End-of-Semester Report | '11

Cervical Biopsy Device

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Abstract
Cervical biopsy procedures are performed after an abnormal PAP smear indicates abnormal cell growth. The most common cervical biopsy procedure is a punch biopsy, which utilizes devices like the Tischler forceps and the Kevorkian forceps. These biopsy devices are not effective at adhering to the surface of the cervix prior to pinching off the tissue sample, leading to tearing, bleeding, and therefore, increased patient discomfort. In order to make improvements upon these current devices, a cervical biopsy device will be developed. This device will utilize the mechanical force of a scooping blade to make a clean cut against the cervix, allowing for a more consistent sample size while minimizing patient discomfort.

Background
In developed countries around the world, the incidence of cervical cancer has been reduced by about 50% due to cervical cancer screening programs, the most common of which is a PAP smear[1]. Each year, about 3 million PAP smears[2] are found to be abnormal, meaning there are signs of abnormal or cancerous cell growth[3]. Upon discovery of abnormal cells, the doctor will likely recommend a colposcopy and cervical biopsy, a combined procedure that utilizes a colposcope to obtain a better view of the patient's cervix as well as extracts 2-4 cervical tissue samples for pathological analysis.[4]

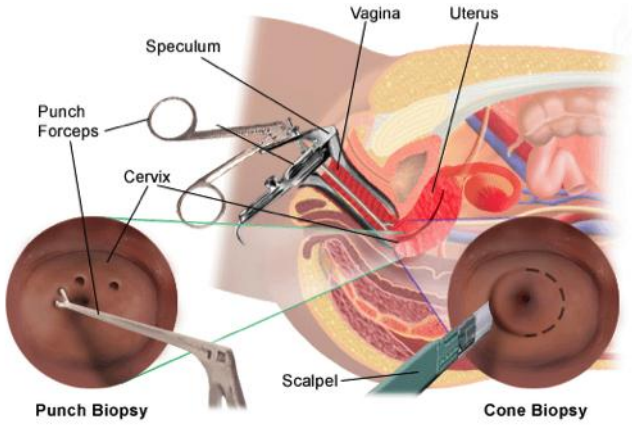

Figure 1: Visualization of cone and punch biopsy procedures[5]

Cervical Biopsy Procedure
During the cervical biopsy, the doctor can chose to perform either a cone biopsy or a punch biopsy, both aided by a magnified video feed from the colposcope. A cone biopsy involves using a scalpel to cut and remove and cone-shaped wedge of cervical tissue while a punch biopsy uses a punch instrument to remove small biopsy samples from the surface of the cervix[5]. Before starting the procedure, it is standard for the doctor to swab the surface of the cervix with vinegar or an iodine-based solution. Vinegar turns the abnormal cells white in color and thus become easier for the doctor to visualize a sample tissue[6]. The samples are sent to a pathologist, who then tests the cervix tissue sample for cancerous cells. Various treatments are then considered on a case-by-case basis.

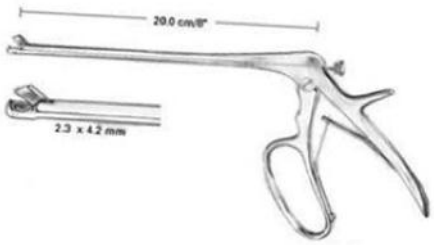

Figure 2: Baby Tischler forceps[7]

Competition
There are currently several devices on the market that doctors can use for cervical biopsy procedures, the most common being the Tischler and Baby Tischler forceps (Figure 2) as well as the Kevorkian forceps. All of these devices are similar in their mechanics as well as how

they obtain the biopsy sample. The ends of these devices, since they are used for punch biopsies, have a mouth-like opening that clamps down on the tissue of the cervix when the handle end is compressed. While these devices are easy for doctors to use and manipulate, it is often difficult to get the device secured against the surface of the cervix while taking a sample[8]. This is largely due to the slippery, mucus-covered surface of the cervix. Ultimately, this leads to increased patient discomfort due to the tearing and ripping of the cervix tissue while obtaining a biopsy sample. In addition, this limitation affects the consistency of the biopsy sample size, which typically has dimensions of about 3mm x 3mm x 2mm, but has a required minimum sample size of 4 mm^3 [9].

