure 19, are necessary for the valve to open when enough pressure is created. These upper fitment and lower fitment were then joined together and placed half inside the tubing and half outside. Since the valve opened upward the upper fitment was placed inside of the tubing; while the lower fitment was placed outside of the tubing. Figure 20 illustrates the assembly of the SureFlo[®] Valve in the fitment and the direction of the airflow throughout the fitment to create the negative pressure.



Figure 18: SureFlo[®] Valve placed in Upper Fitment



Figure 19: Upper Fitment (black) & Lower Fitment (white)

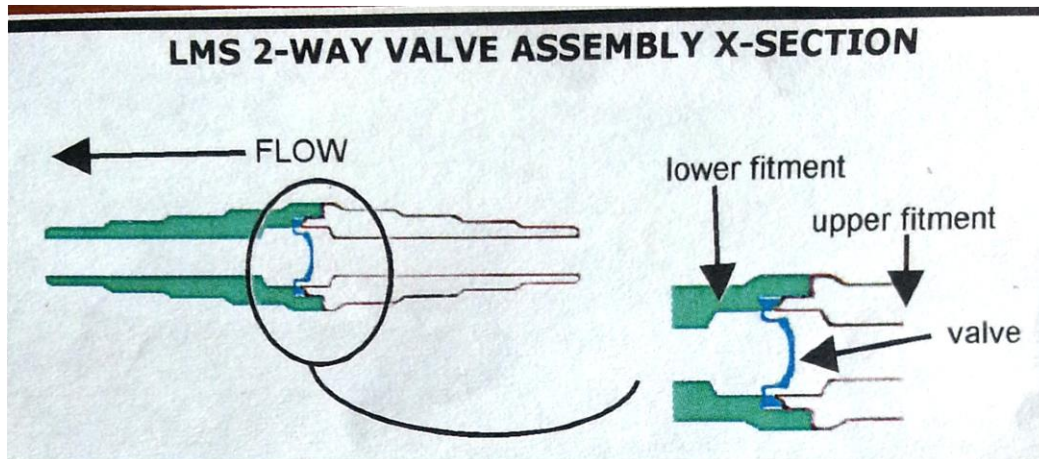


Figure 20: Cross Section Assembly of two-way valve

5.4.2 Spring-Loaded Syringe

We began to consider the design of a syringe driven by a spring. For the sake of clarity, the end of the syringe where the needle is attached will be considered the bottom of the device, while the opposing side is the top. Any relative directional words such as ‘above’ or ‘below’ are used given this assumption. For the concept to function correctly the spring must create net motion between the outer cylinder and the plunger-shaft; therefore, the spring must apply a force between these parts. Also, the spring must be located above the plunger. In general, compression springs perform better mechanically, so a compression spring is preferred. The spring contacts two separate parts, with the purpose of exerting an equal and opposite force on the plunger shaft and outer cylinder, driving the plunger shaft to move upwards relative to the outer cylinder. For this to happen, the spring-shaft interface must be above the spring-cylinder interface. Next, we must consider a mechanism that can hold down the spring, compressed in the “loaded” position. Upon input from the user, the spring needs to be released, exerting a force according to $F = -k\Delta x$ and moving to the extended or “unloaded” position. After the device has reached the “unloaded” position, it needs to allow the user to move the plunger back to the “loaded” position, to eject the biopsy sample. This completes the extension-compression cycle of the syringe. We considered the possibility of a device that could perform the cycle only once, but this design is flawed. If the spring is accidentally released during shipping or handling of the device, it will be rendered

useless. Therefore, we want a design that allows continuous cycling between the “loaded” and “unloaded” positions, so that the syringe can be reset if need be.

To achieve this cyclic motion, we decided to investigate and mimic the mechanism of another cylindrical, plastic, spring-driven device: the retractable pen. A retractable pen has a button at the top, and after it is pressed, the pen either extends or retracts into the pen. It stays in this new position until the pen button is pressed again. We observed the internal components of a Spencer retractable ballpoint pen to understand and apply this mechanism to our design. We found that 2 loose plastic parts interact with long, thin grooves that extrude from the inside surface of the pen body. One of the loose pieces acts as the "button," and is exposed at the top of the pen. The button part can only move axially; it runs along the track of the extruded grooves and cannot rotate. The second loose piece rotates and moves axially. This piece interacts with the button piece with a modified cam-follower relationship with complex geometry.

Figures 21-27 diagrams the motion of these internal components, and the key forces of the mechanism are labeled. The diagram shows only the geometries that are creating our functional mechanism. Also, for clarity, the diagram shows horizontal movement to represent rotation of the components in the pen. This is essentially a planar representation of a cylindrical system. This diagram shows only the key geometry on each part whose interaction leads to the cyclic motion, and preventing motion while the parts are at rest. The key forces creating this motion are labeled. The shapes labeled with a “1” are on the rotating piece; the shapes labeled “2” are on the button piece, while the shapes labeled “3” are the long extrudes on the inside of the pen body. Part 1 has two angled surfaces, with respective angles of θ and ϕ .

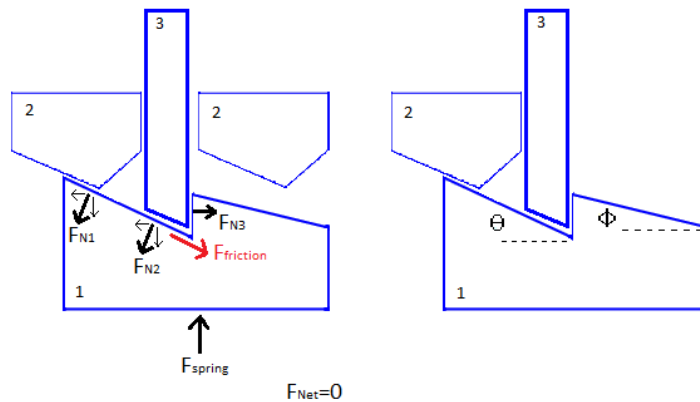


Figure 21: Functional Mechanism: Resting Position

Initially the parts are at rest. The force of the spring (F_{spring}) is pushing up on the rotator piece. The angled surface of part 1 contacts parts 2 and 3, resulting in normal forces F_{N1} & F_{N2} . Part 1 would rotate, signified by moving left on the diagram, but the normal force F_{N3} is preventing that motion. The weight is neglected.

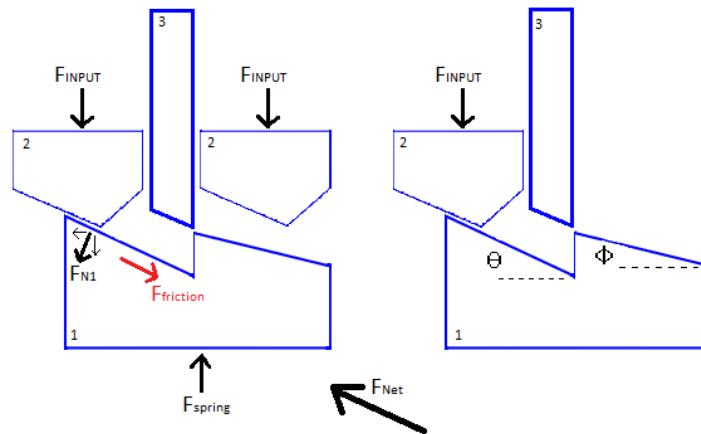


Figure 22: Functional Mechanism – Spring Force on Rotator Piece

The user applies a downwards force (F_{INPUT}) on the button piece, overcoming the spring force and pushing part 1 downwards until it has clearance past part 3. If we look at the instant

where $F_{INPUT}=F_{spring}$, part 1 needs to move left and up diagonally at an angle θ from the horizontal. Figure 23 shows the breakdown of forces driving this motion.

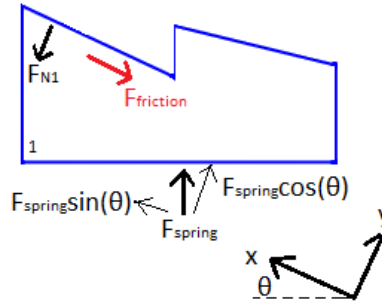


Figure 23: Functional Mechanism – User Input Force

The frame of reference is changed so that the direction of motion is the positive x direction. The spring force is resolved into components in the x and y directions. In order for the part to move, or rotate, $F_{spring} * \sin(\theta)$ must be greater than $F_{friction}$.

$$F_{spring} * \sin(\theta) > F_{friction} \quad (1)$$

$F_{friction}$ equals $F_{N1} * \mu$, where μ is the coefficient of static friction between parts 1 and 2. There is no net motion in the y direction, so from balancing the forces, $F_{N1} = F_{spring} * \cos(\theta)$.

$$F_{friction} = \mu * F_{N1} \quad (2)$$

$$F_{N1} = F_{spring} * \cos(\theta) \quad (3)$$

Substituting equations (2) and (3) into equation (1) yields:

$$F_{spring} * \sin(\theta) > \mu * F_{spring} * \cos(\theta) \quad (4)$$

This can be rearranged to produce the following equation:

$$\tan(\theta) > \mu \quad (5)$$

This analysis shows that the motion of this part does not depend on the magnitude of force applied to it, but only the friction coefficient of the material and the angle at which the contacting surface is inclined. When the input force is released, the spring pushes part 1 upwards, and the second incline surface catches on part 3. Figure 24 below shows this step.

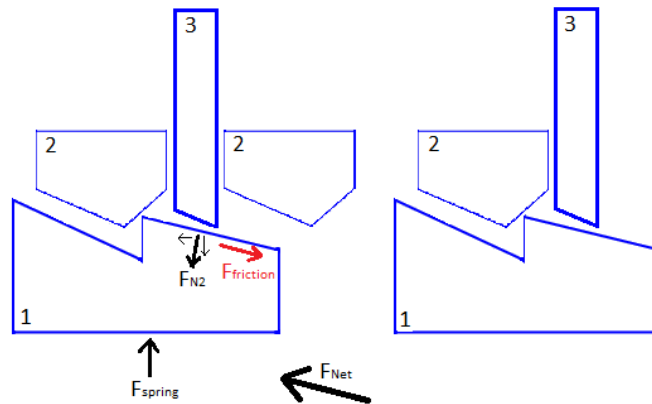


Figure 24: Functional Mechanism –Spring Force Released

The same conditions for motion are required as in the previous analysis, but with the angle of the second surface, φ . Again, the determining equation is:

$$\tan(\varphi) > \mu \quad (6)$$

We will use equation 5 and 6 to determine the values for θ and φ in our design.

As part 1 continues to move in the direction of F_{NET} , it eventually reaches the gap between the repeated geometry. Part 1 now has clearance to move upwards with the force of the spring.

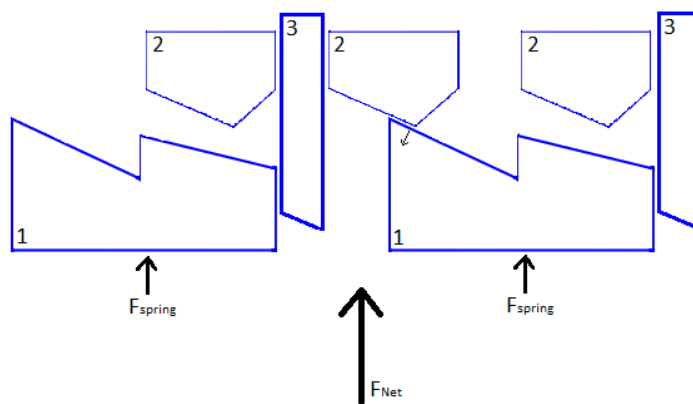


Figure 25: Functional Mechanism – Interaction of Components

When part 1 reached the top of its trajectory, the pen is fully retracted. To extend the pen tip again, the user pushes down on the button (part 2). Figure 26 shows this step.

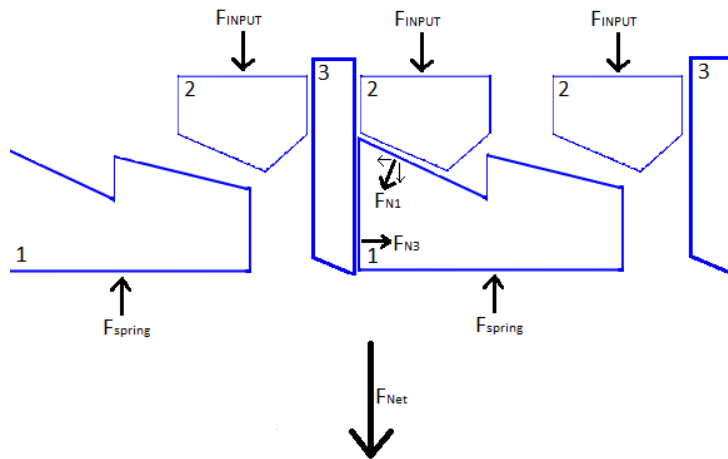


Figure 26: Functional Mechanism – Interaction upon Input Force

The user is applying an input force that is greater than the spring force, so the net motion is downwards. Part 1 is prevented from rotating due to its contact with part 3.

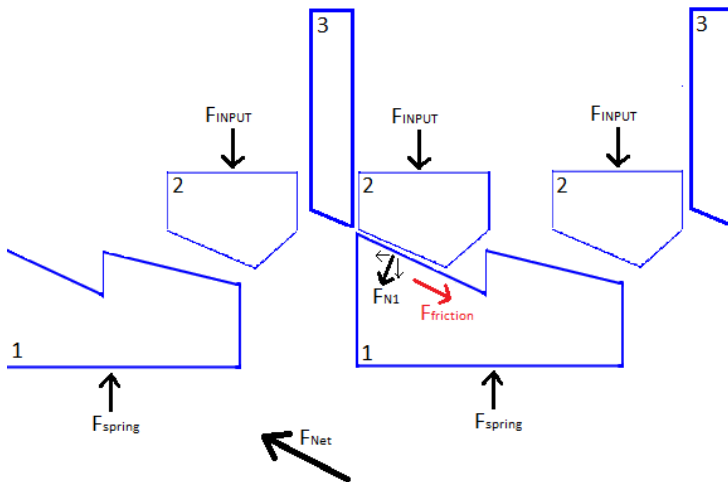


Figure 27: Functional Mechanism – Net Motion

Once the top of part 1 moves below part 3, part 1 moves in the direction of θ , and slides until part 3 rests in the “valley” of part 1. It is back to its initial position.

While designing the spring-loaded syringe, there were a few design constraints to consider. There were ergonomic concerns, defining the outer dimensions of the device. The spring-loaded syringe is used with a four-finger grip, bracing the syringe cylinder between the

first four fingers and the palm. The thumb is placed on top of the ‘button’, to control the release and retraction speed of the plunger. This functional grip limits both the outer diameter of the device and overall length of the device. The client specified that one inch was the maximum diameter the device could be, although a thinner syringe would allow better control. He did not specify a length, but we know that a shorter syringe offers better control. Within the scope of designing this spring-driven device, we will not approach values for diameter or length that are too small to use.

Based on the functions and constraints of the device, the team designed an assembly of six separate parts, including a spring, in SolidWorks. These parts interacted with each other to utilize the retractable-pen mechanism. Figure 28 displays the initial design.

