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EVALUATION OF A NOVEL NOTES ENDOSCOPIC BIOPSY NEEDLE

MELISSA CHRISTINE BUYDASH
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Reviewed and approved* by the following:

Dr. Mary Frecker
Professor of Mechanical Engineering
Thesis Supervisor

Dr. Zoubeida Ounaies
Associate Professor of Mechanical Engineering
Honors Adviser

* Signatures are on file in the Schreyer Honors College.

ABSTRACT

NOTES (natural orifice transluminal endoscopic surgery), a technique conducted with an endoscope inserted through natural orifices, has the potential to completely revolutionize surgical procedures. The technique presents the unique possibility of incision-free (and thus scar-free) surgery. Though progress has been made in NOTES as a minimally invasive surgery (MIS) throughout the past few years, it has become increasingly apparent that several obstacles remain and need to be overcome before NOTES can become a preferred surgical technique. One such obstacle is that of limited instrumentation. The three objectives of this research will help to overcome this obstacle.

The first objective was to develop a testing procedure for the Olympus EZ-Shot. With a testing protocol, better comparisons between developing needles and a readily available needle were able to be made. The second objective was to apply the testing procedure to benchmark a prototype 2-dimensional endoscopic biopsy needle against the Olympus EZ-Shot, and the third was to determine the effect of prototype needle thickness on removal force and mass removed.

The results of this research showed that neither the 300 or 400 micrometer thickness needle performs better than the Olympus EZ-Shot in mass removed or removal force. However, the EZ-Shot removed a large amount of liquid mass in addition to solid mass, so the results may be skewed unfavorably for the prototype needle. The two needle thicknesses tested showed a correlation in which mass removed and removal force increase proportionally with increases in thickness. After measuring actual needle thicknesses, there was also an 84% linearly increasing relationship between actual needle thickness and mass removed. It would be interesting to see if these correlations continue over a larger needle thickness range. This research also showed that average friction force induced by the actuating handle of the EZ-Shot is 2.570 +/- 0.205 N.

These results show that the prototype needle design is a viable one, but improvements need to be made to the testing procedure in order to obtain more conclusive results. The sample used contained a high moisture content which may have significantly altered test results, so a lower moisture sample is desired in future testing to limit mass removed to solid mass only. Additionally, “a scooping” design could be considered for prototype modification to increase mass removal.

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Chapter 1

Introduction

Endoscopic biopsy needles represent a nascent area of NOTES (natural orifice transluminal endoscopic surgery). One objective of this research is to develop a test protocol for the Olympus EZ-Shot, an endoscopic biopsy needle commercially available and used by medical professionals. A second objective is to apply the developed test protocol to compare the performance of the Olympus EZ-Shot to that of a new 2-dimensional prototype needle. A third objective is to determine the effect of needle thickness on removal force and mass removed.

Open surgery is an invasive technique used to investigate and treat various medical conditions. It is the traditional surgical method in which a large incision is made and the surgery is viewed and completed directly through the incision. While usually effective, open surgeries have traditionally led to a high risk of infection, heavy bleeding, and tissue damage in addition to long healing times post-surgery. However, the relatively recent development of minimally invasive surgery (MIS), including laparoscopic procedures, has shown reductions in all of these categories [1-3]. MIS improvements over open surgery techniques have led to an increase in MIS research across the breadth of medical procedures.

Because MIS procedures have so many advantages over traditional open surgeries, they have become more common over the years as the field has progressed. With MIS procedures continually evolving, it is not surprising that medical researchers have attempted endless improvements, some successfully and some not. One development of MIS in progress is that of natural orifice transluminal endoscopic surgery, or NOTES. NOTES procedures are conducted through the use of a flexible endoscope, which is inserted through natural orifices such as the mouth, anus, or vagina. Various accessories, through endoscopic accessory channels, assist the

surgeon during surgical procedures. Some of these accessories include the following: forceps, lights, biopsy needles, cauterizing tools, scissors, and cameras.

Research in the field of NOTES has expanded future possibilities for MIS, but improvements need to be made to accessory instruments in order to make NOTES easier and more reliable in the operating room. Suturing devices, intended for use in transgastric (through the stomach) NOTES procedures, need to be made more maneuverable and versatile than commercially available options [1]. Endoscopic transgastric suturing in animals has been successful, but a direct clinical application in humans remains unclear [4, 5]. Additionally, current imaging methods are iterative, causing a lag in delivery of visual information to the operator of the endoscope [2]. Endoscopic biopsy needles are no exception to these instrumental voids, which is why the endoscopic biopsy needle research presented in this thesis is so important to the continuing growth and success of NOTES in medicine.

Background Information and Objectives

As discussed in the introduction, NOTES is a recently developed technology in the world of medicine, so it is not surprising that very few procedures have been completed successfully on humans. Limitations in available instrumentation have prevented the expansion of NOTES and have stopped NOTES from completely replacing current open or laparoscopic surgeries. As mentioned in the previous section, instruments such as those involved in imaging, suturing, and biopsy translate reduced visual and tactile information to the operator when compared to open surgery procedures [2]. Imaging is delayed, suturing instruments are hard to maneuver, and biopsy needles use a coring or scooping mechanism, which is not consistently effective in

providing enough cells for testing [1, 2, 6]. Additionally, small working channels due to the size constraints of endoscopes have limited equipment design and progress [7].

Combined with a lack of trained NOTES surgeons, these instrumental deficiencies have slowed the development of NOTES into a routine human procedure. Discussions at a meeting between the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) and the American Society for Gastrointestinal Endoscopy (ASGE) in 2005 suggested that NOTES procedures will be best performed by multidisciplinary teams of gastroenterologists and surgeons [1]. Some also suggest a hybrid NOTES/laparoscopic procedure, but such a solution would remove the incision-free advantage of NOTES [8]. In any case, NOTES procedures, by virtue of only recently being developed, have room for improvement and leave many problems seeking novel solutions.

Endoscopic biopsy needles represent one such area of NOTES which is still in the early stages of development. As mentioned in the introduction at the beginning of this chapter, this thesis aims to develop a test protocol for the Olympus EZ-Shot, an endoscopic biopsy needle which is already commercially available. A second aim is to apply the developed test protocol to compare the performance of the Olympus EZ-Shot to that of a new 2-dimensional prototype needle, and a third aim is to determine the effect of needle thickness on removal force and mass removed. Parameters of interest include mass removed and force applied to remove the needle from the sample studied.