Problem Statement

With approximately three million abnormal PAP smears found each year, cervical biopsy procedures are becoming more common. As referenced in the discussion of the competition, current devices have struggled to secure a proper grip on the tissue of the cervix, ultimately making it difficult to obtain a biopsy sample and often leading to inconsistent biopsy sample sizes. This leaves a gap in the market that an improved cervical biopsy device can occupy by addressing these shortcomings.

Design Criteria

When considering the standards necessary to meet while designing a cervical biopsy device, one of the main factors that needed to be addressed was meeting the minimum required biopsy size of $4mm^3$, a value provided by the client after consulting with a pathologist. In order for a cervical biopsy sample to be properly analyzed, it needs to meet this minimum volume. The ability to obtain consistent sample sizes was also necessary for our device. For material requirements, the device needs to be made of a sturdy, non-bendable material that can be sterilized effectively between patients. The device then needs to be appropriately sized due to the maneuverability restriction and size restrictions of obtaining the biopsy through the vagina.

Final Design Development

The basic form of the final design remained fairly consistent from the mid-semester point and onward. It used the same base as the Tischler and Kevorkian forceps for the physician to grip and it relied on the physician to use his or her hand to squeeze the base, resulting in the retraction of the device at the blade.

Initial Design: Spring Mechanism

For the initial design, the team started with a spring mechanism in the tip of the device to generate the force necessary to complete the cut. This mechanism was based on a rod that was a continuation of the base and would extend into the tip and hold back the blade, keeping the spring in a compressed position (Figure 3). The spring would be on the opposite side of the tip as the rod and would be permanently attached to the base of the tip

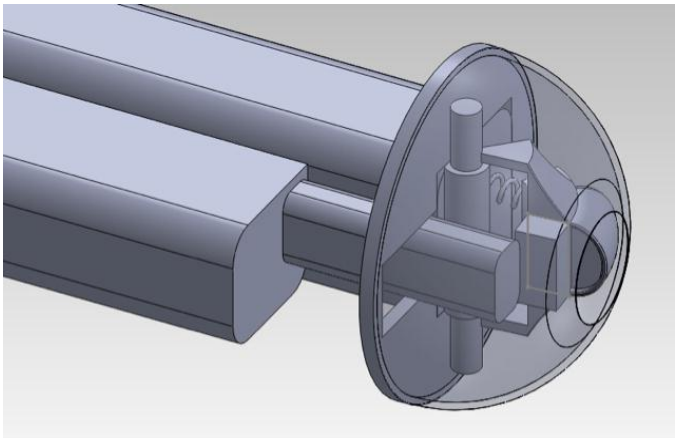

Figure 3: Tip of device in resting position

shell. Then, the blade would have blocks protruding on either side of it (as can been seen in Figure 3) that would keep the sharpened portion of the blade from ever coming in contact with any part of the device directly, leading to dulling of the blade. The force of the compressed spring would be directed on the far side of the blade while the block on the opposite side would be pressed against the rod extending from the base of the device to the tip. This rod would stop the release of the spring until the physician squeezed the base. Upon doing so, the rod would retract and allow for the release of the force residing in the compressed spring. This force would be directed against the blade, which would rotate in place and then complete its allowed rotation to the other side of the tip. As the blade completed this rotation, it would then break the surface of the tip and take a biopsy of the cervix, which would be pressed up against the hole of the device. When finished, the blade would rest on the opposite side of the shell, as seen in Figure 4. To reset the blade and recompress the spring, the physician would then only need to push the base forward, which causes the blade to be pushed back to the other side of the shell and the spring to be returned to its compressed position.