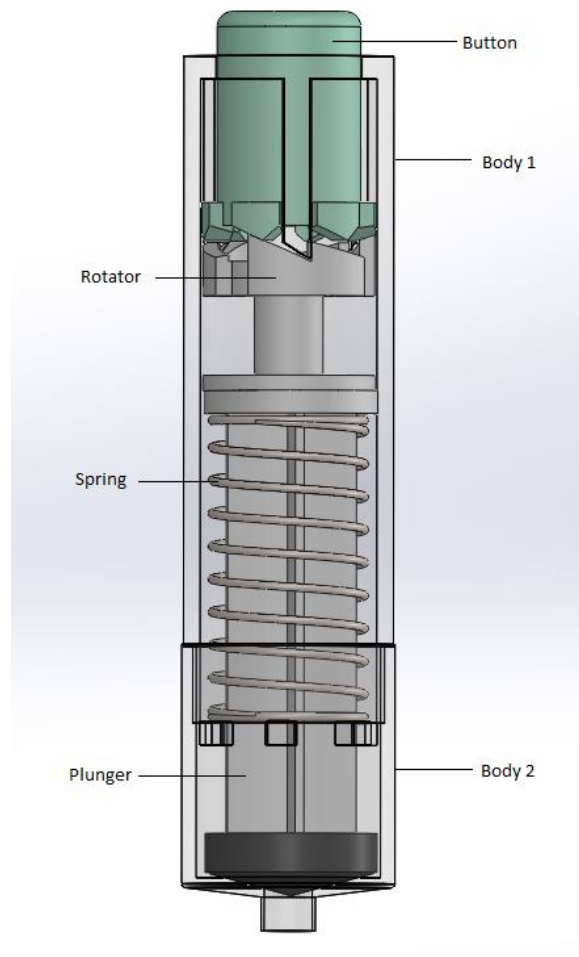


Figure 28: Spring-loaded Syringe Parts

Body 1 and body 2 are bonded together. When the user presses down on the button, the rotator rotates to allow extrudes on the inside surface of body 1 to fit into the gaps of the rotator.

The spring is in compression, and it exerts a force on the top circular surface of the plunger. The other end of the spring contacts 6 small extrudes on the inside surface of body 2, creating the net opposing force between the outer body parts and the remaining internal parts. The spring forces the button, rotator, and plunger upwards a distance of ΔL . The black rubber plunger forms a seal with the inside surface of body 2. When the plunger moves upwards, a vacuum is created, just as in a regular syringe, based on the change in volume. The distance ΔL that it needs to move will depend on the diameter. If the sealed volume needs to change 5 mL, from the equation for volume of a cylinder, ΔL can be calculated from the following equation.

$$\Delta L = (5 \text{ mL}) / (.25 * \pi * D_i^2) \quad (7)$$

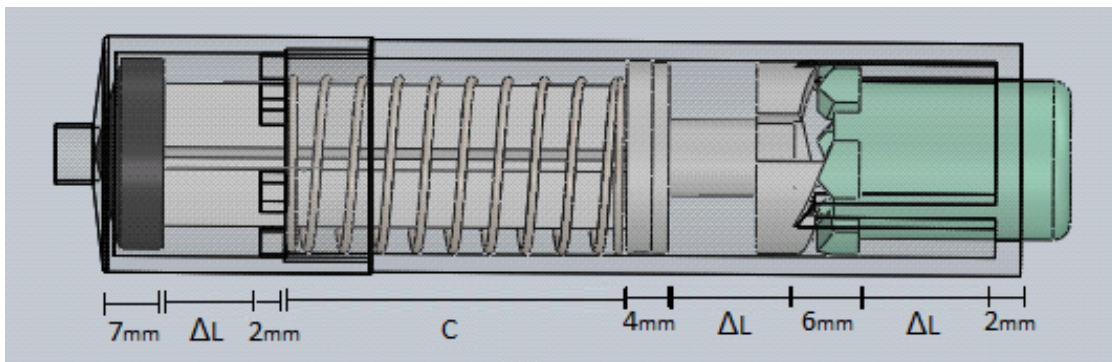


Figure 29: Length Specifications

Figure 29 above shows the diagram used to determine the axial length for each part (besides the spring). For a given ΔL and C , the length of the spring when it is at maximum compression, the axial length of any part can be determined based on where each part needs to travel and stop. For example, the plunger part has a circular surface of thickness 2 mm that the spring contacts. The distance from this distance to the black plunger is $\Delta L + 2\text{mm} + C$. The button has a length of $\Delta L + 2\text{mm} + [\text{Length of forks}]$, plus a small additional amount to extend out of the end of the cylinder.

According to equation (7), ΔL depends on the internal diameter of the device. From Figure 30, an equation for total length of the device as a function of inside diameter is derived.

$$\Delta L(D_i) := \frac{5\text{cm}^3}{(25 \cdot \pi \cdot D_i^2)}$$

$$C := 1.2\text{cm}$$

$$\text{TotalL}(D_i) := 2.1\text{cm} + \Delta L(D_i) + C$$

Figure 30: Equation for Total Length of Device

This relationship calculates the total length of the syringe for a given inside diameter and compressed length of the spring. Ideally a spring with a low length and large spring constant would result in a shorter, more ergonomic device, but real springs will have a length that contributes significantly to the overall length of the device. In our prototype we used a spring with a compressed length of 3.3 cm, for the graphic interpretation of the relationship we've assumed a compressed spring length, $C=1.2$ cm.

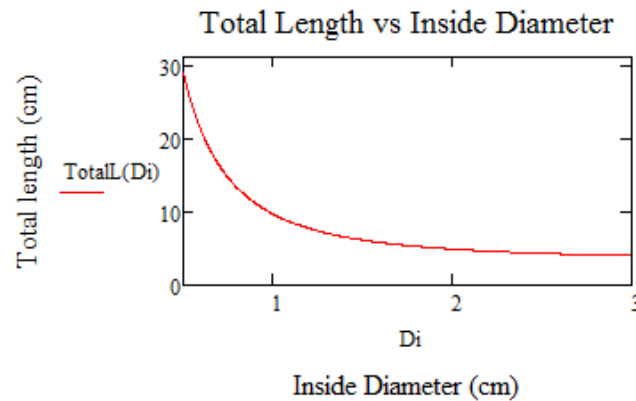


Figure 31: Total Length vs. Inside Diameter

This graph portrays the trade-off between diameter and length of the device. As the diameter goes below 1 cm, the total length of the device increases dramatically. By observing this graph, the team concludes that the ideal diameter for such a device is between 1.5 and 2 centimeters. Ultimately to design this device we would need to find the right compromise between diameter, length, and cost (as any change in volume results in a change in cost). Before digging deeper into this aspect of the design, the team designed and constructed a prototype to test and demonstrate the feasibility of the spring-loaded device.

The basic shape of the rotator and button parts were based on viewing the corresponding parts in a retractable pen. The extrusions on the inside surface of body 1 act as a guide track from the button piece that preventing it from rotating. At the top of body 1, there is a rim with slightly

smaller diameter that prevents the button from escaping out the top of the cylinder. The button has “forks,” which are the small pieces that contact the rotator. These forks extend out past diameter of the button, and contact with the rim at the top of Body 1.

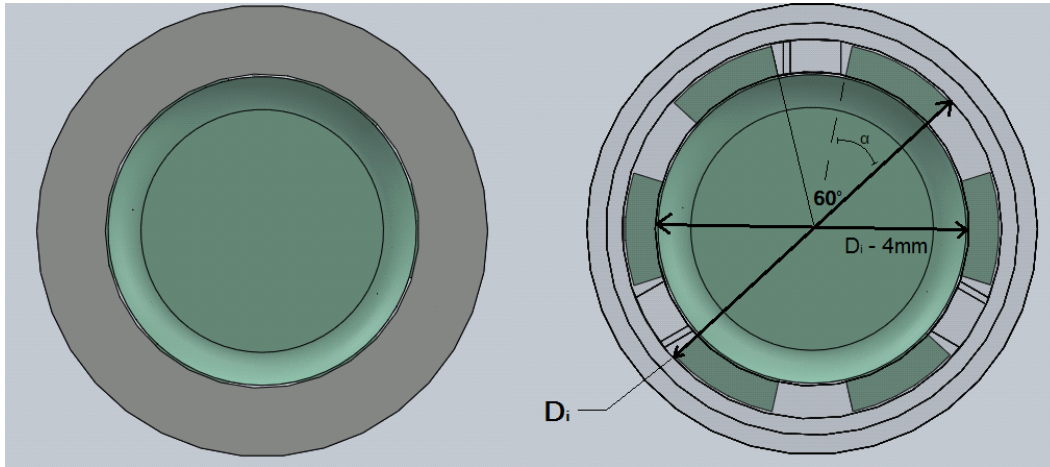


Figure 32: Interior of Button Component

Figure 32 shows two top views of the button and Body 1, where Body 1 is solid then transparent. The inside diameter of the device is labeled D_i . The rim at the top of the device has a diameter equal to $D_i - 4$ mm, which is also labeled. The button has 6 repeated “forks,” which were created with a circular pattern feature in SolidWorks. Since there are 6 forks repeated over 360 degrees, the angle between each fork is 60 degrees. The “extrudes” have a thickness of 3 mm. This value is not very significant; it only needs to fit into the gap between the button's forks. The angle of a single fork is labeled as “ α ”. The space in between each fork is equal to arc length

$$\text{Space between forks} = \pi * (D_i - 4 \text{ mm}) * (60^\circ - \alpha) / 360^\circ \quad (8)$$

This space needs to be slightly more than the extrude width of 3 mm, so we can rearrange this equation to solve for α for whatever value of D_i .

$$\alpha = - (3 \text{ mm}) * 360^\circ / (\pi * (D_i - 4 \text{ mm})) + 60^\circ \quad (9)$$

The rotator, shown in Figure 33, has only 3 fork pieces. Similar to the button piece, the forks extend out to a diameter just under D_i , while the cylinder they extend from has a diameter of $D_i - 4$ mm. This allows the piece to have clearance past the extrusions of body 1, when aligned with the gaps between keys.

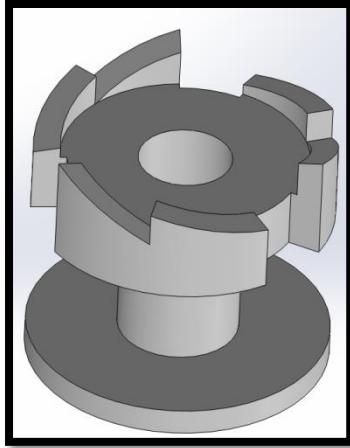


Figure 33: Rotator Component

As discussed earlier, the rotation of the rotator depends on the angles of the 2 key surfaces and the coefficient of friction. These contacting parts are made out of commodity plastics such as polypropylene or polyethylene, which can be molded with relatively smooth surfaces. The coefficient of friction can depend on a lot of factors such as surface roughness, temperature, and sliding velocity, and the value for μ between plastic surfaces can range from 0.1 to 0.4 [8]. To ensure that the part will be able to move, we design for the maximum friction condition of $\mu = 0.4$. Substituting 0.4 into equation (5) and (6) results in the following equations:

$$\tan(\theta) > 0.4, \tan(\phi) > 0.4 ; \quad (10)$$

$$\theta > 21.8^\circ, \phi > 21.8^\circ \quad (11)$$

Both of these surfaces need to be inclined at an angle greater than 21.8° . In our design, θ equals 25 degrees and ϕ equals 23 degrees. Figure 34 shows the sketch whose extruded cut resulted in those surfaces.

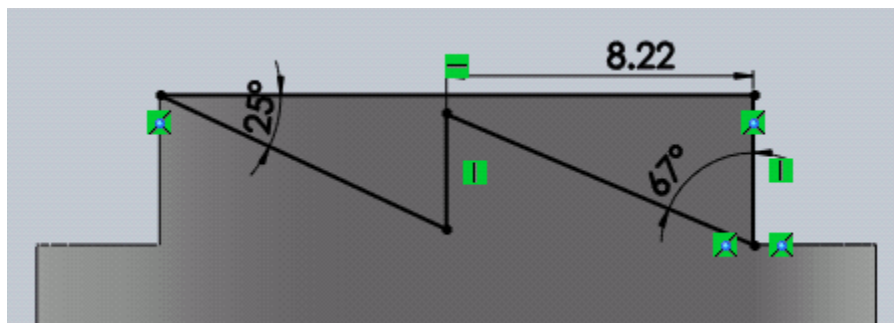


Figure 34: Extruded Cut of Rotator Component

Body 2 can be seen in Figure 35. This piece has 6 internal extrudes against which the spring exerts its force. The axial lengths of these parts depend on the distance ΔL that these parts need to move.

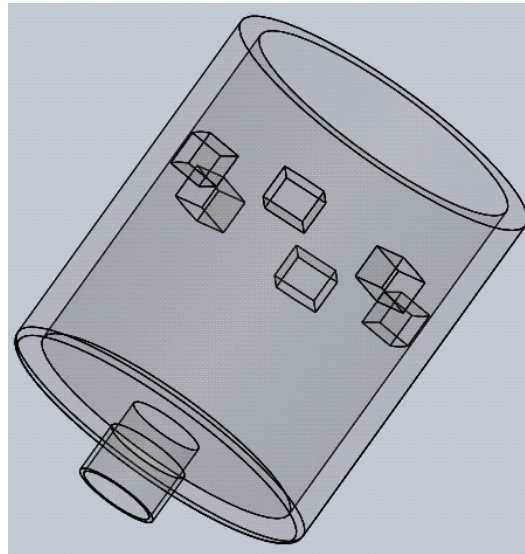


Figure 35: Body 2

To validate this design a prototype was constructed using components rapid-prototyped with WPI's Objet260 Connex, a spring purchased from Hardware Products Company, and the front end of a 25 mL Stylex syringe. The surfaces of parts built with the rapid-prototyping machine are very rough. Also, CAD models for a Luer-lock are not readily available. For these reasons the end of the outer syringe and plunger shaft of a regular syringe were sawed off and epoxied into the assembly. The parts initially modeled were slightly changed to allow for this. The first spring received from the Goddard Hall Machine shop and the second spring obtained from Hardware Products Company. One spring, shown in Figure 36, is made out of Plain Carbon Steel and the other spring, shown in Figure 37 is made out of Brass. The spring coefficient was determined by conducting a test to determine the force required to move the plunger. The carbon steel spring that was ordered had a length of 2 inches, a diameter of 0.875 inches, and a wire diameter of 0.062 inches. This spring is placed over the length of the plunger shaft and is compressed is initially compressed before aspiration. However, during aspiration the spring is uncompressed which allows the plunger to move back, thus collecting the cells. This spring is placed between the rotator component and the button to prevent obstruction between these parts.

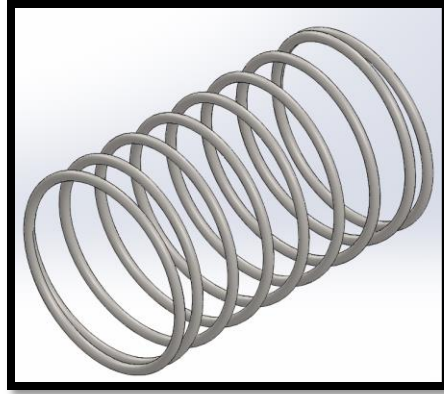


Figure 36: Plain Carbon Steel Spring

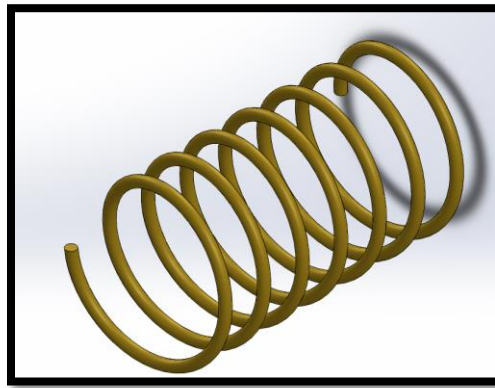


Figure 37: Brass Spring

Next, there are parts that are rapid prototyped using the Objet260 Connex Rapid Prototype machine. These parts include the disc, button, rotator, and two outer body components that were epoxy together with all the rest of the components inside. The other components were taken from a 20 mL Stylex syringe. These pieces include the luer lock attachment, the plunger, and plunger shaft.