In the specific case of endoscopic biopsy needles, instrumental limitations have prevented surgeons from being able to perform procedures precisely and consistently, sometimes forcing patients to undergo a biopsy multiple times in order to achieve success [6]. Before further human trials can proceed, it is crucial that surgeons are not only trained but are also proficient

and reliable in performing NOTES procedures. This will ensure the safety of patients and the ultimate effectiveness and continued development of NOTES.

Literature Review

Gastrointestinal cancers are the most common malignant tumors in the United States, and most of these cancers are diagnosed through endoscopy [9]. According to the National Center for Health Statistics, it was estimated in 1996 that over 1.2 million endoscopic biopsies are performed in the United States each year [10]. Traditionally, treatment of gastric cancers through endoscopy ended with diagnosis. Laparotomies, or surgeries performed through large abdominal incisions, were used for continued treatment. Laparoscopic surgery, a minimally invasive surgery (MIS) performed through small incisions, was later found to result in decreased patient discomfort and recovery time over laparotomies [1-3].

The original initiative behind natural orifice transluminal endoscopic surgery, or NOTES, was the idea of a MIS completely void of incisions [11]. As such, NOTES is believed by surgeons to potentially be a superior treatment for gastric cancers even in comparison to laparoscopic techniques [11]. However, there are several deficiencies that need to be corrected before this can be a possibility. This literature review will address general information about NOTES before discussing its technical limitations in detail. Then, current and developing designs will be studied before the niche for the research presented in this thesis is addressed based on current literature.

NOTES has the potential to reduce patient discomfort and decrease recovery time to an even higher degree than laparoscopic methods have been able to achieve [2]. There is also

increasing clinical data demonstrating that NOTES procedures can be carried out successfully in humans. The peritoneal cavity has been accessed safely through multiple transluminal routes, each with its own advantages and disadvantages [1]. Possible other applications of NOTES include liver biopsy, tubal ligation, partial hysterectomy, splenectomy, and treatment of Barrett's Esophagus [12]. NOTES surgery is possible through a flexible instrument called an endoscope which is inserted through natural body orifices and contains attachments that can provide surgical instruments, imaging, light, or nearly any other surgical necessity (Figure 1-1) [7].

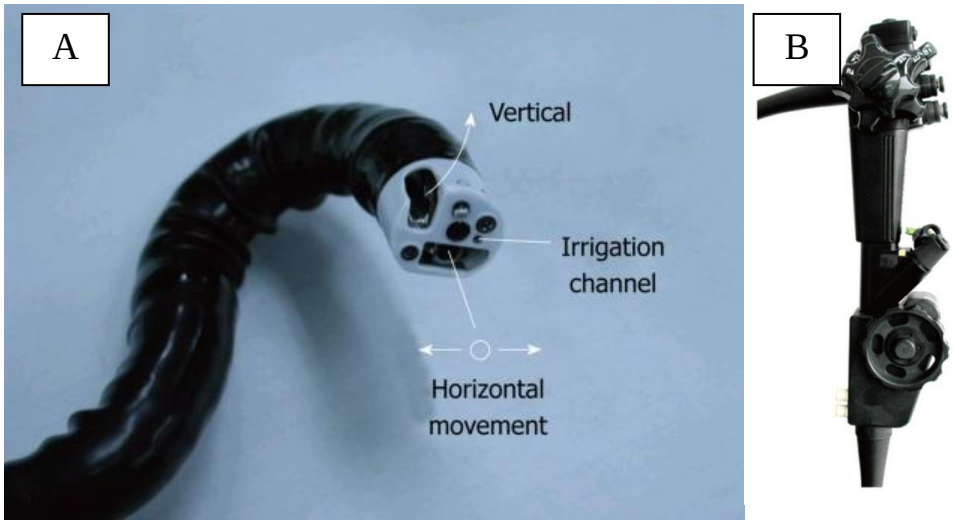

Figure 1-1 NOTES endoscope: (A) endoscope tip, highlighting vertical and horizontal imaging cameras, an irrigation channel, and other channels for lighting/accessories; (B) NOTES scope user interface to control endoscope tip movement and use of accessories [7]

The NOTES procedure does not come without technical limitations, but new attachments and tools to suture, cauterize, and cut are currently being developed to make a wider range of NOTES procedures possible. Even with these advances, only limited visual and tactile information is able to be transmitted to surgeons through the endoscopic instruments by the physical limitations of the endoscope [2]. There remains a need for a superior biopsy needle that can be used through an endoscope to perform non-invasive biopsy procedures. The scope of this

literature review is to study the current developments in the field of endoscopic biopsy needles and to evaluate and justify a 2-dimensional screw-like endoscopic needle design based on pertinent literature.

In general, an endoscopic biopsy needle can be classified into one of two main categories based on the way that it cuts tissue samples. These two categories are 1. end cutting needles and 2. side cutting needles [6]. End cutting needles use a hollow tube with an inner, retractable stylet to cut into the tissue and core out a sample (Figure 1-2 (A)) [13]. Side cutting needles typically have a needle shaft with a forward-pointing tip and a recess that retains tissue close to the needle tip (Figure 1-2 (B)); some have an outer sheath that is fitted over the needle shaft and encases a blade to cut tissue samples [14]. When the needle is inserted into a tissue specimen, the sheath is pulled back to reveal the recess and to allow the tissue to become caught. Then, the sheath is quickly pushed forward again to cut the tissue sample [14].

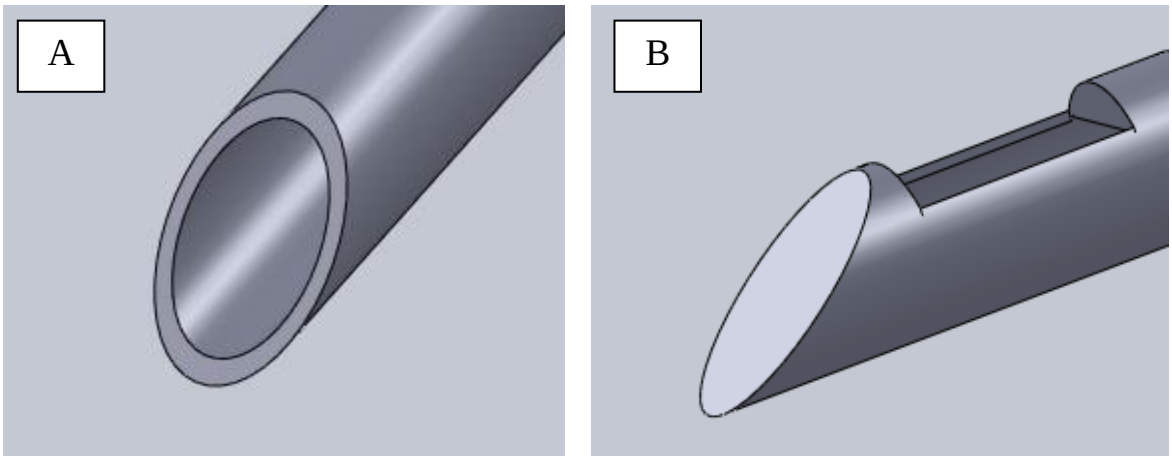

Figure 1-2 Biopsy needle types: (A) end cutting; (B) side cutting

If suction is used to draw a sample into the needle, the needle is called an aspiration needle, as is the case with the Olympus EZ-Shot (the design to which the 2-dimensional screw-like design will be compared) [6]. Based on the terminology presented, the Olympus EZ-Shot is