Although this was where the design began, this is not where it ended. When deciding upon a spring to use, there is little data to prove that the spring would work. Even if the team found data supporting the fact that the spring is capable of generating the force necessary to take a sample, if it did fail halfway through a biopsy, the device would have to rely on tugging in order to tear through the tissue sample, increasing patient discomfort. In this case, there would be no biopsy obtained and the device would fail to perform its function. To ensure that the device would not risk failure halfway through the biopsy, the team turned to a hinge mechanism that relies solely on the force generated by the physician's hand. This force far exceeded the force that any spring small enough to use could create.

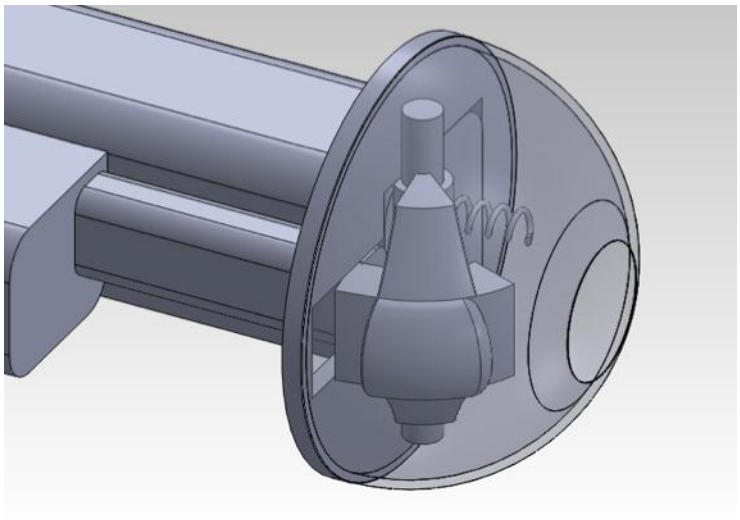

Figure 4: Tip of device after blade completes cutting motion

Final Design: Hinge Mechanism

Our final design (Figure 5) would be made entirely of stainless steel, allowing for it to be sterilized between uses. Overall, it relies on the force of the physician's hand to take the biopsy. The physician would wrap his or her fingers around the base with each finger securely positioned within the ergonomic handle and his or her thumb anchored at the base of the device. The motion of the two base pieces is limited by the slot mechanism, which only allows for the motion necessary to complete the biopsy (Figure 6). This ensures that excessive force outside of the amount necessary to complete the biopsy will not be exerted on the small pieces of the tip. This also works to minimize the possibility of the tip pieces breaking during the use of the device.