The first rapid prototyped part is the disc component. The disc is located in the plunger shaft and allows for union of the plunger to the button component so that by pressing the button the plunger can move downward or upward. The initial design for the disc was not very thick. However, after the first spring-loaded syringe broke, the alteration made to the disc was to make it from 3 mm to 15 mm thick, as seen in Figure 38. Now, by repeated clicking motion, the plunger shaft will not break off the disc.

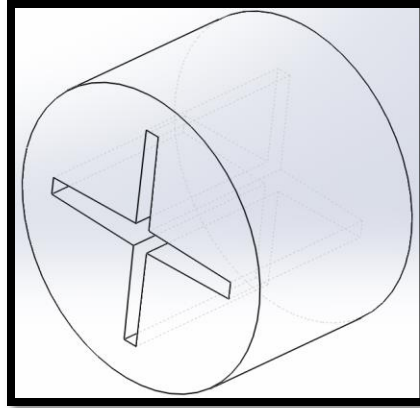


Figure 38: Disc Component

The next component is the button. The button piece allows the clicking motion is initiated that drives the spring to uncompress and aspirate the cells. This piece is very similar to the button seen on a pen. The button also has an extruded part where it engages with the inside of the outer body component for it to move upwards and downwards. The button also engages with the rotator component which rotates when the button is pressed. Figure 39, shows a visual representation of the button component with a circular extruded part.

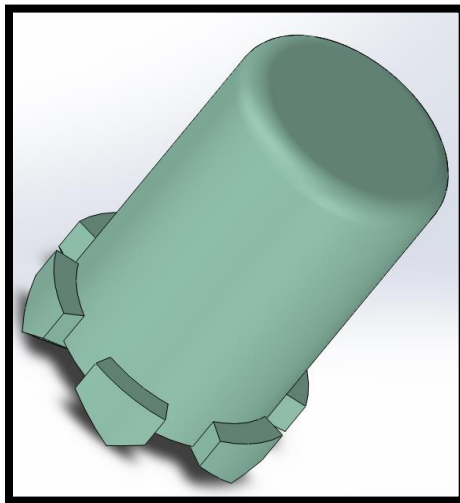


Figure 39: Button Component

The next part that was rapid prototyped was the rotator component. The rotator component, shown in Figure 40, combines the disc with the plunger shaft to the button. This

piece rotates to the left when the button is pressed. The rotator piece also engages the inside extruded part of the outer body to pass through the gap which affects the position of the button.

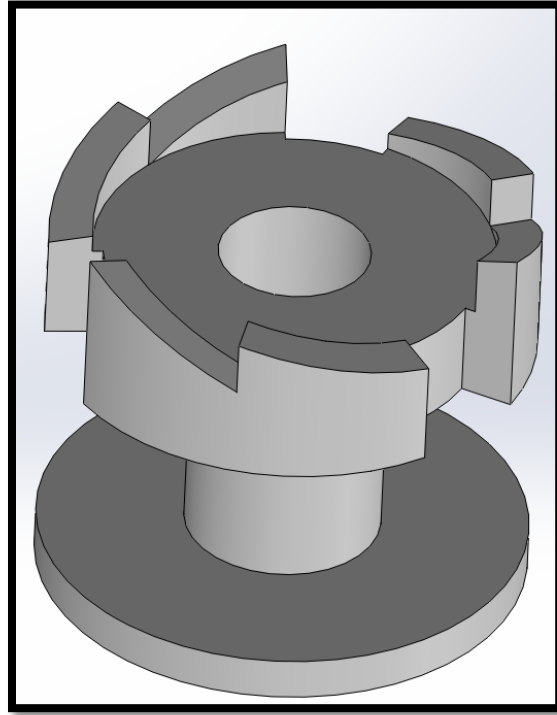


Figure 40: Rotator Component

The next two pieces were prototyped so that they could be glued together with all the other parts inside. The first outer body component, shown in Figure 41, also has an extruded part that engages with the rotator component when the button is pressed.

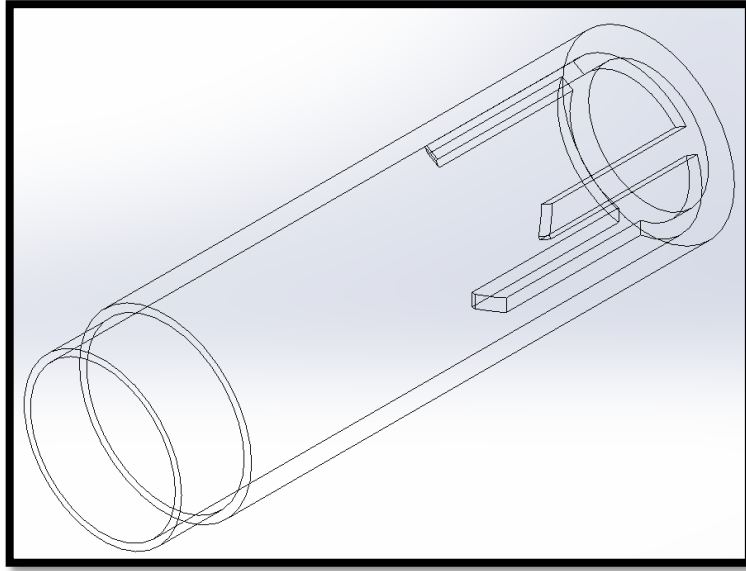


Figure 41: First Outer Body Component

The final piece that was rapid prototyped was the second outer body component. The second outer body component connected the 25 mL Stylex plunger shaft to the disc. Also, the extruded pieces in the interior of this part provided opposite and equal force to spring. This extruded piece prevents the spring from becoming in contact with the plunger and luer lock attachment. The second outer body component is shown in Figure 42.

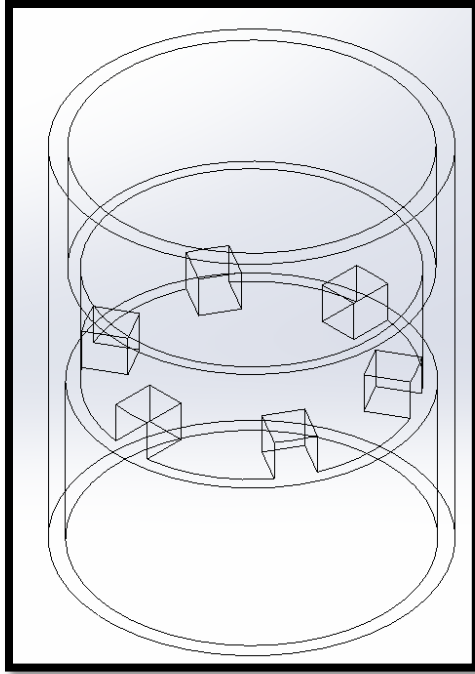


Figure 42: Second Outer Body Component

The remaining parts of the plunger, plunger shaft, and luer lock attachment were obtained from a 25 mL Stylex syringe. The plunger shaft, as mentioned previously, attaches to the disc for the entire mechanism to function as a retractable pen. The cross section length is too large to fit in the disc. The length of the cross section of the plunger shaft had to be less than 15 mm. Therefore, to cut the length from each of the four sides, the team used a band saw available in Goddard Hall Machine shop to cut 3 mm from each side by cutting along the entire length of the plunger shaft. The band saw cut in a straight line with the assistance of a straight metal bar. The excess material from the cut was removed by an xacto-knife. These steps were repeated for each of the three remaining sides of the plunger shaft. Figure 43, shows a Computer Aided Design of the plunger shaft attached to a plunger and a disc. The plunger shaft was glued into the disc.

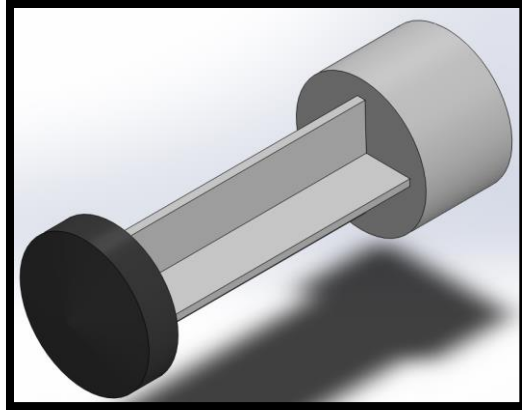


Figure 43: Plunger shaft with plunger attached to disc

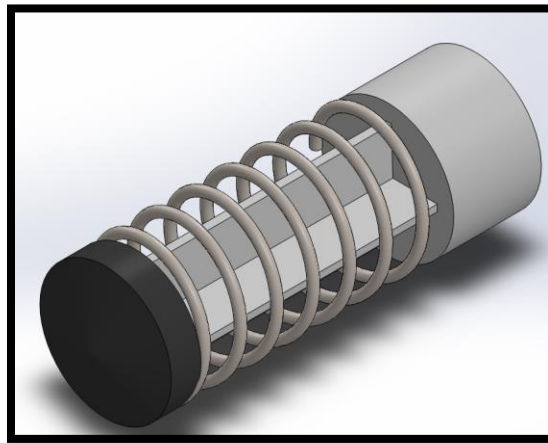


Figure 44: Plunger shaft, plunger, disc, and spring components

After assembling the front half of the spring loaded syringe, the back half also needs to be assembled together. First the click component, is passed through the outer body component of syringe, so that empty spaces of the click component are on the same path as the extruded piece on the outer body. Once the button component is completely passed through the outer body of the syringe, the next piece is the brass spring, followed by the rotator component.

The luer lock was cut using the same technique to cut the luer lock of the 10 mL BD syringe. The luer lock attaches to the front of the spring-loaded syringe so that it can attach to the needle. Figure 45, shows the assmebly of the luer lock attachment with the needle.

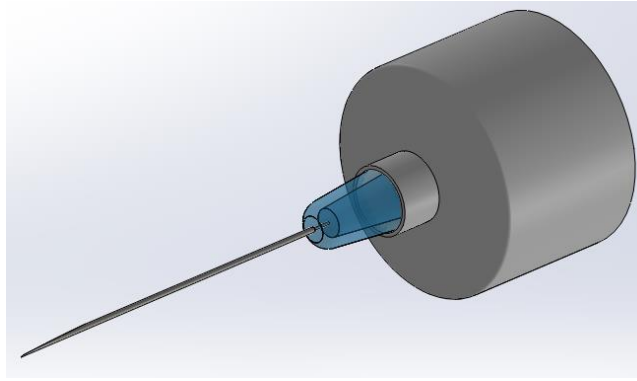


Figure 45: Luer Lock Attachment with 22 Gauge Needle

Now, the outer component had to be combined with the groove component with the disc and spring so that the entire assembly could function as a pen. The epoxy was applied to the area where the two components are going meet.

5.5 Determining Expected Pressure from Prototypes

A key engineering parameter for our compressive design is the amount of negative gauge pressure it can generate. According to data recorded during a fine needle aspiration on rat liver, roughly 5-6 psi is desired for our device to match the capability of a regular syringe. This value was determined under the condition that the needle tip was clogged, and maximum vacuum was achieved. The team, however, found that it was possible to aspirate rat tissue with less pressure, so design success does not hinge on this value. Another metric is that it should be capable of displacing 5 mL of volume during the aspiration. Both of these values are important in determining the ultimate dimensions and geometry of the device. Determining pressure capability of the syringe depends on the initial volume and Boyle's Law, $P_1V_1=P_2V_2$. Figure 46 below labels the corresponding initial volume and pressure (P_1 & V_1) and final volume and pressure (P_2 & V_2) of our system.

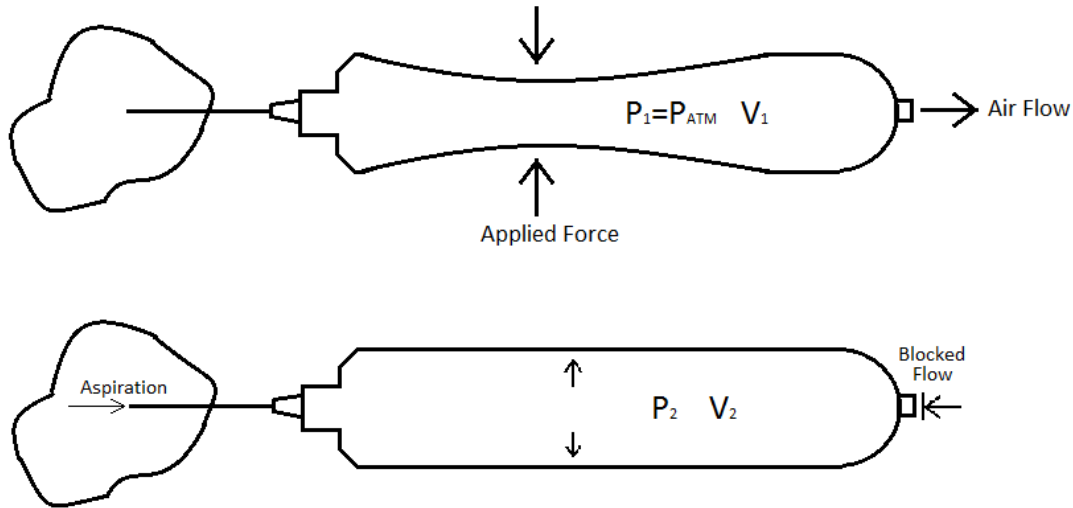


Figure 46: Diagram of Compressible Tube

Since we know P_1 =atmospheric pressure, which we assume to be 14.7 psi, and that -5 gauge pressure (psig) is desired, we can conclude that $P_2 = 14.7 \text{ psi} - 5 \text{ psig} = 9.7$ absolute pressure (psia). By rearranging the Boyle's Law equation, $V_1/V_2=P_2/P_1$. P_1 will always be atmosphere, and we are designing for P_2 . This relationship shows that our desired vacuum pressure depends on the volume ratio of initial to final volumes. Since gauge pressure is measured as the difference from atmospheric pressure, a smaller P_2 yields a larger vacuum in the device. Decreasing the volume ratio V_1/V_2 will result in a larger vacuum, but the device still must stay within ergonomic bounds.

While the initial volume may vary depending on the degree of pressure applied and technique of the user, we assume that it is consistent, and it will be defined by $V_2-\Delta V$. The inside diameter is the controlling factor of ΔV ; logically, if there is a greater space to squeeze, ΔV will be greater. V_2 is the internal volume of the syringe at rest, assuming it has fully reformed. The volume is cylindrical, neglecting the volumes of the luer-lock and back-valve; it is equal to $\pi L*(D_i/2)^2$, where D_i is the internal diameter and L is the length. As a starting point for our design, we will use an outside diameter, D_o , of 15 mm. That is the outside diameter of a typical 10 mL syringe; current surgeons conducting FNA's are familiar with this size. We initially estimate a wall thickness, t , of 0.5 mm, which is within the bounds of injection molding and other types of plastic molding. Inside diameter is calculated as:

$$D_i = D_o - 2t = 15\text{mm} - 2(0.5 \text{ mm}) = 14 \text{ mm} \quad (12)$$

From previous testing, compressing 14 mm tubing with the palmar grip results in a volume displacement of ~5 mL, so $\Delta V = 5 \text{ mL}$ or 5 cm^3 ($1 \text{ mL} = 1 \text{ cm}^3$). P_2 is assumed to be 9.7 psia.

Under the following assumptions:

$$V_1 = V_2 - 5 \text{ cm}^3 \quad (13)$$

$$V_2 = \pi(D_i/2)^2 L \quad (14)$$

By substituting these relationships into the modified Boyle's Law equation, and rearranging it, we solve for L, length of the syringe:

$$\begin{aligned}
 P_2 &:= 9.7 \text{ psi} & \Delta V &:= 5 \text{ mL} \\
 P_1 &:= 14.7 \text{ psi} & D_i &:= 14 \text{ mm} \\
 L &:= \frac{\Delta V}{\left(1 - \frac{P_2}{P_1}\right) \left[\pi \left(\frac{D_i}{2}\right)^2\right]} = 9.549 \text{ cm}
 \end{aligned}$$

Equation 1: Manipulating Boyle's Law to Solve for Lengths of Prototypes

5.6 Molding Compressive Tube in Finite Element Analysis

Finite element analysis (FEA) was used to determine the maximum stress endured by the hollow cylinder under a compressive load. It also provided insight into the stress concentration device and allowed the team to view the deformation of the material. With this information the optimal material properties and wall thickness could be determined. The analysis was conducted using a Static Structural model in ANSYS Workbench 14.0. Stresses were reported in Von-Mises Stresses (equivalent stress) and the stress concentration and body deformation was visually analyzed. A linear model was assumed.