an end cutting aspiration needle (Figure 1-3). It uses a hollow needle with a stylet which is placed into the sample. The stylet is then removed, suction is applied with a syringe, and the hollow needle is advanced into the sample several times while the suction is applied to aspirate tissue into the needle. The suction is removed before the needle and the contained sample are removed from the tissue. Finally, a 20cc syringe is used to force the obtained sample out of the hollow needle and onto a slide for testing.

Figure 1-3 The Olympus EZ-Shot needle, an end cutting aspiration needle

Biopsy needles vary greatly based on their intended use. In many cases in which a hollow needle is used to remove a biopsy sample, a stylet is used to fill the hollow needle and prevent tissue from entering the needle until desired or from traveling too far up into the needle [6]. Biopsy needles unintended for endoscopic use are similar to endoscopic biopsy needles in purpose (end cutting versus side cutting), but they generally have fewer design constraints due to unpresent stresses incurred through endoscopic flexing [15]. It is beneficial to examine and understand how components of these related designs might be useful in endoscopic biopsy needle design, so relevant designs are presented next.

A study conducted at MIT revealed that side cutting needles do not always cut samples from tissue; instead, they simply push the tissue aside and fail to collect an adequate sample size [6]. The same study also showed flaws in end cutting needles. The most obvious flaw was that, although the end cutting needles were reliable in cutting core samples in the tissue, they were not able to reliably sever the samples perpendicular to the core to actually remove them for further testing [6]. Another study showed that end cutting needles in particular produce very inconsistent tissue retrieval by failing to capture any tissue 27% of the time [16]. To combat these issues, MIT researched and developed prototypes of an endoscopic biopsy needle with flexural members that reliably provided a greater sample mass. However, a removal force higher than that of traditional wedge-shaped endoscopic biopsy needles was necessary in order to remove the sample [6].

Another recently patented surgical biopsy instrument under development is not a needle at all but a pair of actuating jaws. The jaws are opened and closed through a pressure or thermal gradient created by a handheld generator [17]. The foundation of this surgical instrument is minimally invasive surgery through use of energy-based surgical devices (EBSD). However, these devices are capable of harming surrounding healthy tissue, putting them at a disadvantage compared to commercially available products [17]. If this possibility could be eliminated through further research, EBSD could certainly prove to be a viable solution.

There are also multiple endoscopic biopsy needles which are already commercially available in the medical industry. Aside from the EZ-Shot, Olympus also manufactures and sells the PowerShot (NA-11J-KB) and their original fine needle (<1 millimeter) aspiration system (NA-10J-1) [18]. Only the EZ-Shot and PowerShot are designed for use in an endoscope. The

EZ-Shot is designed for a single use, while both the PowerShot and the NA-10J-1 are reusable [18].

Cook Medical also manufactures a needle which is meant to be used through the accessory channel of an ultrasound endoscope [19]. Like the EZ-Shot, it is intended for single use applications in which a core tissue sample is desired, but it is unique in that it can be operated conveniently with only one hand [19].

Visual NOTES limitations are being mitigated by surgeons through the use of endoscopic ultrasound-guided (EUS) techniques [20]. In this setup, an ultrasound transducer is used externally to view movement of a biopsy needle in reference to the tissue of interest. An ultrasound transducer works by producing sound waves, which echo off of tissues and are sent to a computer. The data is then interpreted and turned into an image for the surgeon to view [21]. It should be noted that special care needs to be taken to avoid puncturing and damaging vascular structures even when EUS techniques are used, as the shadows produced by ultrasound are not always particularly clear [20].

All biopsy needles have one common goal—to remove the maximum amount of tissue possible with the lowest removal force. This helps to not only reduce healing time and patient discomfort but also to minimize bleeding complications during and after surgery [22]. When combined with the inherent need for an endoscopic biopsy needle to be small enough in diameter to enter the body through an endoscope, yet large and strong enough to withstand stresses caused by endoscope deformation and tissue puncture, the endoscopic biopsy needle design problem becomes increasingly complex. Minimizing the risks involved with endoscopy is realized by using needles smaller than 18 gauge [22].

Proper modeling of needle insertion into tissue is necessary to provide an accurate representation of surgery [2]. Before in vivo testing can take place, extensive ex vivo tests must first be completed and verified. One notable variable is the design of the stylet. The stylet can be either round or beveled (sharp) [20]. Although bevel-tipped needles lead to more bending than cone or triangular tips, they continue to be more widely used due to manufacturing ease [2].

The force required to insert a biopsy needle into tissue can be represented by a summation of three forces: needle stiffness, friction, and cutting [2]. However, the severity of these forces depends to a high degree on the tissue of interest. Density of arteries and veins, placement, and variations between different patients makes it extremely difficult to directly apply ex vivo results, even with the most accurate model, to in vivo testing. However, combining these empirical results with finite element modeling may help combat some of the discrepancies and provide more representative results [2].

Another significant variable in endoscopic biopsy is that of the user. A round stylet is less damaging than a bevel-tipped stylet to the instrument channel and, as such, is used more often by novice endoscopic surgeons [20]. In most cases, the needle and stylet are advanced to the tissue sample and subsequently cut and trap tissue inside the hollow needle, as described earlier in this literature review when discussing the two types of biopsy needles. However, there are cases in which a “punch” technique, or a very rapid puncture of the tissue of interest, is the only way to penetrate the tissue and retrieve a sample [20]. In these cases, needle bending is more often observed, which may cause unwanted injuries or damage to the endoscopic channels [20].

A final variable worth considering is overall needle geometry. Currently, a needle tip geometry that maximizes cutting efficiency has not been found [23]. An increased

understanding and application of biopsy needle design could lead to an increased consistency in biopsy needle performance and an increase in retrieved sample size [16]. In order to completely define needles that are symmetric about one or more planes, three parameters are required: needle radius, number of planes, and tilt angle. Asymmetric needles are not as simple to define. Symmetric one-plane needles are sometimes called bias bevel needles and three-plane needles are also known as Franseen needles [16].