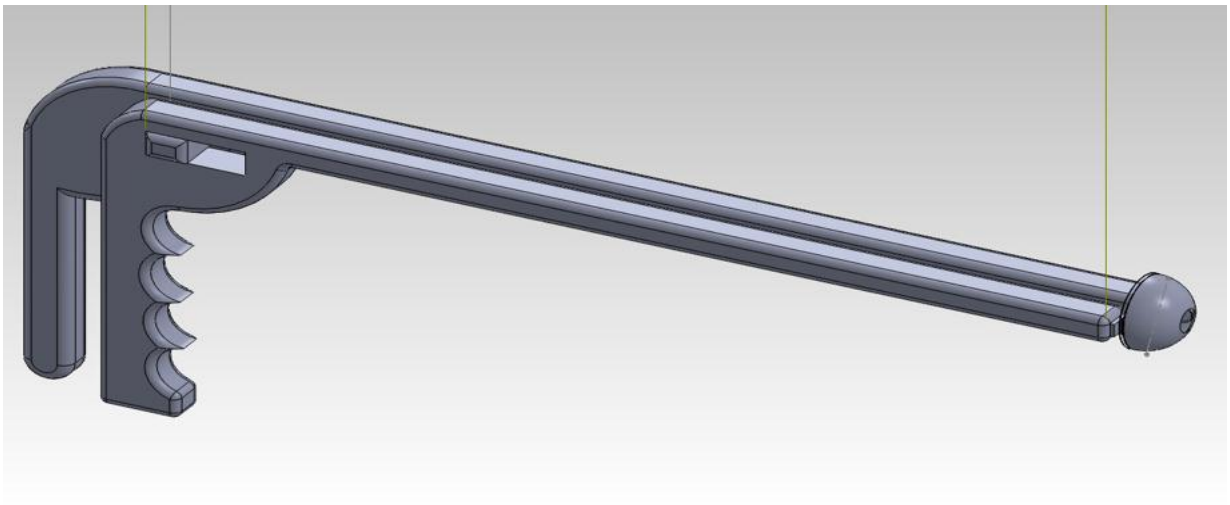

Figure 5: Final hinge design

The neck of the device, which is the portion of the device that will be inserted into the vagina, has a length of 23 cm. This is slightly longer than current devices on the market and will allow for a wider range of patient anatomies.

The tip of the design is responsible for completing the cut and retaining the biopsy sample for retrieval. The biopsy is obtained through a system of rods that will pull the arched blade though the tissue. This system can be seen in Figure 7, which shows the tip of the device prior to compressing the handle.

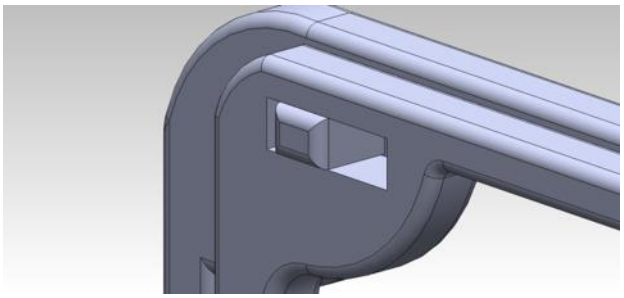

Figure 6: Slot mechanism of the device

Once the physician has set the tip against the surface of the cervix, the physician can squeeze the base. This motion will cause the connected rods within the tip to also move. By retracting these rods, the blade will rotate and cut through the cervical tissue in the process. The physician will continue to squeeze until the base can no longer move due to the slot mechanism. From here, the device can be retracted and the physician can use tweezers to pull out the biopsy from the tip. The system is then reset by pushing apart the handles at the base.

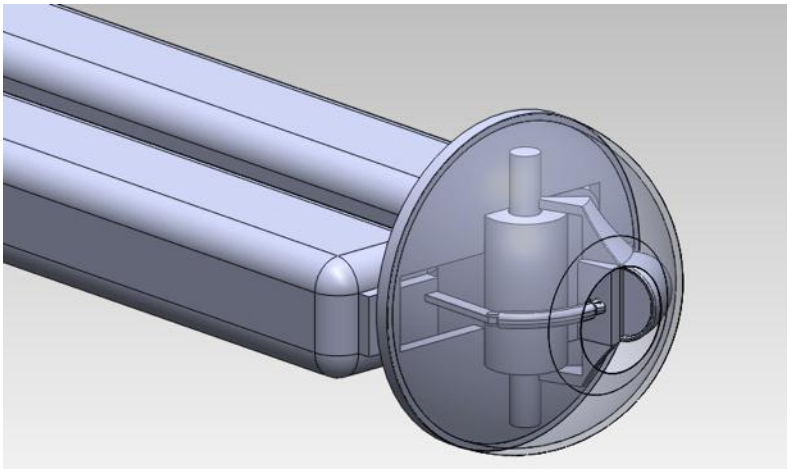

Figure 7: Tip of device

Testing

Since the final prototype was constructed with plastic via the 3-D printer, the actual device itself could not be used for testing.

However, three different tests were designed in order to prove that the device would indeed perform as expected when manufactured out of metal. The three tests targeted the tip of the device, specifically the volume of the biopsy sample, the force necessary for the sample to protrude through the hole on the tip, and the cutting force needed to retrieve a proper biopsy.