Opposing 40 Newton (N) vertical forces were applied above and below the cylinder. The 40-newton value was chosen instead of 44.5 N, because the user would not have optimal control if they had to pinch the device at their maximum strength. In reality the user would apply a grip force on surfaces of different sizes above and below, but in this model the forces were applied on surfaces of equal size, shape, and position. These surfaces had a length of 2.5 cm, to represent the width of the users' fingers. The front end (C) contains an attachment for needles made of a

stiff, non-flexible material, so this face was fixed. It was assumed that the back-valve is also stiffer, so the back end (D) was fixed radially and torsionally, but could move axially.

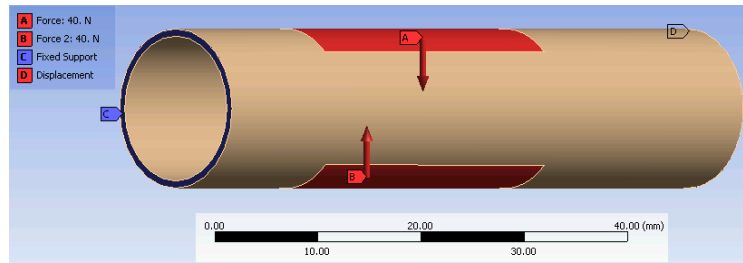


Figure 47: Opposing 40 N Forces on cylindrical body

Initially the cylinder had an inside diameter of 14 mm and a thickness of 1 mm. Length was determined using Boyle’s law as shown earlier. A fine mesh was used, which was automatically generated by the ANSYS software. The initial setup had 15300 elements and 30860 nodes, but these numbers slightly changed when the size of the model was altered.

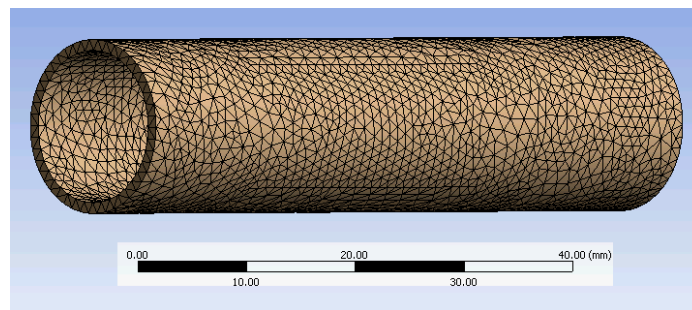


Figure 48: Fine Mesh Cylindrical body

The elastic modulus, wall thickness, and diameter (and corresponding length) were all changed iteratively. A cylinder with the ideal combination of modulus and thickness should be completely compressed under a load of 40 N, while remaining in the elastic region of its deformation. This means that stress endured in the material is under the material’s yield stress. “Complete compression” in this case means that opposite ends of the cylinder’s inside diameter are in contact, but no further, or less, than that. By designing for this condition, we maximize the “reformation strength,” or the force with which the compressible body expands to its original shape. This is the force that acts against the vacuum increasing inside the body, so the internal negative pressure is also maximized.

5.7 Instron Testing with Prototypes

The team used the Instron machine, as seen in Figure 49, to determine the compression force required to compress the body of the syringe. Using the Bluehill software on the computer in Goddard Hall, the team used the three-point bending test to achieve the maximum force required to compress each of the tubing prototypes. The data obtained was compared to grip strength from literature; specifically the palmar pinch because this gripping technique is utilized in operating the compressive device. The palmar pinch grip strength was based on the weakest individual in the study. This force was approximately 10 pounds or 44.5 N [17]. We designed the compressive design based on the weakest individual because now any individual with different ranges of grip strengths can use the device. If we simply designed the device for stronger individuals then the weaker individuals would not be able to use it. The team conducted three point bending tests using the Instron 5444 Machine in Goddard Hall. The flexure fixture was applying a force at 3 mm/min until either the user stopped the three point bending test or the machine automatically stopped the testing. Before every run, the load balance was zeroed to ensure that there is no force remaining from the previous run. From testing the compressive prototypes on the Instron both the Polyurethane and the Silicone designs showed results that were well below the 44.5 N limit, which was determined from the study.



Figure 49: Compression of prototype with Instron Machine

5.8 Product Testing

The team conducted tests using our two prototypes on rat liver obtained from Sprague Dawley female retired breeders. Our team conducted fine needle aspiration biopsies on these rat tissue using the syringes that the team prototyped to not only mimic the technique as it would be done on humans but also to determine the optimal negative pressure necessary to collect enough tissue cells that would then be sent to pathology. Figure 50 displays the first compressive syringe prototype with all the components.



Figure 50: PVC tubing with Duckbill Valve & Luer Lock attachment to a 22-Gauge Needle

The following is a diagram that shows the components used to complete a successful Fine Needle Aspiration procedure. Figure 51, shows the components including rat liver along with either 22 to 25 gauge needles, and forceps to maintain the rat liver against the side of the bowl. The diagram also shows the prototypes used to conduct the biopsy and Phosphate Based Saline solution to keep the rat liver hydrated in the container. The technique of aspirating the tissue with the prototype and ejecting the tissue into the second container is seen in Figure 51 and Figure 52.

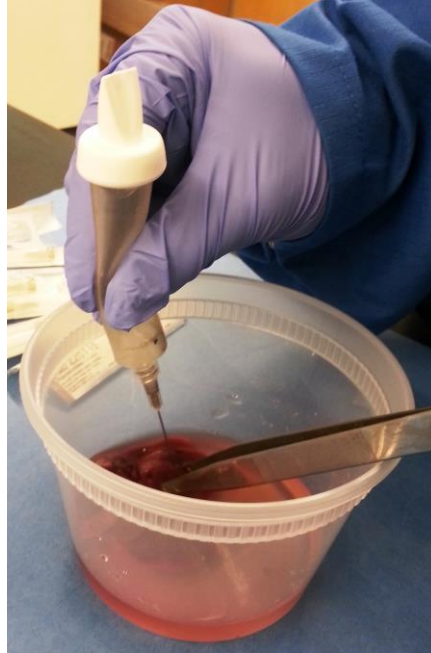


Figure 51: Aspiration of Rat Liver Tissue

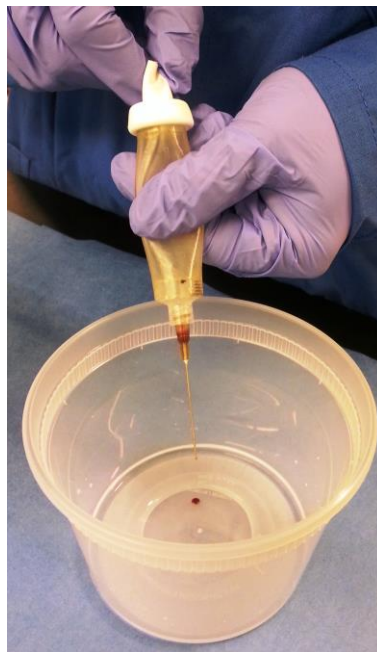


Figure 52: Ejection of Sample

Chapter 6: Results

After completing the testing procedures of the standard syringe and the prototypes, results were collected for analysis of the conventional syringe, the five compressive syringes, and the spring loaded syringe prototype.

6.1 Plunger Force Analysis

Using a force gauge stand, the force created by the plunger was determined. The trials were conducted with only the standard syringe, the syringe with a sealed luer lock attachment, and the syringe in water. The following tests would help the team analyze the force that our designs need to produce.

The average force of the plunger for solely the conventional syringe was 7.07 ± 0.94 N. For the syringe with the sealed Luer Lock the average force of the plunger was 13.3 ± 1.35 N. There were two separate syringes used for the experiment of the force plunger analysis in water. For Syringe 1, the average force of the plunger was 6.0 ± 1.25 N. For Syringe 2, the average force of the plunger was measured to be 2.95 ± 0.38 N.

6.2 Force Pullout test

The team also investigated the force it took to move the plunger. A force gauge and test stand was used to conduct this test. This test was conducted in water, milk, and rat liver. The plunger force analysis was conducted with the needle in milk because it has a similar viscosity to blood. We used rat liver because the liver is an organ that is similar to human tissue in which a Fine Needle Aspiration is conducted on. Performing tests using milk and rat liver would simulate an environment similar to the one used for needle biopsy. We performed various numbers of trials with a minimum of two different syringes.

The results of the data this assessment in water for Syringe 1 and 2 were averaged to be 3.2 ± 0.448 N and 3.8 ± 1.29 N. The overall average for the pullout analysis in water of both syringes was 3.5 ± 0.869 N. The average forces for this test in rat liver for syringe 1, 2, 3 were 8.67 ± 2.47 N, 9.08 ± 2.14 N, and 8.85 ± 2.48 N. The total force to withdraw the plunger while the needle was in the rat liver was 8.87 ± 2.36 N. Regarding the pullout test in milk, there were two syringes used for the first group of trials. The pullout force for Syringe 1 and 2 for the first

set of the trials were 2.3 ± 0.89 N and 6.0 ± 1.71 N, respectively with the total average of 4.15 ± 1.3 N. There was a second group of trials with the assessment in water conducted with the same syringes that was used in milk, but the needle was changed to eradicate any mixing of the water and milk that may have been present in the needle. For this test, the average force to extend the plunger for Syringe 1 and 2 were 3.5 ± 1.87 N and 5.5 ± 0.94 N, correspondingly. The overall average for the assessment in water with the Syringes 1 and 2 used in milk was 4.5 ± 1.41 N.

6.3 Instron Machine Testing

The Instron Machine helped us understand the amount of compression force was applicable to the various tubing used for the compressive syringe prototypes. The different materials that were analyzed with the Instron machine were polyethylene, polyurethane, polyvinyl chloride and silicone. The polyvinyl chloride tubing had the highest average load at maximum compressive stress (43.71 ± 3.803 N) with polyethylene (32.89 ± 0.414 N) having the second highest. Following polyethylene was the silicone tubing with average compressive stress of 19.80 ± 0.826 N. The polyurethane tubing had the least average compressive stress 16.21 ± 0.251 N. The compression data from each of the compressive prototypes are shown in Table 2.

Compressive Prototypes	Average Force at Maximum Compressive Stress (N)
Polyethylene	32.89 ± 0.414
Polyurethane	16.21 ± 0.251
Poly-vinyl chloride	43.71 ± 3.80
Silicone	19.80 ± 0.826

Table 2: Average Force at Maximum Compressive Stress

6.4 Pressure Data of Standard 10 mL BD Syringes

The team acquired pressure data of a standard Becton Dickinson 10 mL syringe that is currently used to conduct Fine Needle Aspiration. The overall average pressure for the various for Syringes 1, 2 and 3 was 6.42 ± 0.017 psi.

	Trial	Negative Pressure (psi)
Syringe 1	1	6.45
	2	6.46
	3	6.46
	4	6.47
	5	6.47
	Average	6.46
	Standard Deviation	± 0.00837
Syringe 2	1	6.25
	2	6.30
	3	6.29
	4	6.31
	5	6.30
	Average	6.29
	Standard Deviation	± 0.0235
Syringe 3	1	6.5
	2	6.55
	3	6.52
	4	6.52
	5	6.53
	Average	6.52
	Standard Deviation	± 0.0182

Table 3: Pressure Data of Standard 10 mL BD Syringes

6.5 Pressure Data of Prototypes

The following pressure data was collected by attaching the pressure transducer to each of the prototypes via the luer lock attachment to obtain pressure readings to compare to the pressure data acquired from a standard 10 mL BD syringe.

Trials	Pressure of Polyethylene (psi)	Pressure of Silicone (psi)	Pressure of Polyurethane (psi)	Pressure of PVC (psi)	Pressure of Polyurethane w/ LMS valve (psi)	Pressure of PVC w LMS valve (psi)
Trial 1	4.20	3.06	3.20	2.38	2.71	2.81
Trial 2	4.03	3.20	3.22	2.41	2.85	2.91
Trial 3	3.05	3.06	3.13	2.41	2.71	2.83
Trial 4	3.55	3.12	3.15	2.36	2.78	2.81
Trial 5	3.62	3.17	3.09	2.34	2.95	2.81
Trial 6	3.54	3.65	3.17	2.23	2.91	2.78
Trial 7	3.53	3.29	3.09	2.25	2.98	2.94
Trial 8	3.53	3.08	3.18	2.30	2.93	3.00
Trial 9	3.58	3.08	3.15	2.36	2.87	2.77
Trial 10	3.53	3.80	3.28	2.39	2.80	2.65
Average:	3.62	3.25	3.17	2.34	2.85	2.83
Standard Deviation	± 0.310	± 0.262	± 0.0583	±0.0636	± 0.100	±0.0984

Table 4: Pressure Data of Prototypes

6.6 FNA Pressure Data using standard 10 mL BD syringe

After collecting pressure data of the standard syringe, the team collected pressure data during a FNA procedure. To do so, the team utilized a three-way valve by connecting it to a 22 and 25 gauge (1 ½ inches in length) and the VWR pressure gauge. To test the FNA procedure, rat liver waste tissue was acquired from a Biomedical Engineering Graduate Course.

	Trial	Negative Pressure (psi)
Syringe 1 & 22 Gauge Needle	Trial 1	5.98
	Trial 2	6.04
	Trial 3	6.02
	Trial 4	5.98
	Trial 5	6.08
	Trial 6	5.92
	Trial 7	6.14
	Trial 8	5.90
	Trial 9	6.03
	Trial 10	6.10
	Average	6.02
	Standard Deviation	± 0.076
Syringe 2 & 25 Gauge Needle	Trial 1	5.82
	Trial 2	6.06
	Trial 3	6.13
	Trial 4	6.23
	Trial 5	6.26
	Trial 6	6.28
	Trial 7	5.73
	Trial 8	6.25
	Trial 9	6.11
	Trial 10	6.25

	Average	6.11
	Standard Deviation	± 0.193

Table 5: FNA Pressure Data using Standard 10 mL BD Syringe

6.7 FNA Pressure Data using prototypes

After conducting the FNA procedure using the standard syringe, pressure data was collected using selected prototypes to acquire the pressure and determine if the aspiration collected adequate tissue sample. The three prototypes that were analyzed during FNA were the silicone tubing and duckbill valve, the polyurethane tubing and the duckbill valve and the spring-loaded syringe.

	Trial	Negative Pressure (psi)
Silicone Tubing (duckbill valve & 22 Gauge Needle)	Trial 1	1.30
	Trial 2	1.20
	Trial 3	1.52
	Trial 4	1.55
	Trial 5	1.35
	Trial 6	1.41
	Trial 7	1.44
	Trial 8	1.30
	Trial 9	1.38
	Trial 10	1.53
	Average	1.40
	Standard Deviation	± 0.11
Polyurethane tubing (duckbill valve) & 25 Gauge Needle	Trial 1	1.57
	Trial 2	1.61
	Trial 3	1.53
	Trial 4	1.73
	Trial 5	1.80
	Trial 6	1.68

	Trial 7	1.53
	Trial 8	1.55
	Trial 9	2.05
	Trial 10	1.97
	Average	1.70
	Standard Deviation	± 0.19

Table 6: FNA Pressure Data with Prototypes

The spring-loaded syringe was also tested with FNA pressure assessment. The following tables display the various pressure data obtained the Spring-loaded Syringe had an approximate average of about 2 psi.