A study at the University of Michigan showed that biopsy performance is directly related to the needle tip geometry, more specifically rake and inclination angles, which directly affect the bevel angle. In the study, the largest biopsy samples were obtained using two-plane needles with low bevel angles (high rake and inclination angles) [16]. However, only bevel angles between 20 and 30 degrees were tested, leaving room for external factors to greatly affect the results outside of the tested range.

Another study performed on bovine liver and phantom gel compared the effectiveness of end-cut biopsy needles at different speeds in addition to inclination angles [24]. The bovine liver had a Young's modulus of 3.5 kPa and the phantom gel had a Young's modulus of 12.4 kPa [23]. To cut tissue, a machine was built which uses a pneumatic cylinder as an actuator to insert blades (used to represent needle geometry on a larger scale) into the samples. The study determined that several factors, including tip geometry, edge sharpness, and cutting speed can all affect the ability of the needle to retrieve tissue. Higher speed, in particular, was shown to produce a much higher necessary insertion force. High inclination angles, in accordance with the previous University of Michigan study, were found to greatly benefit tissue cutting [24].

Not addressed in previous research of endoscopic biopsy needles is the study of 2-dimensional alternatives to the 3-dimensional, hollow needles that are mass produced for the

traditional coring method of biopsy. However, a 2-dimensional alternative could potentially reduce manufacturing costs and failure rates. Niebel et al utilized a lost mold rapid infiltration forming (LMRIF) process to manufacture planar screw-like needles (Figure 1-4) [25]. This design eliminates the need for a stylet, which reduces the human control component of an endoscopic biopsy and could potentially increase endoscopic biopsy success rates.

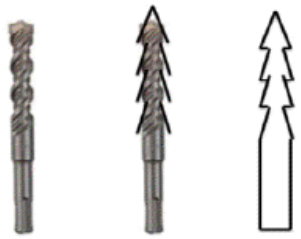

Figure 1-4 2-D simplification of screw design

The design was tested with large-scale (10x) and meso-scale (13 millimeter length, 0.8 millimeter width, 0.8/1.5 millimeter thickness) prototypes. Tests involved inserting the needles into an apple at 90 degrees to the surface and measuring the removal force required with a force gauge. Needles were weighed before and after apple insertion, yielding both removal force and mass of removed material [25]. Several removal methods were tested, but a multiple insertion method was determined to be the most practical. This research will involve a continuation of this study with meso-scale prototype needles, using a similar multiple insertion method and the same materials as the previous large-scale and meso-scale tests.

Conclusion

NOTES has the potential to completely revolutionize medicine and surgery, in particular. As progress has been made in NOTES throughout the years, it has become increasingly apparent that several obstacles remain and need to be overcome before NOTES can become a preferred surgical technique. One such obstacle is that of limited instrumentation. The three objectives of this research will help to overcome this obstacle by attempting to improve available instrumentation. As mentioned in the introduction, the first objective is to develop a testing procedure for the Olympus EZ-Shot. With a testing protocol, better comparisons between developing needles and readily available needles can be made, leading to optimal instrumental performance during NOTES procedures. The second objective is to apply the testing procedure to benchmark a prototype 2-dimensional endoscopic biopsy needle against the Olympus EZ-Shot, and the third is to determine the effect of needle thickness on removal force and mass removed.

Chapter 2

Methods and Materials

The methods and materials used for this research can be best explained in three parts, namely the following: development of the Olympus EZ-Shot test protocol, preparation for the setup of prototype and EZ-Shot needle testing, and the testing procedure used for comparison between the prototype needle and the Olympus EZ-Shot.

Development of Olympus EZ-Shot Test Protocol

Users may perform biopsies differently with the Olympus EZ-Shot, but this is problematic in a laboratory testing environment and could lead to drastic differences in results and ultimately influence the design of a new endoscopic biopsy needle. In order to prevent this and develop a testing procedure for comparing the Olympus EZ-Shot to the new prototype needle (and possible future prototypes), a test protocol for the Olympus EZ-Shot was created to serve as a common and constant reference point.

Dr. Abraham Mathew, a gastroenterologist at the Hershey Medical Center, collaborated in the development of the test protocol and provided suggestions throughout the process. He also verified the final testing procedure to be consistent with medical practice. The materials necessary to complete a test with the Olympus EZ-Shot are the following: an Olympus EZ-Shot aspiration needle, a stopcock, a 20cc syringe, a glass slide, and a sample upon which the "biopsy" will be performed. The stopcock and 20cc syringe can be easily attached by twisting them onto the top of the actuating handle clockwise after the stylet has been removed (see Figure 2-10 and Figure 2-12 for further clarification).

The most variable parameter between users is depth of needle penetration and movement within the sample. Through trial and error testing, it was determined that large (4 centimeters or more) movements remove larger samples than either the new prototype needle or the Olympus EZ-Shot at smaller depths. However, the 20cc syringe, which is first filled to capacity and subsequently used to expel the mass from the biopsy needle, prevents use at these larger depths. This is because expelling the larger masses from the hollow needle requires a larger pressure than it is possible to apply manually with the 20cc syringe. In a medical biopsy procedure, this would not be practical. After further testing, the largest mass able to be removed using a 20 cc syringe was achieved with a working depth of 1-2 centimeters. This working depth was used for testing and comparison to the new prototype needles.

The EZ-Shot was tested both with and without use of its actuating handle (Figure 2-1). This was done for two reasons. First, it was desired to quantify the force of friction in the actuating handle. Second, because the prototype needles are not attached to an actuating handle, comparisons between the EZ-Shot and the prototypes would be more meaningful if tests with the EZ-Shot were also completed in the absence of an actuating handle.

Figure 2-1 Olympus EZ-Shot actuating handle

In the next section, the test protocol for the Olympus EZ-Shot will be presented (Figures 2-2 to 2-14). Then, the preparation of the testing setup, including that of the prototype needles and the EZ-Shot, will be discussed. For the purpose of this thesis, an apple was chosen as the "sample" for testing. Although an apple may not be directly comparable to tumor tissue, it does provide consistent removal force and mass removal data that is applicable for comparison between different biopsy needle designs.

Olympus EZ-Shot Aspiration Needle Test Protocol

Step 1

Protrude the needle out of the sheath by 1 centimeter by moving the handle to the 1 centimeter position.