Swipe Cut Test

The first test performed was the Swipe Cut test. This test was carried out by drilling a small hole with a diameter of about 0.63 cm near the center of a circular metal sheet of 1 mm thickness. The metal sheet was then placed on top of a piece of fruit or a chicken drumstick and increasing pressure was applied until the specimen bubbled through the hole. The client recommended using kiwi for any tests performed, so kiwi and other similar fruits were utilized in the three different tests; chicken drumsticks were also tested due to their similar properties (texture, composition, etc.) to cervical tissue. After the specimen bubbled through the hole, a razor blade attached to a metal rod was used to horizontally cut across the sample and obtain a biopsy (Figure 8).

Figure 8: Swipe Cut test of chicken

The sample biopsy for each cut was placed on a sheet of graph paper and a picture of the graph sheet with all of the biopsy samples was analyzed by using an imaging analysis program called ImageJ. Using this program, the area of each sample was determined. Making the assumption that each biopsy had a thickness of 1 mm, based on observation, the volume in mm^3 was determined by multiplying the area of each biopsy by the assumed thickness. The results of the Swipe Cut test are graphed in Figure 9.

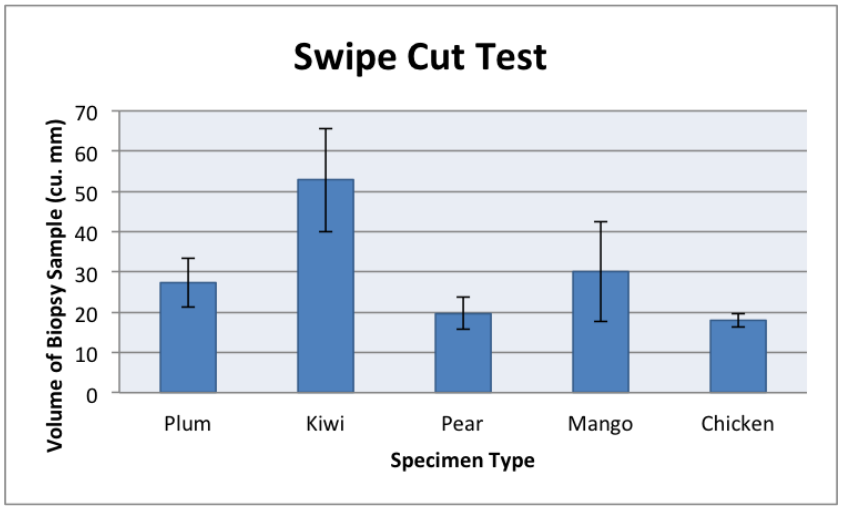

Figure 9: Swipe Cut Test Results

After analyzing the biopsy samples, it was determined that each specimen produced biopsies that were well above the ideal volume of 4 mm^3. Since increased biopsy size may lead to increased bleeding and patient discomfort during the procedure, future designs of the device should reassess the size of the hole at the tip so that less of the specimen bubbles through and a smaller biopsy is cut. Nonetheless, when considering the standard error mean of the Swipe Cut test results, the chicken biopsies proved to be the most consistent. This conclusion is very significant because the chicken drumsticks are definitely more closely similar to the mechanical properties of the cervix than the other fruits used for the test. Thus, based on the Swipe Cut testing, the blade of the device should have no problem cutting through the tissue of the cervix to obtain a biopsy sample.

"Bubble" Test

The second test – the "Bubble" test – was very similar to the Swipe Cut test in that it utilized a rectangular metal sheet with a 0.63 cm-diameter hole in the middle. Each of the four corners of the sheet also had a small hole so that four strings could be tied to the corners. A piece of fruit or chicken was then skewered with a metal rod and held under the sheet. Weights of known mass were added to the strings so that an increasing amount of force was applied to the fruit or chicken (Figure 10). Once each specimen bubbled through the hole of the metal sheet, the mass applied was recorded and converted to Newtons. The results of the "Bubble" test are graphed in Figure 11.