Trial	Negative Pressure (psi)
Trial 1	1.92
Trial 2	1.95
Trial 3	1.93
Trial 4	1.90
Trial 5	1.95
Trial 6	2.02
Trial 7	1.91
Trial 8	2.38
Trial 9	2.39
Trial 10	2.45
Average	2.08
Standard Deviation	$\pm .228$

Table 7: Round 1- FNA Pressure data with Spring-loaded Syringe (21-gauge Needle)

Trial	Negative Pressure (psi)
Trial 1	2.11
Trial 2	2.10
Trial 3	1.85
Trial 4	2.08
Trial 5	2.45
Trial 6	2.29
Trial 7	2.13
Trial 8	1.93
Trial 9	2.61
Trial 10	2.34
Average	2.19
Standard Deviation	±.233

Table 8: Round 2- FNA Pressure Data with Spring-loaded Syringe (21-gauge Needle)

Trial	Negative Pressure (psi)
Trial 1	2.45
Trial 2	2.56
Trial 3	2.15
Trial 4	2.38
Trial 5	2.23
Trial 6	2.23
Trial 7	1.78
Trial 8	2.20
Trial 9	2.12
Trial 10	2.09
Average	2.22
Standard Deviation	±.216

Table 9: FNA Pressure Data with Spring-loaded Syringe (22-gauge Needle)

6.8 Tissue Sample

After performing FNA using the compressive designs, the next step was to examine the amount of tissue collected. The collected tissue samples were not sent to pathology for investigation. However, after conduct testing with the client, the team was informed that the collected tissue samples were sufficient by the compressive prototypes.

Figure 53 showed two runs for collecting tissue cells in a container from Silicone compressive prototype, labeled 1 & 2, and the Polyurethane compressive prototype, labeled 3.

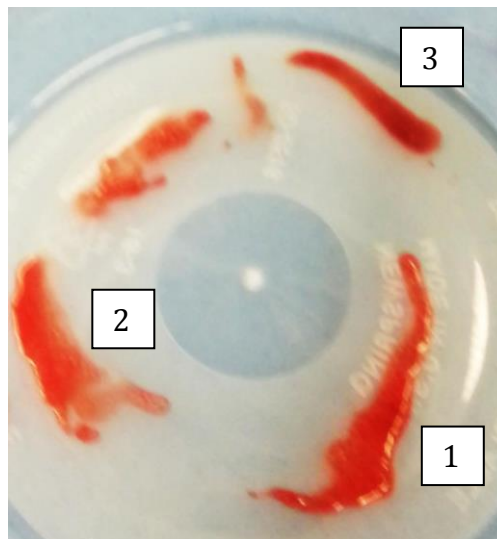


Figure 53: Tissue Cells Acquired from Silicone & Polyurethane Compressive Prototypes

Chapter 7: Discussion

After compiling the results from the experiments to validate the various compressive syringe prototypes and the Spring-loaded syringe prototypes, the results were thoroughly analyzed.

7.1 Plunger force and Pullout Analysis

The data acquired from the plunger force data was used to determine specifications for the spring in the spring-loaded syringe. The lowest average force was the testing with the syringe in water. The pullout assessment was conducted with the standard syringe in milk, water and rat liver. The highest average force to extend the plunger was the testing done in the rat liver because rat liver has the higher viscosity when compared to water and milk. The lowest average force was the analysis done in water, which is logical because it has the lowest viscosity in comparison to milk and rat liver.

7.2 Pressure Drop data from each prototype not related to FNA

There were various pressure results collected from analyses with the conventional syringe and the different prototypes. The data gathered from the standard 10 mL syringe was the desired goal that the team was trying to achieve with the prototypes. The average gauge pressure of the Polyethylene, Polyurethane, and Silicone compressible tubing attached to duckbill valves acquired a gauge pressure that was approximately half of the gauge pressure from the 10 mL syringe. The team hypothesizes that there are many factors that contribute to the variation of pressure conventional syringe to the prototypes that were created. The variation in the pressure is related to the duckbill valve and the luer lock attachment being epoxied on to the compressible tubing. Initially, the epoxy did not create an airtight environment upon suction; therefore, the air leaked through causing a lowered pressure drop. Also the flaps of the duckbill valve did not always shut completely, preventing air from leaking through; thus causing the pressure to equalize faster.

The team also checked the pressure drop from the prototypes attached to a SureFlo[®] Valve. The team compared the pressure drop of the polyvinyl chloride (PVC) and polyurethane (PU) compressible tubing attached to a SureFlo[®] Valve to the pressure drop of polyvinyl chloride and polyurethane compressible tubing attached to a Duckbill Valve. The change in pressure from the prototypes with the SureFlo[®] Valves was seen to be lower than that of the prototypes with the

Duckbill valves.

7.3 Finite Element Analysis

To make sure this model was appropriate for our project, the conditions of our Instron compression test were used for an analysis. The material properties of aromatic polyester polyurethane A85, which was the material we purchased, and the dimensions of our prototype were used. According to the Instron testing, the tube compressed fewer than 18 N; consequently an equivalent load was placed. The load surface was slightly smaller in length (1 cm) to mimic the width of the compressing bars of the Instron.

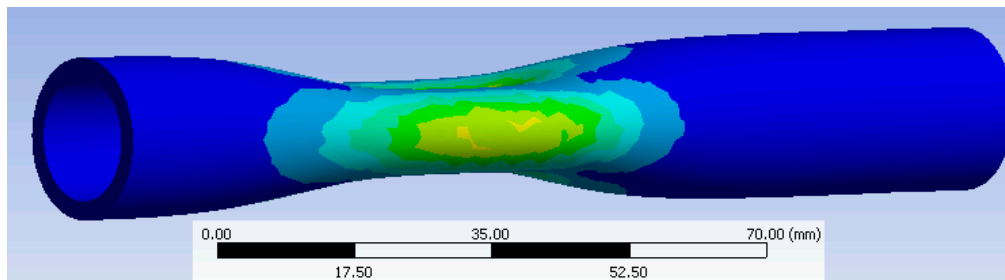


Figure 54: FEA Model - 18 N Load

We see that the material compresses nearly all the way. We would expect the cylinder to compress all the way, as we saw in real life, but this leads us to believe that using the linear finite element model is appropriate for our project.

Initially the finite element model was used to observe the deformation and internal stress of the hollow cylinder when elastic modulus and wall thickness are changed. Figures 55 to 57 illustrate the deformation under varying wall thicknesses. These use a modulus of 172 MPa and a Poisson's ratio of 0.45, the properties for LDPE.

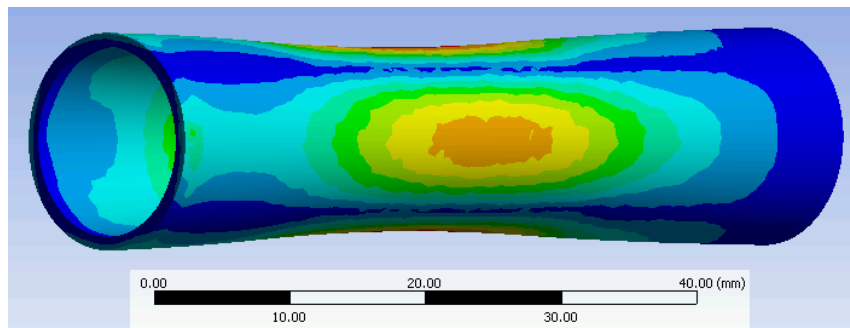


Figure 55: FEA Model- 0.1 cm Thickness

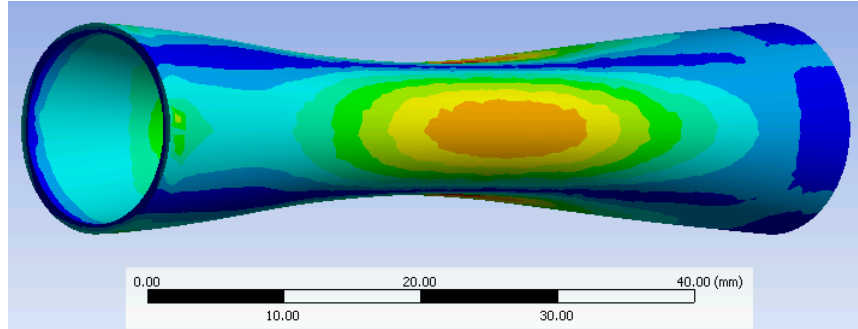


Figure 56: FEA Model - 0.07 cm Thickness

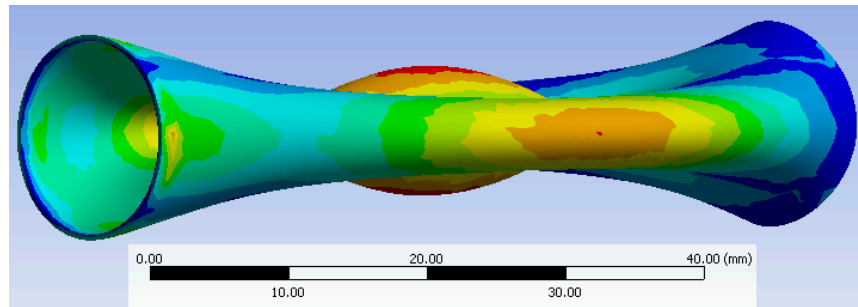


Figure 57: FEA Model - 0.04 cm Thickness

The cylinder with a wall thickness of 0.1 cm had a maximum internal stress of 6.57 MPa. The cylinder with a 0.07 cm thickness endured a maximum stress of 11.7 MPa, and the cylinder of 0.04 cm thickness had a maximum internal stress of 27.91 MPa.

Figures 58 through 60 show the deformation of the model at thickness is 0.7mm and elastic moduli of 300, 50, and 1, respectively. A Poisson's ratio of 0.45 is assumed for each model. The maximum internal stress was 12.02 MPa for each.

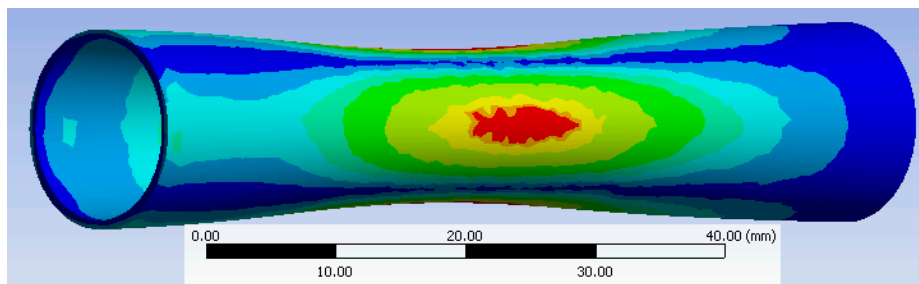


Figure 58: FEA Model- 300 MPa Modulus

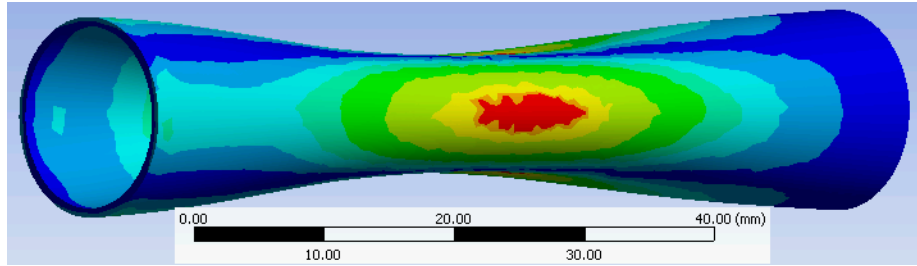


Figure 59: FEA Model - 150 MPa Modulus

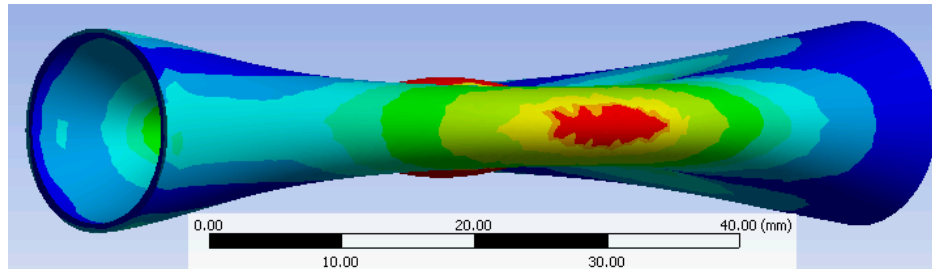


Figure 60: FEA Model - 50 MPa Modulus

The initial comparison comparing wall thicknesses and moduli helped direct our materials search towards more flexible, elastic materials. We considered some commodity plastics such as polypropylene and polyethylene, due to their low cost and common usage in the medical field, but the finite element analysis showed that these materials were far too stiff for this application. Polypropylene has a young's modulus of 800-1000 MPa and low-density polyethylene has a modulus of 180 MPa, while the model demonstrated that elastic moduli in the 1-100 MPa range might be more suitable. After continuing to iterate the model, the ideal material properties of the cylinder were determined. A wall thickness of 0.5 cm was used, because this is the minimum wall thickness that can be created with injection molding technology [8]. The minimum value for thickness was used to minimize the volume of the part, and a lower volume means lower material costs.

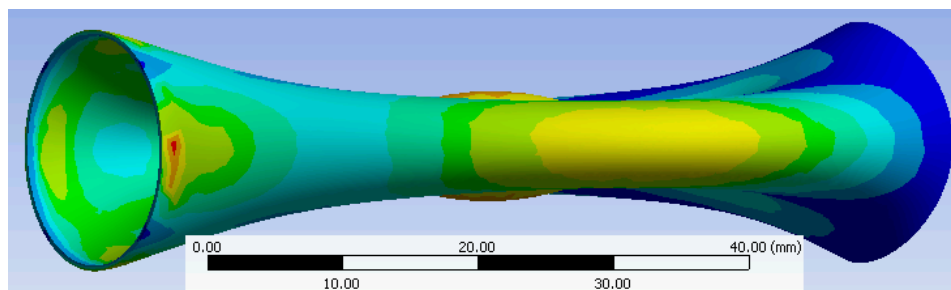


Figure 61: FEA Model - Final Design

The final design optimized by this process is a cylinder with an inside diameter of 1.7 cm, a wall thickness of .05 cm, and a length of 6.5 cm. The elastic modulus used was 40 MPa. The maximum internal stress was recorded at 26.12 MPa. The ideal material, as determined by this analysis, has an elastic modulus of 40 MPa and a yield stress that is greater than 26.12 MPa. Thermoplastic polyurethane elastomer (TPU) was the material proposed for our design. Depending on composition, reinforcement, and manufacturing process the modulus for TPU can range from 13 MPa to over 1000 MPa. Specifically, aromatic polyester TPU A85 has an elastic modulus ranging from 28-40 MPa and a yield stress of 40 MPa. These dimensions were used for the model sent to Nypro for a cost estimate.

A more complex FEA model was developed to ensure that the cylinder would reform to its original shape under 6 psi of negative pressure. This was a non-linear, large deformation analysis. The set-up incrementally applied a 40 N load, and incrementally removed the load. As the load was removed, a negative pressure was applied incrementally to the inside surface of the cylinder. The model intended to account for the non-linearities of the material, as well as the hysteresis encountered during the unloading phase. Ultimately this goal was unachieved, as it required an expertise with the ANSYS software that was above the skill level of the team. If there were more time, the team would like to investigate this concept more to prove the mechanical functioning of the device.

7.4 Pressure Drop with Fine Needle Aspiration in Rat Liver

The client was present during FNA testing and had the opportunity to grip the various compressive syringe prototypes. After the doctor held each of the prototypes, the polyethylene compressive device and the PVC compressive device were disregarded because its stiffness was higher than necessary. Therefore, the polyurethane and silicone compressive device were the prototypes that the team used to perform the FNA procedure.