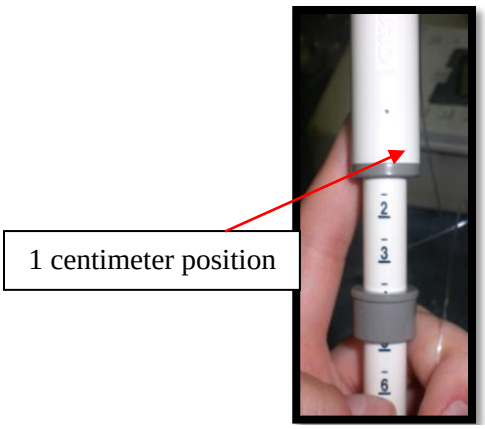

Figure 2-2 Move the handle to the 1 centimeter position

Step 2

Place the stopper below this point and twist the silver knob clockwise to prevent the handle from moving.

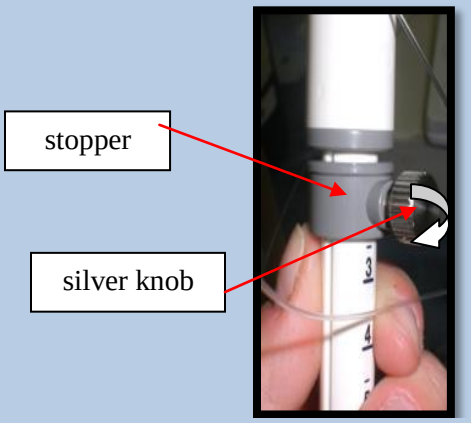

Figure 2-3 Turn the knob clockwise to immobilize the needle

Step 3

Twist the cap on the handle clockwise to bring the stylet inside the hollow needle.

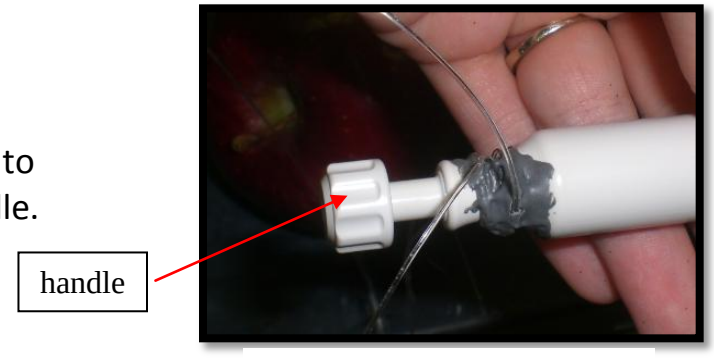

Figure 2-4 Expose the stylet by twisting the handle

Step 4

Insert the needle normal to the surface of the sample until the sheath comes into contact with the sample's surface.

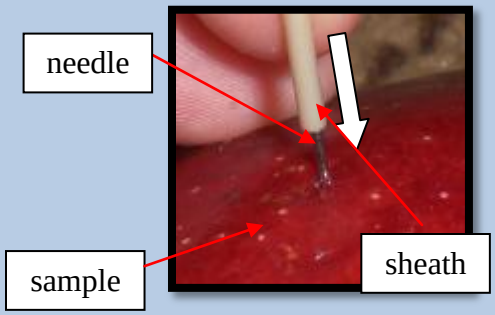

Figure 2-5 Insert the needle into the sample

Step 5

Have another person hold the sheath to keep the needle in place. Repeat Step 1 and Step 2 for a needle protrusion of 2 centimeters while leaving the needle in the sample. Twist the cap on the handle to remove the stylet from the apparatus completely.

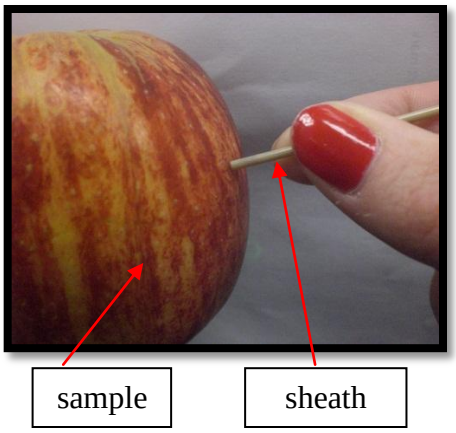

Figure 2-6 With the needle in the sample, bring the needle to the 2 centimeter position

Step 6

Ensure that the stopcock is in its "open" position and twist it onto the top of the handle.

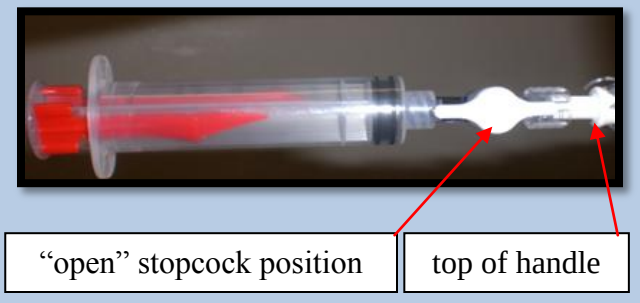

Figure 2-7 Attach the stopcock in the open position

Step 7

Apply suction by pulling the syringe back to the second red stopper.

Note: Do not be concerned if the stopper is difficult to pull back. It will not break.

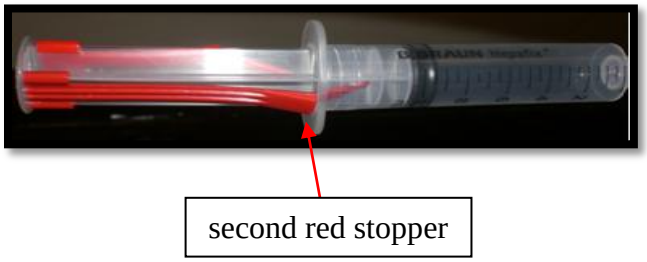

Figure 2-8 Use the stopcock to apply suction

Step 8

Keep suction applied. Loosen the stopper on the handle again by twisting the silver knob counter-clockwise, and move the needle between 1 and 2 centimeters seven times within the sample (see Step 1 and Step 2, if necessary). You have now removed cells from the sample.

Figure 2-9 Mobilize the needle by twisting the silver knob clockwise, then immobilize the needle by twisting the silver knob clockwise

Step 9

Return the stopcock to its "closed" position and remove the stopcock from the top of the handle. You have now removed the suction that was applied to draw cells into the needle.