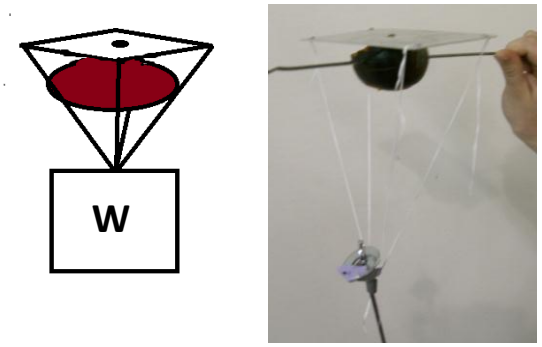

Figure 10: "Bubble" test schematic diagram and photograph

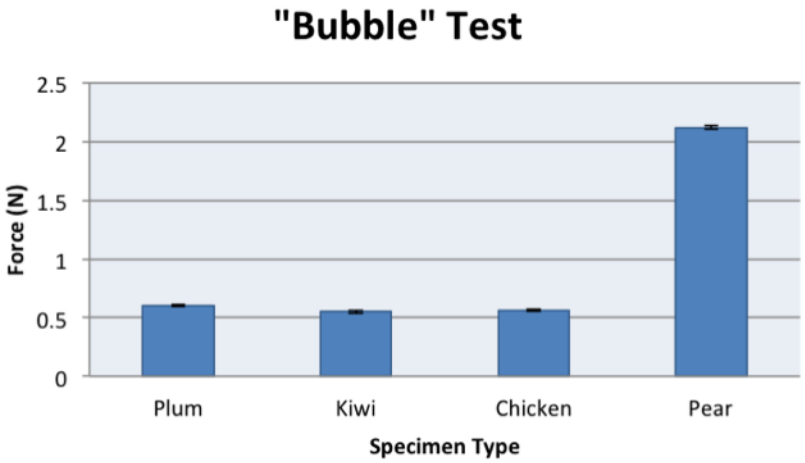

Figure 11: Bubble Test Results

Based on the results of this test, it was determined that the cervical biopsy device should be pushed against the wall of the cervix with between 0.5-2 N (.11-.45 lb) of force. Since these force values are most definitely attainable by the physician using the device, it is clear that the device should not have an issue in sufficiently contacting the cervical tissue to cut a biopsy sample.

Cutting Force Testing

Figure 12: Cutting Force test without weight (left) and with weight added (right)

The Cutting Force test measured the force required to make a sufficient cut into the testing subjects. These testing subjects included a plum, a kiwi and a pear, both peeled and unpeeled. Chicken drumsticks were also used for testing.

For the testing setup, a razor blade is attached to a metal rod, as shown in Figure 12. The rod and blade was then clamped vertically over the fruit or chicken with only horizontal forces to balance the weight. Weights are added onto the rod until a sufficient cut was made. The team deemed a sufficient cut to be when the slanted edge of the razor blade was completely embedded into the fruit or the chicken. After the weights were recorded, they were converted to kilograms and multiplied by the acceleration of gravity to get the force. The results of the Cutting Force test are presented in Figure 13.

Each testing subject yielded a different force due to the hardness inconsistency. Nonetheless, the minimum cutting force was around 1.50 Newton, which is about 0.337 pounds. It is important to note that this force is only the force that cuts into the subject. It does not take into consideration the scooping motion of the blade and the nonproductive forces necessary. In order to test the scooping motion, a fully