The change in pressure was collected during an FNA were conducted in rat liver. The pressure drop was measured using the polyurethane and silicone compressible tubing attached to duckbill valves that was less expected pressure. The team compared the pressure drop of an FNA procedure using the prototypes to that of a 10 mL standard syringe. The team used two different sized needles 22 and 25 gauge because these size needles are most commonly used during FNA procedures. Syringe 1 had a 22-gauge needle attached and the average gauge pressure during the FNA was approximately 6.02 ± 0.076 psi and syringe 2 with a 25-gauge needle, had an average

gauge pressure of 6.11 ± 0.193 psi. There is not a significant difference between the two syringes. Therefore, the needle did not change much of the pressure data of the syringe. The silicone tubing had a 22-gauge needle attached and the average pressure obtained was 1.40 ± 0.11 psi. The polyurethane tubing was tested with a 25-gauge needle attached and the average pressure was 1.70 ± 0.19 psi. The average pressure results of the two prototypes were less than half of the average of the standard syringes. The average pressure between these two devices was half than the desired amount. This is because the wall thickness of these devices was small (small volume within the cylinder), resulting in a lower displaced pressure.

Due to the SureFlo[®] valve not being able to equalize the pressure while the needle was inserted into the tissue, the polyurethane tubing with LMS valve and the PVC tubing with the LMS valve were not evaluated. Equalizing the pressure while in the tissue is essential for the tissue not travel up the needle and into the body of tubing because ejecting the sample becomes difficult. Therefore, equalizing the pressure while in the tissue ensures that the tissue collected remains in the needle or in the luer lock attachment.

Although, the pressure of the two prototypes were not as high as expected the client was satisfied with the amount of sample they were able to collect. The amount of sample that the prototypes are able to collect is an important aspect of the procedure. The higher amount of sample acquired, the higher chances of the determining what type of cells are present in the lesion.

7.5 Client Feedback

After testing the Silicone and the Polyurethane prototypes with the duckbill valve, the doctor was pleased with the amount of suction that these prototypes create. Even though the negative pressure that these designs create are less than the standard 10 mL syringe, the doctor's main objective was to see if these designs improve on aspirating accurate tissue cells. Furthermore, the doctor was satisfied with the amount of tissue cells that were aspirated from the Silicone and polyurethane compressive prototypes.

7.6 FNA Spring-loaded Syringe Pressure Data

Aside from conducting FNA procedure with the compressive device, the team also conducted FNA using the spring-loaded prototype. The team connected the spring-loaded syringe to a 22 or 21 gauge needle and a pressure transducer and conducted FNA on Sprague Dawley rat liver. The average gauge pressure using a 21-gauge needle was 2.22 ± 0.216 psi. The average gauge pressure using two 21-gauge needles were 2.07 ± 0.238 psi and 2.19 ± 0.233 psi. The increase in pressure was likely because the 22-gauge needles have smaller diameters than the 21-gauge needles.

Furthermore, though the negative pressure obtained was similar to that of the compressive device, the spring-loaded syringe showed inconsistency in acquiring tissue sample from the FNA. Upon releasing the compression of the pre-compressed spring the clicking mechanism did not consistently aspirate enough cells from the rat liver. Sometime the aspiration collected enough tissue and other times the aspiration did not collect any tissue at all.

7.7 Instron Maximum Force Data

After the compressive design was prototyped and tested the team wanted to see if doctors with different grip strengths could use the device.

These silicone and polyurethane compressive devices required less force to compress than that of the polyvinyl chloride and the polyethylene compressive devices. Therefore, for bulk manufacturing the team proposed that the device has similar elastic properties to silicone or polyurethane tubing.

7.8 Evaluation of Compressive Designs

The team evaluated each of the compressive designs based on different parameters. These parameters include autoclavable, injection moldable, young's modulus (material stiffness), yield stress, cost per pounds, and shelf life. Based on these parameters the team would decide which of these materials would be the best candidate for bulk manufacturing. Table 10 highlights the parameters of each of the materials that were considered for prototyping the compressive device.

	Polyamide (Nylon) Type 6,66 Copolymer	Polypropylene (unfilled, copolymer, impact, high flow)	Low Density Polyethylene (branched homopolymer)	Silicone Elastomer (VMQ thermally conductive)	Polyurethane	PVC (Flexible Shore A85)	Thermoplastic Polyurethane Elastomer
Young's Modulus (MPa)	689.48	820.47	171.68	7.51	2068.42	30.00	20.48
Yield Stress (MPa)	28.61	32.89	8.96	3.40	40	19.00	31.9
Cost / lb. (\$)	2.10	0.95	0.98	2.50	1.69	2.12	2.31
Autoclavable	Yes	Yes	No	Yes	No	No	Yes
Injection Molding	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Medical Grade Available	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Table 10: Evaluation Matrix of Compressive Prototype Materials

From Table 10, the most suited material for the compressive prototype is one that meets all the parameters. For the final design, the team chose Thermoplastic Polyurethane Elastomer (TPU) and Silicone Elastomer because they met all the parameters that were specified.

Thermoplastics have a shelf life of approximately one year when stored at a temperature of between 35^o – 95^o F. Thermosets on the other hand have shelf of less than six months because they are often less stable.

7.9 One-way Valve Evaluation

From the two valves, we chose the Duckbill Valve as the preferred valve because the LMS SureFlo[®] Valve was unable to equalize the pressure within the device. Equalizing the pressure is essential when the doctor compresses the body of the compressible device to prevent the tissue from being shot up the needle and into the body of the device. Therefore, equalizing the pressure allows the tissue to remain in the needle. Only after conducting FNA with the client,

the team realized that the SureFlo[®] Valve would not be suitable. The Duckbill Valve is appropriate for this application because the doctor has the ability to equalize the pressure during this procedure. Table 11 summarizes the differences between the two valves that were considered for the project.

	Duckbill Valve	LMS SureFlo [®] Valve
Opening Pressure	N/A	Range 0.38-6 Psi
Pressure release	User	Unable
Attachment	Molded	Secondary bonding step (epoxy)
Material	Silicone	Silicone Valve & plastic fitment
Autoclavable	YES	No

Table 11: Comparison between the Valves

7.10 Comparison of Compressive Device & Spring-loaded Prototypes

Through FEA and evaluation of results from FNA pressure data, the silicone and polyurethane tubing with duckbill valves were the most desirable prototypes. As previously mentioned, the client was pleased with the amount of sample from both prototypes. Our client did prefer the grip of the silicone prototype to that of the polyurethane grip. Due to inconsistent data and the feedback from our client, it was determined that the spring-loaded syringe would not be our final design. Our client, Dr. Karam informed our team that this prototype is too bulky for use in FNA. One of the objectives our device stated previously was that our device needed to be inexpensive. The Spring-loaded syringe does not meet this requirement. The spring-loaded syringe is easy to use but the compressive device is easier to use. The compressive device has a better grip and motor control than the syringe-loaded syringe.

7.11 Comparison of Compressive Device & Spring-loaded Prototypes

Through FEA and evaluation of results from FNA pressure data, the silicone and polyurethane tubing with duckbill valves were the most desirable prototypes. As previously mentioned, the client was pleased with the amount of sample from both prototypes from performing FNA. Our client did prefer the grip of the silicone prototype to that of the

polyurethane grip. Therefore, the duckbill valve was the best way to control pressure throughout our prototype. Due to inconsistent data and the feedback from our client, the spring-loaded syringe would not be considered as our final design. Our client, Dr. Karam informed us that this prototype is too bulky for use in FNA. One of the objectives our device stated previously was that our device needed to be inexpensive. The spring-loaded syringe does not meet this requirement. The spring-loaded syringe is easy to use but the compressive device is easier to use. The compressive device has a better grip and enhanced motor control than the syringe-loaded syringe for successfully conducting a FNA procedure. The compressive device eliminates the need of having a highly skilled physician or doctor to conduct the procedure because aspiration occurs simply by compressing the body of the tubing and reforming back to its original shape after the force is removed.

7.11.1 Cost Comparison of Compressive Device and Spring-loaded Syringe

After discussing design details with Tim Baird from Nypro Medical, we received a cost estimate for manufacturing the Thermoplastic Polyurethane Elastomer (TPU) compressive device along with a duckbill valve via injection molding. The TPU compressive device attached to the duckbill valve was chosen as the final design based on costs and performance during FNA testing. The design sent to Nypro was a cylinder with an inside diameter of 1.7 cm and a wall thickness of 0.03 cm as determined by the FEA model. The device must be molded in 2 parts and assembled; this estimate assumes a semi-automatic ultrasonic welder is used. Table 12 shows the cost estimate that we were provided to us for injection molding the TPU compressive device with the duckbill valve.

Year	Assemblies/Year	Assemblies/Run	Assy/Run 10% Scrap	Annual Labor	Annual Parts	Per Assy Cost	Sale Price
1	50,000	10,000	11,000	\$2,979.17	\$49,025.15	\$1.121	\$1.457
2	75,000	15,000	16,500	\$4,468.75	\$72,037.73	\$1.102	\$1.433
3	100,000	20,000	22,000	\$5,958.33	\$82,828.09	\$0.982	\$1.276
4	150,000	30,000	33,000	\$8,937.50	\$122,742.13	\$0.973	\$1.264
5	200,000	40,000	44,000	\$11,916.67	\$162,656.17	\$0.968	\$1.258

Table 12: Injection Molding Estimates

The estimate assumes a single operator at \$18.00/hr splits time between three machines between two injection-molding units and the ultrasonic assembly unit. Years 1-2 use 1-cavity molds, while years 3-5 use 2-cavity molds. With the two cavity molds, twice as many parts are molded at the same labor rate, so cost decreases. The production rate increases each year, absorbing some of the overhead and resulting in reduced cost. The sale prices include a 30% profit margin. Even though the cost of manufacturing and selling a TPU compressive device is more than a standard 10 mL syringe (less than \$1), it provides better control, enhanced grip, and single handed so that the physician/doctor can maintain a real-time image of the lesion during a FNA procedure.

Furthermore, the compressive device is more cost efficient than the spring-loaded syringe because the spring-loaded syringe has many parts, which would lead to high manufacturing costs.

7.12 Impact of Compressive Device

While our design team believes that the Compressive Device for FNA will improve the efficiency of the procedure, we understand the impacts on other aspects such as economics, politics, ethics, the environment and manufacturability.

7.12.1 Economic Impact

As previously mentioned in the literature review, the numbers of cancer cases are great and the ways to determine whether cancer is present and allowing for early detection of cancer is significant. In addition, fine needles aspiration is widely used to collect a sample of cells to be sent to pathology, which determine if cancer exists in the suspected region of the body. Due to the widespread practice of FNA, there is a large market for the devices used for this procedure. Therefore, a device that is not expensive will improve the FNA procedure will be beneficial.

7.12.2 Political Ramifications

Political ramifications need to be examined due to the fact that clinical testing is required before any device that is FDA approved and available on the market. Animals will be used to perform clinical testing which can be controversial to various organizations. For example, the People for Ethical Treatment of Animals (PETA) is an animal rights organization that strong support humane treatment of animals. Therefore, to avoid any conflicts with PETA and similar groups, all appropriate protocols should be followed.

7.12.3 Environmental Impact

The compressive device could impact the environment significant. There is typically a minimum of three syringes used per FNA procedure sometimes more if there is not an adequate amount of sample obtained. Since the syringes are disposable and comprised of different plastics it can be harmful to the environment. Our device has proven to obtain a sufficient amount of sample and can improve the procedure overall with feedback from our client, Dr. Adib Karam. If enough samples are acquired with the compressive device, which is also disposable, then the amount of syringes used will be no more than three. This will lead to a decrease in disposing of plastics materials because FNA is practiced widespread.

7.12.4 Manufacturability

The team evaluated the manufacturability of the compressive device by discussing details with Tim Baird from Nypro Medical. Injection Molding would be the best option to manufacture our device. The device could easily be manufactured due to the design of our device and the lack of elaborate components. Injection molding will be the most efficient process to manufacture the compressive device due to the numerous FNA procedure performed.

7.12.5 Sustainability

The compressive device is a sustainable solution to performing Fine Needle Aspirations. Being able to reduce the complications of the current procedure and obtaining quality samples will allow the device to be used for a long time. Concerning manufacturing costs, the price per device will decrease as the production rate increases. The cost of this device will be more than the current standard syringe by approximately one dollar but the compressive device offers better grip and control, which doctors will prefer over the current standard. Our client has showed much interest in our device even if it will be slightly more expensive than the conventional 10 mL syringe.

7.12.6 Health and Safety

The health and safety regarding the implications of this device is a main concern. There are no small elaborate components of the device, which can increase the risk of manufacturing problems. The lack of smaller components increases the stability of the device. This device will be used on humans, but before use on humans there will be much testing including on animals to validate the safety and accuracy of the device.

7.12.7 Ethical Concern

FNA is a minimally invasive and safe procedure therefore the risks are low with presenting a new device for this procedure. Our device uses the same needles as current FNAs, so it does not present any ethical concerns. Also, the clinical testing will be detailed and follow protocol in hopes that the device will provide a more comfortable and efficient procedure for patients as well as for doctors.

7.12.8 Societal Influence

After the manufacturing and marketing of this device, there will be changes occurring to the society. There will be notifications about this device and its benefits to encourage purchase.

Chapter 8: Conclusion

The team developed a new device that addressed and satisfied the requirements of our client. The compressive syringe prototype with the silicone tubing and the duckbill valve achieved the most desired results in regards to the amount of tissue sample collected. This compressive syringe has the ability to improve the Fine Needle Aspiration procedure by means of providing comfortable, single-handed function of the device and obtaining sufficient tissue sample from lesion. In addition, the compressive syringe was more cost efficient than the spring-loaded syringe.

8.1 Silicone Tubing & Duckbill Valve

The client preferred the grip of the silicone grip to the grip of the polyurethane tubing. Due to the SureFlo[®] Valve not being able to work, the duckbill valve was chosen. The duckbill valve performed as hoped during the FNA pressure testing. The cost to manufacture the compressive device would be a more expensive than the standard syringe by almost a dollar but the compressive device provides better grip and motor control, which would improve the efficiency of FNA procedures.

8.2 Spring-Loaded Syringe

From the obtained data, it was established that the spring-loaded syringe could not produce consistent results. In addition, the grip and the size of this prototype would not be preferred over the compressive device or even the conventional 10 ml syringe that is used now.

8.3 Recommendations

Before this device can enter the market, it needs to be further optimized by an expert in medical plastics and manufacturing. While this report offers a proof of concept and a detailed description of our work, further pre-production analysis must be done. One recommendation would be to conduct in vivo FNA procedures on animal models. In addition, we would like to send tissue samples to pathology to test for accuracy and amount. Concerning manufacturing, we would like to go through with production compressive device via injection molding. With further testing and results, our team would like to obtain additional feedback from doctors and physicians.