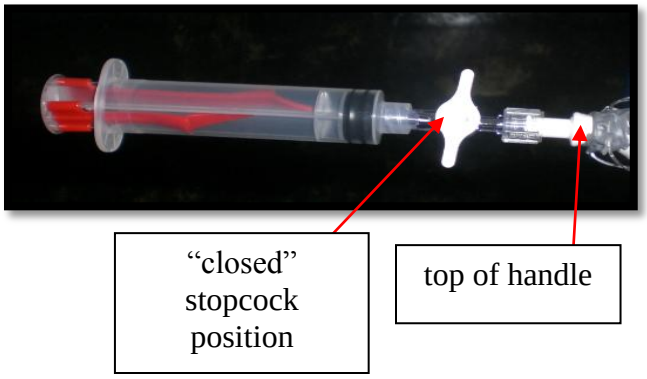

Figure 2-10 Remove suction applied by the stopcock

Step 10

Move the needle to the 0 centimeter position, and re-tighten the metal knob by twisting it clockwise. This completely removes the needle from the sample.

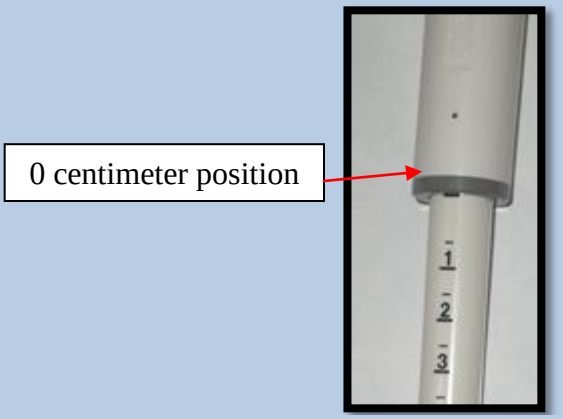

Figure 2-11 Move the needle to the 0 centimeter position

Step 11

Fill the 20 cc syringe to capacity with air. Attach it to the handle.

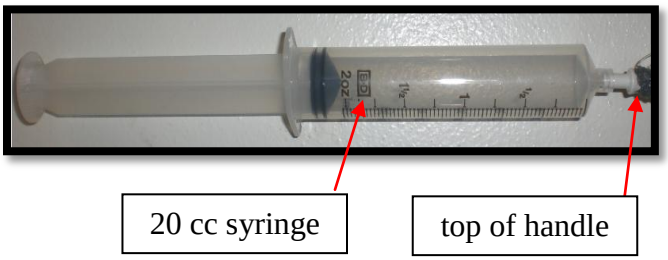

Figure 2-12 Attach the 20 cc syringe

Step 12

Protrude the needle out of the sheath by 1 centimeter by moving the handle to the 1 centimeter position.

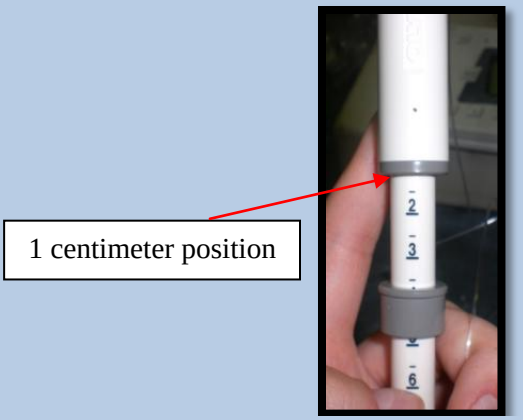

Figure 2-13 Return the needle to the 1 centimeter position

Step 13

Slowly apply force to the syringe to push the mass out of the needle and onto a glass slide for testing.

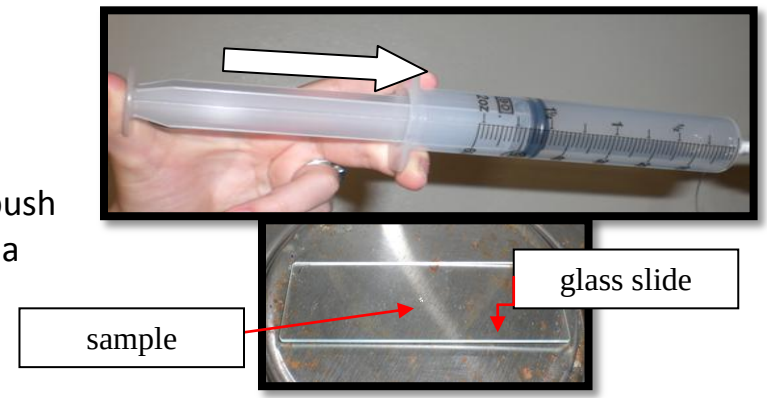

Figure 2-14 Eject the mass removed onto a glass slide

Preparation of Needle Test Setup

After the test protocol for the Olympus EZ-Shot was created, the next task was to assemble all materials necessary for comparing the Olympus EZ-Shot to the prototype needles. The design and manufacturing processes for the prototype needles were completed by Cassandra Niebel and Gregory Hayes, respectively [25, 26]. However, the needles needed to be mounted in such a way that they could be attached to an IMADA DPS-1 digital force gauge to determine removal force, yet be weighed both before and after testing with a Sartorius MC210S balance to determine mass removed from the sample.

The developed solution involved using super glue to secure the prototype needles between two washers (Figure 2-15 (C)). Ten needles (five 300 micrometers thick and five 400 micrometers thick) were manufactured for testing. Along with the primary goal of comparing the prototype needle design to the Olympus EZ-Shot, two secondary goals—determining the effect of needle thickness on removal force/mass removed and quantifying the effect of friction in the actuating handle—were also able to be addressed through the testing procedure.

Each prototype needle was a different length beyond its top tooth (Figure 2-15 (A)). This was because the materials science team wanted to test the manufacturing process at longer, more "wire-like" lengths. For consistency, each needle was glued between two washers just above the highest tooth (Figure 2-15 (B) and Figure 2-15 (C)) for use in the testing setup (Figure 2-16).

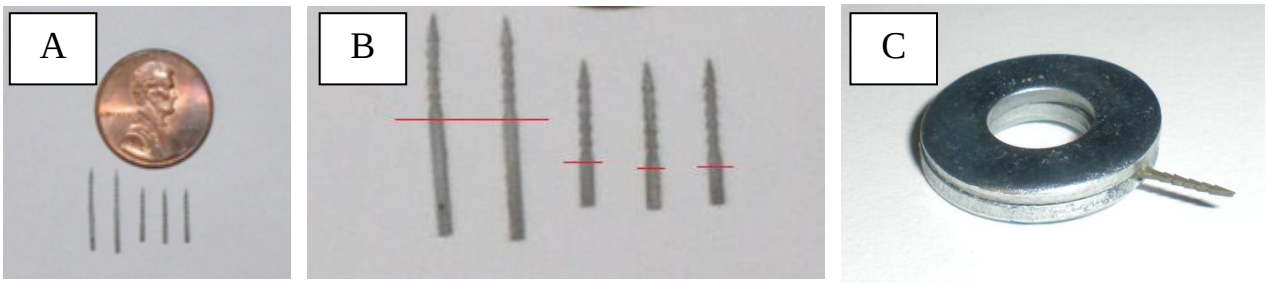

Figure 2-15 Prototype needles (300 micrometer thickness shown): (A) five next to a penny for reference; (B) five marked just above the highest tooth; (C) one glued between two washers

This eliminated any possible variation due to each prototype needle being a different length. The washers provide an easy access point for the DPS-1 force gauge when a hook attachment is used, making it simple to consistently remove the prototype needle from the force gauge for mass measurement after the test has been completed.