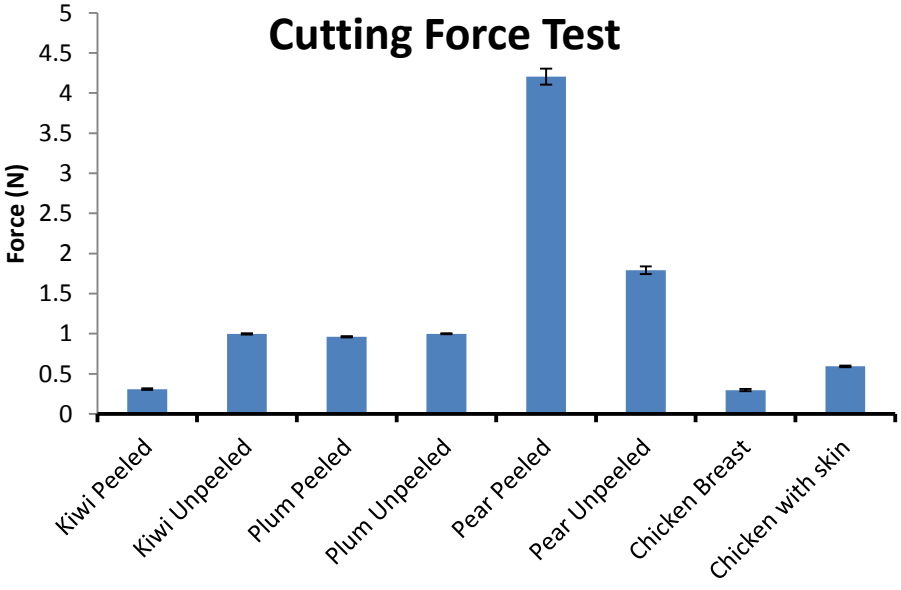

Figure 13: Cutting Force test for different specimen

functioning device is needed. This will be further discussed in the Future Work section. The 0.337 pound force is, however, adequately small. It is reasonable to conclude that a physician will be able to easily provide the force required to take an appropriate sample size.

Budget

The team spent $2.63 on razor blades and $16.85 on testing materials, including the chicken drumsticks and fruits used for testing. The scrap metal used for testing was obtained for free from the College of Engineering Student Shop. The team used SolidWorks to design and ultimately print a three-dimensional plastic prototype. This prototype did not add any additional costs. Therefore, the team only spent $19.48 in the process of creating the device. Since the actual envisioned device would be made out of stainless steel, its cost would be dependent on consultations with surgical device companies as well as the number of devices to be manufactured. The need for cost estimates of the steel version of the device is further addressed in the Future Work section.

Ethical Considerations

Due the invasive nature of a cervical biopsy, patient safety and comfort are imperative design factors. The final design needs to ensure that the sharp blade will not cause accidental cutting of surrounding tissue. Since human anatomy severely limits the device's orientation, the device should be easily maneuvered. In addition, the device should minimize patient discomfort as well as procedural duration. This requires quick and clean cut of cervical tissue. After the sample has been cut, the design should also enclose the sample so that no loose tissue remains in the body. The physician should be more efficient by using the device. After the device is manufactured with stainless steel, it needs to be tested in labs for patient safety and sample consistency. The main ethical concern is clinical testing. A certain standard need to be met before the device can reach the clinical testing stage. The device must exhibit minimal tissue tugging and maximal efficiency. In addition, the device should not cause any type of infection after biopsy procedure. Top priorities should be patient safety and comfort.

Future Work

In the immediate future, adjustments are needed in the dimensions of the device. Specifically, the rod portion of the device should be narrower to better suit different patients. Features of the blade such as strength and speed can also be improved. A shaper blade can shorten the procedure time. Furthermore, the blade should be detachable. If the blade gets dull, it can be sharpened or a new blade can replace it. Other than the specific components of the device, cost and manufacturability also require attention. Due to the size of device components, manufacturability may present difficulties. Important parts of the device such as the curved blade need to be custom-made which increases the cost of production. If some other parts also need to be custom-made, then the device is not able to compete in the market. It is, therefore, imperative to get an estimate of production cost.

If the device were pursued in future semesters, this may entail inclusion of external suction. This can be achieved by making the rod hollow. More importantly, a working prototype should be created. The actual device should be made of stainless steel with an adjustable rod length to accommodate different patient anatomy. This allows testing with the device. The device will be used on testing subjects such as fruit and chick breast to see whether the samples exhibit

consistency and adequacy. This is an extension of the cutting force test that takes into consideration the motion of the blade. After extensive testing in the lab on various subjects, clinical trials also need to be performed. Eventually, overall evaluation of sample consistency, procedural efficiency, patient comfort, manufacturability and cost per device will determine whether the device has a place in the market.

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