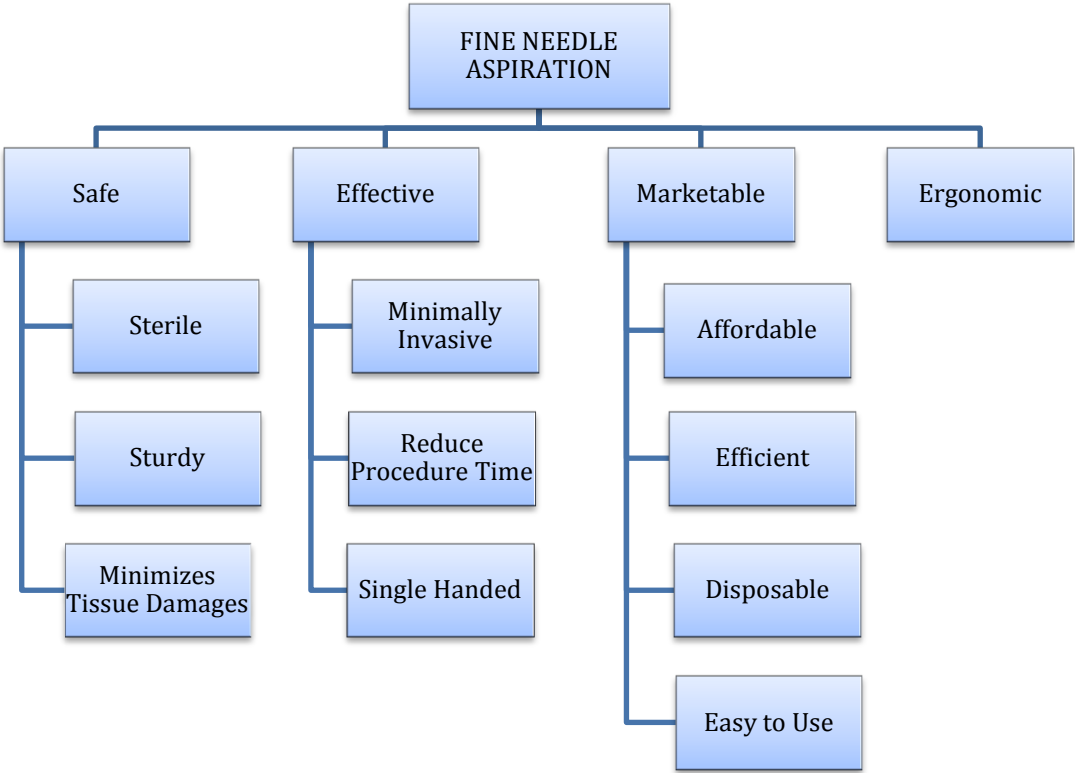
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Appendix A: Objectives Tree



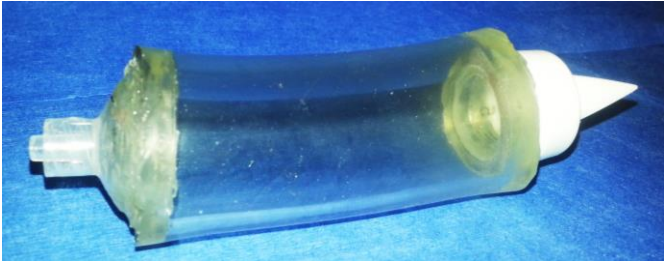
Appendix B: Pairwise Comparison Chart

Pairwise Comparison Chart	Sterile	Minimizes Tissue Damage	Minimally Invasive	Reduce Procedure Time	Affordable	Easy-to-Use	Efficient	Single-Handed	Ergonomic	TOTAL
Sterile		1	1	1	1	1	1	1	1	8
Minimizes Tissue Damage	0		0.5	1	1	1	0	0	1	4.5
Minimally Invasive	0	0.5		1	1	1	1	0	1	5.5
Reduce procedure Time	0	0	0		0	0	0.5	0	1	1.5
Affordable	0	0	0	1		0	0	0	1	2
Easy-to-Use	0	0	0	1	1		0	0	1	3
Efficient	0	1	0	0.5	1	1		0	1	4.5
Single-Handed	0	1	1	1	1	1	1		1	7
Ergonomic	0	0	0	0	0	0	0	0		0

Appendix C: Polyurethane tubing with SureFlo® Valve



Appendix D: Polyethylene tubing with duckbill valve



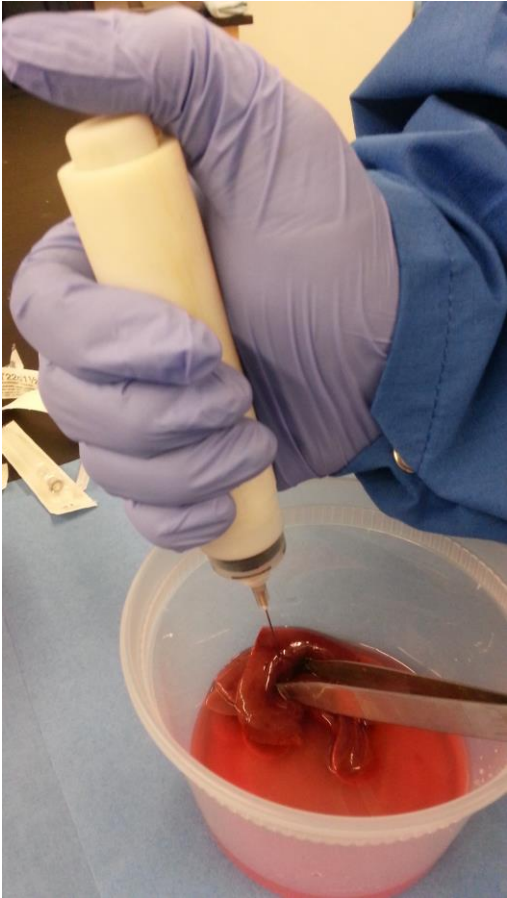
Appendix E: Silicone tubing with duckbill valve



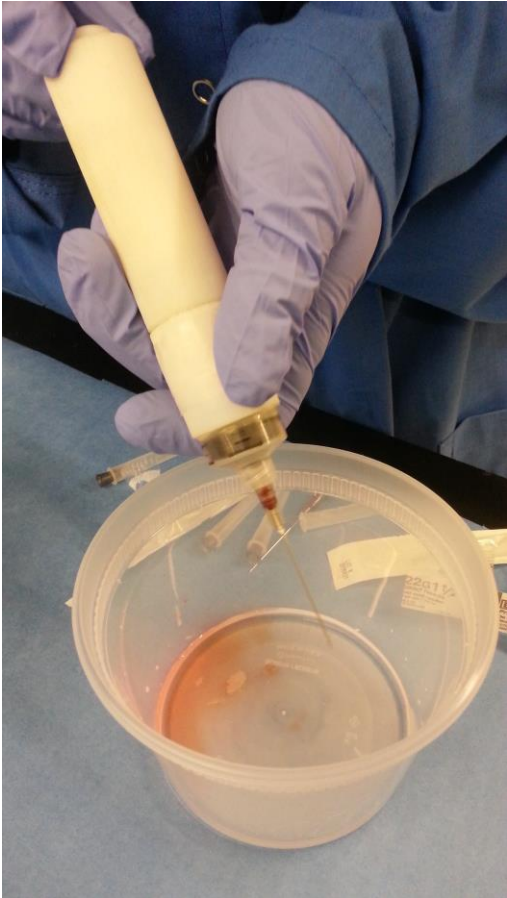
Appendix F: PVC tubing with SureFlo[®] Valve



Appendix G: FNA with spring-loaded syringe in rat liver



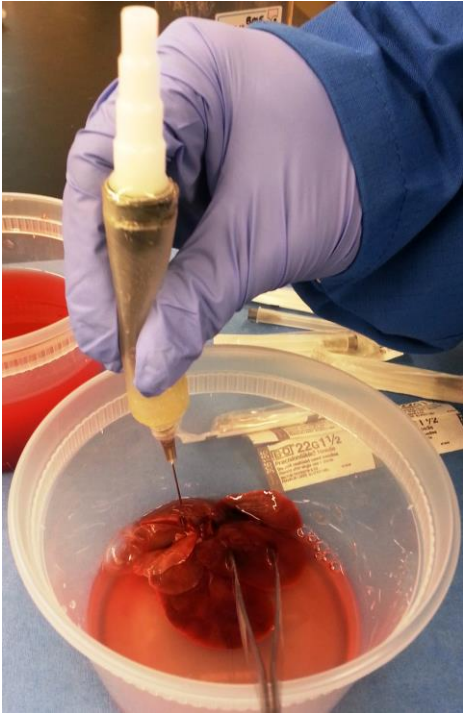
Appendix H: Ejection of Sample from Spring-loaded Syringe



Appendix I: FNA in rat liver with PVC tubing and SureFlo® Valve



Appendix J: FNA using SureFlo® Valve



Appendix K: Plunger Force Testing

Plunger Force Analysis of Only Syringe

Trial	Force (Newton)
Trial 1	6.5
Trial 2	6.0
Trial 3	6.0
Trial 4	7.75
Trial 5	7.0
Trial 6	8.25
Trial 7	8.0
Average	7.07
Standard Deviation	±0.94

Plunger Force Analysis with Sealed Luer Lock

Trial	Force (Newton)
Trial 1	10.2
Trial 2	16.0
Trial 3	13.6
Trial 4	13.0
Trial 5	13.0
Trial 6	14.2
Trial 7	14.4
Trial 8	13.6
Trial 9	12.8
Trial 10	14.2
Trial 11	13.4
Trial 12	12.4
Trial 13	14.2
Trial 14	11.4

Trial 15	13.6
Average	13.3
Standard Deviation	± 1.35

Plunger Force Analysis of Syringe 1 in Water

Trial	Force (Newton)
Trial 1	5.2
Trial 2	4.4
Trial 3	5.0
Trial 4	7.8
Trial 5	5.8
Trial 6	4.4
Trial 7	6.4
Trial 8	7.4
Trial 9	7.4
Trial 10	6.0
Average	6.0
Standard Deviation	± 1.25

Plunger Force Analysis of Syringe 2 in Water

Trial	Force (Newton)
Trial 1	2.4
Trial 2	3.2
Trial 3	3.0
Trial 4	3.2
Average	2.95
Standard Deviation	± 0.38

Appendix L: Pullout Test Results

Pullout test with water

Trials	Force (Newton) - Syringe 1	Force (Newton) - Syringe 2
Trial 1	2.8	2.0
Trial 2	3.0	3.6
Trial 3	3.2	4.4
Trial 4	3.2	3.6
Trial 5	3.5	3.6
Trial 6	2.8	3.6
Trial 7	3.2	2.0
Trial 8	3.6	2.0
Trial 9	3.0	4.4
Trial 10	3.2	3.6
Trial 11	4.2	3.6
Trial 12	4.0	3.6
Trial 13	4.0	3.6
Trial 14	3.8	6.4
Trial 15	3.6	6.2
Average	3.2	3.8
Standard Deviation	±0.448	±1.29

Pullout test with rat liver

Trials	Force (N) – Syringe 1	Force (N) – Syringe 2	Force (N) – Syringe 3
Trial 1	7.2	3.6	3.0
Trial 2	10.0	11.2	4.8
Trial 3	9.6	7.2	9.6
Trial 4	4.0	8.0	11.6
Trial 5	4.8	10.0	8.8
Trial 6	5.6	12.4	6.4
Trial 7	11.6	9.6	10.4

Trial 8	12.8	8.0	10.4
Trial 9	10.0	9.6	9.2
Trial 10	8.4	8.4	9.6
Trial 11	10.0	8.0	9.2
Trial 12	10.0	9.0	7.2
Trial 13	8.0	10.0	10.2
Trial 14	10.2	9.2	11.2
Trial 15	7.8	12.0	11.2
Average	8.67	9.08	8.85
Standard Deviation	±2.47	±2.14	±2.48

Pullout test with milk

Trials	Force (N) – Syringe 1	Force (N) – Syringe 2
Trial 1	5.0	2.4
Trial 2	3.2	7.6
Trial 3	2.4	8.0
Trial 4	2.4	3.6
Trial 5	2.0	8.4
Trial 6	2.4	6.8
Trial 7	2.4	6.2
Trial 8	2.0	6.4
Trial 9	2.0	6.0
Trial 10	1.6	6.4
Trial 11	2.4	6.8
Trial 12	2.0	6.0
Trial 13	1.6	3.2
Trial 14	1.6	6.4
Trial 15	1.2	6.2
Average	2.3	6.0
Standard Deviation	±0.89	±1.71

Pullout test using milk syringe in water, needle changed

Trials	Force (N) – Syringe 1	Force (N) – Syringe 2
Trial 1	1.2	7.2
Trial 2	4.8	7.6
Trial 3	4.8	5.0
Trial 4	1.2	6.0
Trial 5	1.2	5.8
Trial 6	4.8	5.0
Trial 7	4.8	4.4
Trial 8	1.6	4.4
Trial 9	0.8	4.8
Trial 10	4.8	5.0
Trial 11	4.8	5.2
Trial 12	5.2	6.0
Trial 13	5.2	4.8
Trial 14	1.6	5.8
Trial 15	5.2	5.2
Average	3.5	5.5
Standard Deviation	±1.87	±0.94

Appendix M: Instron Machine Testing with Compressive Tubing

Polyethylene Tubing

Trial	Load at Maximum Compressive Stress (N)
Trial 1	32.72
Trial 2	32.61
Trial 3	32.47
Trial 4	33.39
Trial 5	33.28
Average	32.89
Standard Deviation	± 0.414

Polyurethane Tubing

Trial	Load at Maximum Compressive Stress (N)
Trial 1	16.4
Trial 2	15.9
Trial 3	16.04
Trial 4	16.19
Trial 5	16.51
Average	16.21
Standard Deviation	± 0.251

Polyvinyl Chloride Tubing

Trial	Load at Maximum Compressive Stress (N)
Trial 1	40.03
Trial 2	42.41
Trial 3	50.07
Trial 4	43.80
Trial 5	42.24

Average	43.71
Standard Deviation	±3.803

Silicone Tubing

Trial	Load at Maximum Compressive Stress (N)
Trial 1	20.01
Trial 2	20.87
Trial 3	19.66
Trial 4	18.57
Trial 5	19.88
Average	19.80
Standard Deviation	±0.826

Appendix N: Additional Background

MQP – FNA additional background

1. Identify top five manufacturers of disposable syringes and biopsy needles. From an engineering perspective, what are the differences and similarities of each?

There are various manufacturers of disposable syringes in the United States. Examples of five of the top manufacturers are Becton Dickinson & Co (BD), Kendall, B. Braun Medical, Hamilton[®] Company and Angiotech. All of these companies produce and sell syringes, needles or both. BD sells both as well as other diagnostic systems and pharmaceuticals. Kendall sells both as well as other pharmacy products. B. Braun Medical manufactures syringes, needles, and other products involving renal therapy, wound care, anesthesia, and drug delivery. Hamilton[®] Company makes only syringes and needles. Angiotech manufactures various devices including syringes, needles, ophthalmic devices, surgical devices and more.

2. How are they manufactured / sold / distributed/ disposed of or recycled? Include the following:

- a. Specifications
 - b. BOM's
 - c. Distribution channels
 - d. Manufacturing costs
 - e. Sales prices
- a. Specifications of a standards syringe are: 10 mL, single-use syringe/needle combination luer lock tip. The needle length and size can vary depending on use. The syringe is usually comprised of a plastic. Depending on the type of syringe, it can also be made of glass or both plastic and glass. The plunger is made of plastic typically. Most syringes are latex free due to allergies to latex of users and patients.
- b. The bill of materials (BOM) will include the type of material the company is using to produce the syringe. Also, the needle will be incorporated to BOM. Syringes are not always sold with needles. Most manufacturers provide option to buy only the syringe or a syringe with an attached needle. The needle size can be chosen as well. The needles are attached with the luer lock tip.

Part Number	Description	Quantity
1	Needle bevel	1

2	Needle Shaft	1
3	Needle Hub	1
4	Luer Lock tip	1
5	Barrel	1
6	Plunger	1
7	Plunger top	1

- c. The distribution channels of the companies are significant as they in a way control the means of consumers purchasing their products. Most of the companies sell their products in the U.S. and internationally. Direct consumers of the product or through sales representatives market them. There are various resellers that market the products such as the different websites on the Internet.
- d. The cost to manufacture a syringe can vary on the size, components and material. The larger the size, the increased amount of material needed, causing the manufacturing costs to increase. Due to the wide use of syringes, bulk manufacturing is the best way to go forward with production. Injection Molding is a preferred option due to the high volume of syringes that are produced.
- e. Majority of syringes or needles are sold in bulk rather than individually. This is because most consumers purchase in bulk. Also, the companies bulk merchandising save resources. In most cases, buying in bulk is cheaper per unit than buying single products [6].