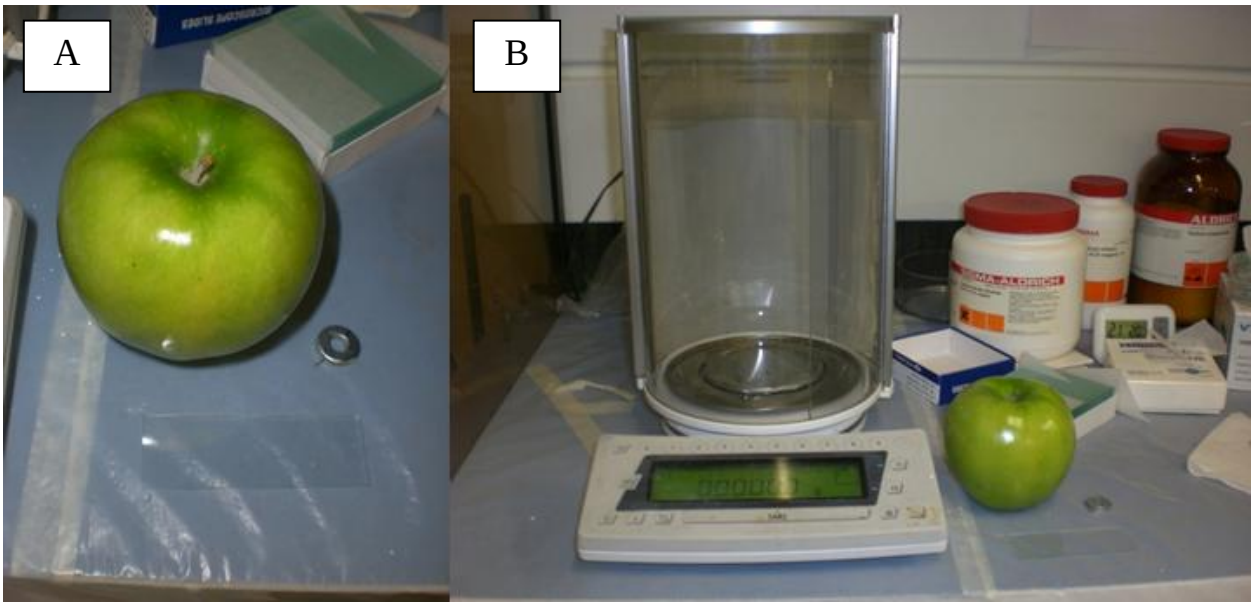

Figure 2-16 Needle test setup: (A) sample, glass slide, and prototype needle secured between two washers; (B) sample, glass slide, and prototype needle aside Sartorius MC210S balance

The Olympus EZ-Shot, for comparison to the prototype needle, also needed to be modified for force gauge attachment both with and without the handle actuator, as described in the previous section of this thesis. Obtaining mass removed could be easily measured by ejecting the mass collected onto a slide as described in the test protocol. Therefore, it was not necessary to detach the needle from the handle actuator in order to do accomplish both testing scenarios.

To attach the Olympus EZ-Shot to the force gauge with the actuator, fishing line (50 pound) was tied around the handle of the EZ-Shot just below the knob connected to the stylet,

given approximately six inches of length, and subsequently tied to an S-hook (Figure 2-17). All knots were secured with JB-Weld epoxy for maximum security. By using this setup, the force gauge could be attached to the S-hook and pulled back while the needle remained in the sample in order to determine removal force accurately.

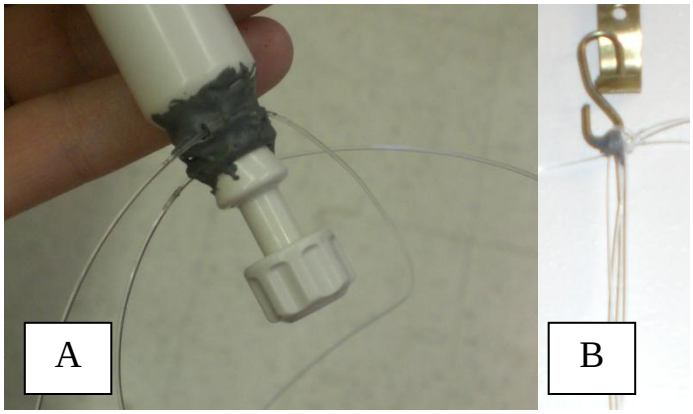

Figure 2-17 Actuating handle force gauge attachment: (A) fishing line tied to actuating handle and secured with epoxy; (B) fishing line tied at opposite end to S-hook

To attach the Olympus EZ-Shot to the force gauge without the actuator, the 50 pound fishing line was used again and tied around the sheath two inches above the sheath opening from which the needle protrudes. Super glue was used to secure the fishing line to the sheath, and a similar S-hook setup as used on the handle actuator was implemented for a second time (Figure 2-18). During the testing process, the needle length was left free so as not to increase or decrease the reading on the force gauge.

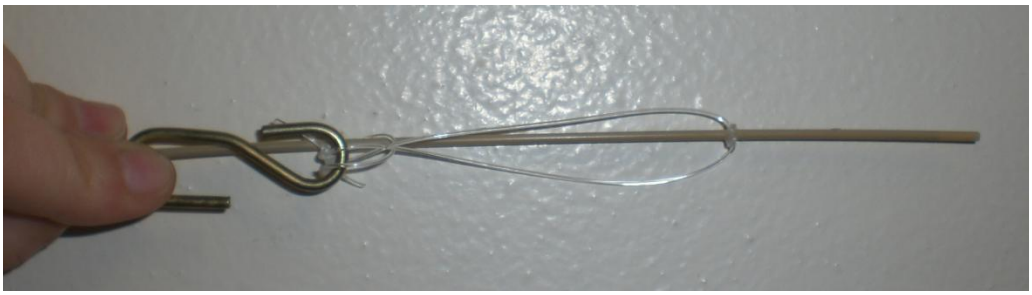

Figure 2-18 No actuating handle force gauge attachment

Testing Procedure for Prototype Needles and Olympus EZ-Shot

At the beginning of each test, a slide was placed on the Sartorius MC210S balance. A reading was recorded, and the scale was tared (Figure 2-19).