3. How are syringes tested during manufacturing?

There are various standards for testing syringes during manufacturing. The ISO 7886 and ISO 8537 are the major syringe testing standards. For product quality, Good Manufacturing Practices (GMPs) standards need to be met. Specific requirements for ISO 7886 include: cleanliness, limits for acidity and alkalinity, limits for extractable metals, lubricant, tolerance on graduated capacity, graduated scale, barrel, piston/plunger assembly, nozzle, performance, packaging, labeling. For syringes, examining the mechanical properties is critical. There are various force and pressure tests that are conducted. The ISO 7886 standards provide various methods for determining force of aspiration and expression. One test that is used involves a

syringe that is half filled with water and a mechanical force testing system, which could be an Instron machine. The water filled syringe is set up on the system vertically with the syringe outlet attached to the reservoir. The system pulls the plunger of the syringe down and aspiration force is detected. Then, the motor of the system is reversed to obtain the expression force. There are several other ways that can be used to assess the syringe and its function [7, 8].

4. How are these items sterilized prior to use? Describe special packaging materials used, various means of sterilization; materials used; pros and cons of each method; cost of processing

The syringe or needle is not the only component that needs to be sterile. Since the needle or syringe will be packaged, the packaging must also be sterile. Examples of packaging materials include but are not limited to: wraps, rigid containers and pouches. There are various requirements that the package of the disposable syringes need to follow. The requirements include: having very tight and strong seams to prevent contamination, easy peel openings for packaging, it has to be sterile and non-pyrogenic, and correct labeling on the package. The material for packing must be chosen carefully because it needs to undergo sterilization and maintain sterility. There are machines that package the materials. The packaging can be sterilized in the one of the methods that is discussed later.

The various means of Sterilization are dry heat sterilization, ethylene oxide, moist heat sterilization, and radiation sterilization. Dry Heat Sterilization uses hot air that is not from water vapor. This sterilization process utilizes conduction to have all parts of the material reach a high temperature to reach sterilization. This process can be used for sharp instruments, powders, etc. The advantages of dry heat sterilization are that it is nontoxic, not harming to the environment, involves relatively low costs, and non-corrosive for metal and sharp instruments. The disadvantages of the process include that it is very time-consuming and high temperatures used therefore select materials can undergo this type of sterilization. An example of a typical process for a material would have an applying temperature of 170 degrees Celsius for an hour. When comparing this process to steam or wet air sterilization higher temperatures and longer times are used for dry heat sterilization. Another type of sterilization is moist heat or steam sterilization. Steam sterilization is a simple process, which involves exposure of the product to steam at

various temperatures and high pressure. This process denatures proteins and lipids associated with microorganisms. In regards to wrapped surgical packs, high pressure ensures sterilization. Autoclave is the most widely used steam sterilization method. Autoclaving can be used for needles and other select metal instruments, clothing, stainless steel equipment, filters, component parts of other equipment, etc., and also for liquids in sealed or ventilated containers. The benefits to this sterilization method are that it is nontoxic, inexpensive, time efficient, simple, and effective. The drawbacks of steam sterilization include the high temperatures that not compatible with materials that have low melting temperatures, causing natural polymers to denature and that the process is incompatible with polymers. Concerning the cost, the initial purchase cost can be expensive and maintaining an autoclave can also get costly. Another common method is Ethylene Oxide sterilization. Ethylene oxide sterilization is a chemical process consisting of four primary variables: gas concentration, humidity, temperature and time. Ethylene oxide is an alkylating agent that inhibits DNA from microorganisms from replicating. Ethylene oxide is a colorless gas that is very toxic and flammable. The benefits of the process are the low temperature needed and sterilize heat or moisture-sensitive medical equipment can be used for this method. The disadvantages of the ethylene oxide sterilization include the lengthy cycle time, the cost, and potential toxicity. The cost depends on the prices of gas, which is increasing. Medical device manufacturers widely use this method. The final type of sterilization that is going to be discussed is radiation sterilization. Radiation is applied to various instruments. The typical process for radiation sterilization is placing the instrument in a sealed pouch, which will be undergoing radiation. The different types of radiation sterilization includes gamma radiation, X-rays, and use of high-energy electrons. Gamma radiation is a sterilant and it is released from radioisotopes such as cobalt-60 or caesium-137. The advantages of radiation sterilization are no toxicity, great reliability, and there is no need for pressure or vacuum aspect for this method. A major drawback of this process is the high initial cost. Although the initial investment for this method is costly, the overall cost is low. Several products that utilize this technique are sutures, gloves, gowns, facemasks, dressing, syringes, surgical stapler, etc. [5, 9, 12, 13, 14]

5. Review the chemistry/ biology of various sterilization methods on various pathogens; bacteria, virus, pyrogens, etc.

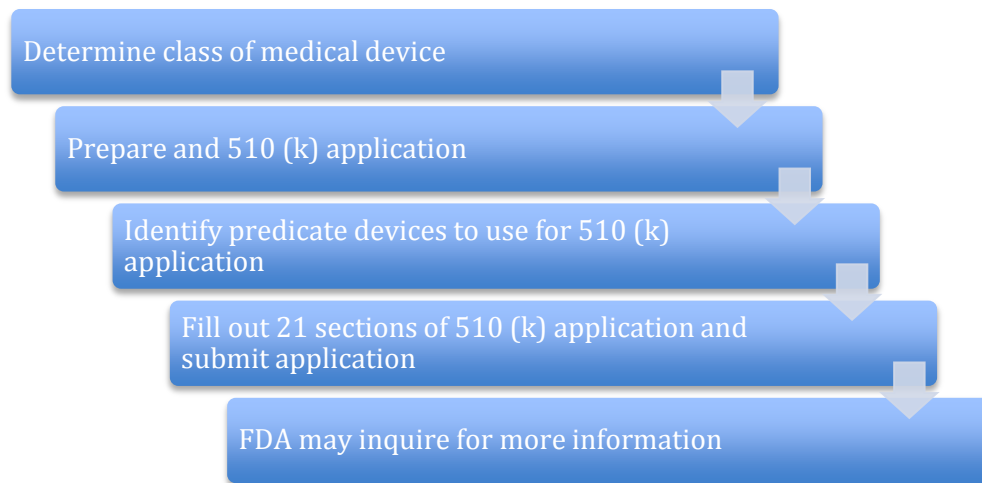
Sterilization is the method by a material or surface is freed of all microorganisms.

Examples of microorganisms include bacteria, viruses and more. There are different sterilization methods and they eradicate the unwanted microorganisms in various ways. The sterilization methods that will be discussed are Dry Heat Sterilization, Steam Sterilization (Autoclaving), Ethylene Oxide (EtO) Sterilization and Radiation. EtO is known to kill most viruses, bacteria and fungi. Ethyl is the alcohol that is present in ETO and it denatures proteins and damages cell membranes. This gas also inactivates all microorganisms although bacterial spores (especially *B. atrophaeus*) are more resistant than other microorganisms. For this reason *B. atrophaeus* is the recommended biological indicator. Autoclaving will inactivate bacteria, viruses, bacterial spores and fungi. Steam sterilization causes denaturation of proteins. With proper timing and pressure, all microorganisms are inactivated. Dry heat sterilization can kill microorganisms as well by extreme oxidation of the cells. Dry heat can eradicate bacteria at 100 degrees Celsius for 60 minutes. In regards to bacterial spores, which are more difficult to remove, dry heat sterilization must be applied for 60 minutes at temperature of 160 degrees Celsius. Radiation uses radioisotopes, such as Cobalt-60, which emits gamma rays. Water in the product that is being sterilized is important during the radiation sterilization process. The water molecule leads to the formation H_3O^+ and OH^- or hydroxyl radicals. The radical uses an electron from the bacteria, which leads to decomposition of the bacteria [9, 12, 13, 14].

6. What are the regulatory considerations a manufacturer must consider when bringing a new syringe or needle to the market? Include a review of the approval process, the class of medical device, relevant documents and regulations, etc.

In order to receive Food & Drug Administration (FDA) approval of a new syringe to the market, one has to follow the steps of the approval process. The first step is to determine the class of the device you are designing. A syringe or needle would be in Class II. For Class II devices, FDA clearance is required. In order to continue this process, one would need to set up a 510 (k) application, which can be found on www.fda.gov. The 510 (k) application determines the equivalency of device that is on the market and what the new product can offer that other devices cannot. Once the application is submitted, the FDA has 90 days to evaluate it. During these 90 days, the FDA will inquire about more information. If your syringe is cleared, then the FDA will send the applicant with a letter saying, “have determined that your device is substantially

equivalent to legally marketed predicate devices – and you may therefore begin to market your device subject to the general controls provisions of the Food, Drug and Cosmetics Act.” This letter essentially states that your product is approved to be sold in the United States. Testing of the device and clinical trials would also be required. One must also register their device of the FDA website. The manufacturer of the syringe or needle would have to comply with the FDA Quality System Regulation or Good Manufacturing Process. Then you have to wait for approval from the FDA [8].



7. Review past history and report on at least three complaints or problems related to syringes and needles and describe: what happened? What changes were made to prevent reoccurrence?

One problem that came up with syringes involved GlucoPro Insulin Syringes manufactured by Nipro Medical Corporation. The issue was that the needle was becoming detached from the syringe, which can lead to the needle remaining in the skin after insulin is injected and other problems. Nipro Medical Corporation sent out a recall for all these syringes. This occurred in January 2010. There was a request for returning the product. The companies should conduct more testing for the syringes during manufacturing. The companies need to be very precise when manufacturing and testing so the best quality is ensured when consumers are purchasing their products.

Another case involved consumers discovering various colored particles in the syringes. After extreme investigation, the FDA announced that the syringes the company that AM2PAT were manufacturing were contaminated. AM2PAT was closed in the year 2008. FDA had tried to resolve the issue making safety their top priority. B. Braun Medical, a company in Pennsylvania made a recall on AM2PAT syringes. FDA did not learn of this recall until about a week later. Before knowledge of the recall, FDA inspectors made a visit to the AM2PAT plant, and reported other issues such as rust contamination and incorrect labeling of the syringes. Approximately six weeks later, FDA announced the recall of the syringes by B. Braun Medical. It was found that the particles in the pre-packaged syringes could lead to brain damage and clotting. There was clear miscommunication with the FDA. After knowing of the recall in early 2007, FDA inspectors did a thorough inspection of AM2PAT and many more violations were recorded. FDA told the company owner to make changes before the next visit. After the following FDA visit, the FDA announced that fixed the previous issues were fixed or in the process in being fixed. In summer of 2007, another complaint of an AM2PAT syringe was made. Another inspection was scheduled but the FDA officials discovered that AM2PAT was relocated. There had been about one million contaminated syringes distributed. There were about 4 deaths and 160 illnesses directed with the distribution of AM2PAT's contaminated fluid filled syringes. There was another FDA visit to the relocated AM2PAT site. For this visit, there were two FDA investigators and a microbiologist present including interviewing the employees and a thorough investigation of the company site. The reason for the contaminated syringes was radiation sterilization method was not functioning properly. There was fraudulent paperwork that was discovered as well. The company was shut down but the owner left the country. There was prosecution of management of AM2PAT. The FDA should have taken strict actions when they heard of a recall and perform an in depth investigation from the beginning. In addition, there should have been better communication between FDA authorities. Sterilization was the major problem in this case. There was not proper sterilization of the syringes in the facilities, which lead to several illnesses and a few deaths. The FDA has improved their communication and inspections involving sterilizations.

Diagnostics Inc. (BDI) issued another syringe recall that I am going to discuss in November 2012. The item that was recalled was the Isovue[®] (iopamidol injection) pre-filled power injector syringes. This syringe is disposable. Particles were found in the syringes that were

deemed as being hazardous. It could possibly cause a stroke. The contaminated syringes were distributed all around the United States. After realization of the particles in the syringes, BDI sent out notifications and is asking for the consumers to return the product. There were potential connections of the Isovue[®] Syringes with various side effects including: urticarial, dyspnea, and pruritis. This is similar to the situation that occurred with AM2PAT. It seems that there was a problem with the sterilization that caused the issue. [1, 2, 6]

8. Review patents and intellectual property claims to review three recent design innovations related to syringes and/ or needles. Discuss the engineering details of each and identify the significant aspects of the engineering/ design improvements changes. Describe the impact in the market of these new/ improved devices.

The number of patents on design innovation involving syringes is endless. There is a syringe with an improved plunger that was innovated. The purpose of this syringe was to inject gas and liquid chromatography samples from the syringe. There is a flexible sleeve that wraps around the plunger. The flexible sleeve creates a seal between the barrel and the plunger. The syringe has an extended barrel with a cannula attached to the front end. The cannula stretches to the bore. Inside the bore is the location of the plunger. The plunger has a long rod that is surrounded by the flexible sleeve. This sleeve is said to address the issue of lost motion of the current standard for the device used. The tip of the plunger is made of polytetrafluoroethylene (PTFE), which causes this lost motion. Lost motion occurs during ejection of the sample, which can cause inaccurate analysis, and performance of the chromatograph. The plunger needs to function directly with the PTFE tip and the lost motion causes the opposite. This flexible sleeve design will help the plunger correspond with the plunger tip and remove any friction. The claims of this device include: a barrel with first and second ends and a bore there through, a cannula attached to first end, a moveable plunger, a rod with an end portion that has a smaller diameter than that of the rod, and a flexible sleeve in a shape of cylinder that surrounds the end part [10].

In the year 2009, Becton, Dickinson and Company filed for a patent for a more cost effective single-use auto-disable syringe. There are other patents that have locking elements different to this one, but they have not been accepted as much as it was hoped. A major reason for the lack of widespread use is due to the cost. Developing countries cannot afford these. Reducing the material costs and the cost to purchase will enable the use of a single-use syringe on a large scale. This syringe has a locking element, which is useful for prevention of re-use of

the syringe. This syringe is essential in developing countries where diseases are spread by reuse of syringes. This design innovation involves a locking piece, which locks the plunger rod to prohibit the reuse of a syringe. This locking piece does not interrupt the normal functions of the device, but when there is attempt of reuse then it will damage the syringe. The goal is to have this locking element in a syringe that is smaller than most, causing the manufacturing costs to be lowered. If the manufacturing costs are low, it will be easier for developing countries to purchase. The claims of this device include: a syringe barrel, a plunger rod assembly with stopper, interface flange, a body that is the length from the stopper to the flange, a group of teeth, a locking element located in chamber, and the locking element interacting with interior of syringe barrel [3].

In the year 2009, there was a needle biopsy device that was filed to be patented. The incision created by the needle is very significant in incision biopsies. There are needle biopsy devices on the market today that make different kinds of cuts, but the important objective of the needle designs are that they are safe enough to be used for soft tissue biopsies. There is an inner cutting needle that interacts with the outer needle that makes this invention unique. This needle biopsy device purpose is to be utilized with a tru-cut biopsy system, which includes a standard syringe body and piston. A benefit of this needle device is that it helps with the aiming of the device and obtaining a sufficient sample from the target tissue. This device can also be used for cystic lesions. The various parts of this design are: a syringe body, moveable piston, outer needle or cannula, needle tip, needle connection head, head connection surface, tissue aspiration reservoir, cutting inner needle, inlet, conveying space, transition channel, connection and outlet. The needle biopsy design improves on the amount of sample received. The claims of this biopsy device are: injection syringe body, a hollow of syringe body, a moveable piston, outer needle attached to syringe body, a needle tip, a needle connection head surface, a cutting needle that is at the hollow on the inside of outer needle, and a transition channel that is created by the needle in hollow [4].

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