Figure 2-19 Taring of the Sartorius MC210S balance after initial placement of a glass slide

Next, a first prototype needle, including its washer setup, was weighed (Figure 2-20 (A)). This measurement was recorded as initial mass. Then, the needle was inserted into an apple normal to the surface until the tooth closest to the needle base (Figure 2-15 (B)) was immersed (Figure 2-20 (B)).

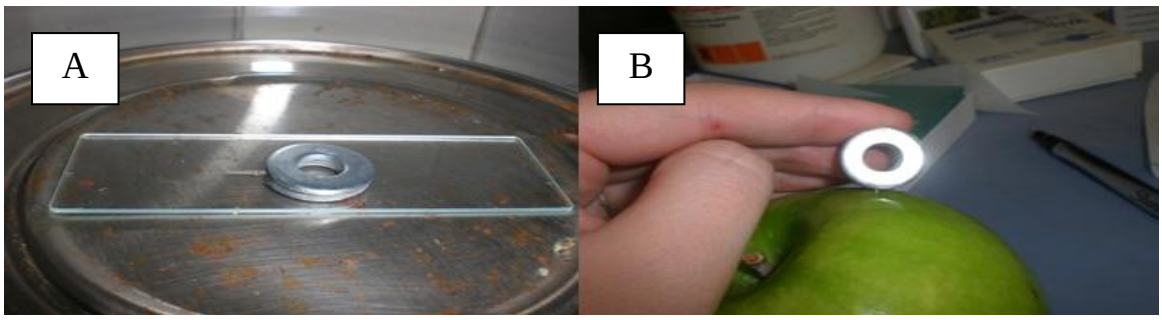

Figure 2-20 Testing procedure for prototype needles: (A) determining the initial mass of the washer and prototype needle setup; (B) inserting the needle into the sample to remove mass

Consistent with a multiple insertion method, the needle was manually inserted three more times normal to the surface of the apple. Next, the IMADA DPS-1 digital force gauge was attached to the washers holding the prototype needle together, set to record the maximum force**,** and used to remove the prototype needle from the apple (Figure 2-21). The maximum removal force was recorded. The needle and washers were set again onto the same glass slide and weighed. This mass, referred to as final mass, was also recorded. The initial mass was subtracted from this final mass to determine the mass removed from the sample by the needle.

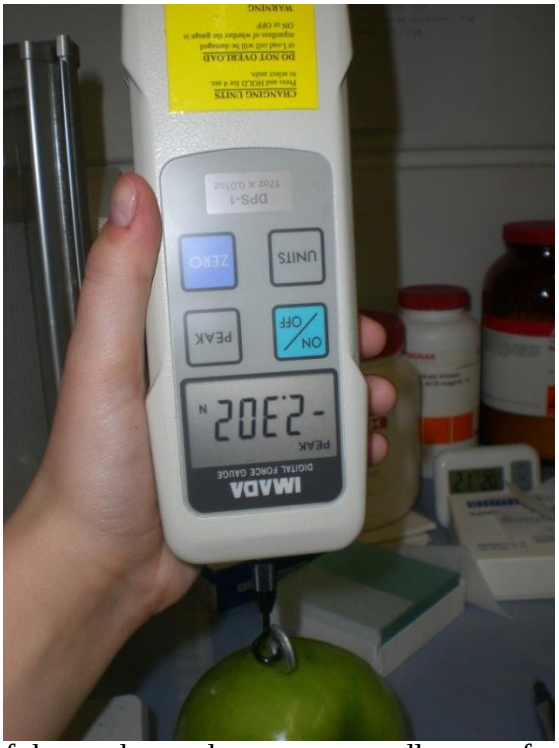

Figure 2-21 Removal of the washer and prototype needle setup from the sample using the IMADA DPS-1 digital force gauge to obtain the maximum removal force required

After each test, a new glass slide was used for measuring both initial and final mass, and the needle being tested was cleaned thoroughly using V WR Light-Duty Tissue Wipers. Eight

prototype needles (four at each thickness) were tested fifteen times each. These results were compared to those obtained through fifteen tests completed with the Olympus EZ-Shot.

Tests for the Olympus EZ-Shot were completed using a method similar to the one used to test the prototype needles. One Olympus EZ-Shot needle was tested 15 times with the actuating handle and 15 times without the actuating handle. The testing procedure began by placing an unused glass slide onto the Sartorius MC210S balance and taring the balance as described previously.

Then, the Olympus EZ-Shot test protocol presented in the "Development of Olympus EZ-Shot Test Protocol" section was followed. However, instead of simply removing the needle from the mass manually as shown in Step 10, the IMADA DPS-1 digital force gauge was attached to the S-hook connected to the sheath or to the S-hook connected to the actuating handle, dependent upon which test was being performed. Similar to prototype testing, the IMADA DPS-1 force gauge was set to display the maximum force, which was subsequently recorded for comparison to the data obtained for the prototype needles.

Chapter 3

Results

The testing methods presented in Chapter 2 were completed as described. This chapter will present the results from the testing. The results are broken down into three sections. The first section, Quantitative Prototype Test Results, presents all raw data, including mass removal and removal force required data for four needles of 300 micrometer thickness, four needles of 400 micrometer thickness, Olympus EZ-Shot with actuating handle, and Olympus EZ-Shot without actuating handle. The second section, Prototype Needle Data, reports combined data from all needles of 300 micrometer thickness and all needles of 400 micrometer thickness. In this section, the raw data for the prototype needles will be averaged to provide meaningful data that can be compared to the Olympus EZ-Shot. The third section, Olympus EZ-Shot Data, will present comparison data between Olympus EZ-Shot tests completed with and without the actuating handle. This data will be used to quantify the friction force induced in biopsy procedures by the actuating handle. The results are discussed in Chapter 4 and Chapter 5.

Quantitative Prototype Test Results

In order to evaluate the endoscopic biopsy needle prototype, quantitative data was obtained through the testing procedure described in Chapter 2. This section summarizes the raw data results obtained during testing. As presented in Chapter 2, four 300 micrometer needles and four 400 micrometers needles were each tested 15 times. For each test, mass removed and removal force required were measured. Full tables including initial and final mass measurements can be found in the Appendix. However, for simplicity and ease of understanding, only the mass

removed will be presented here. The notation x00-y will be used to differentiate the tests, where x00 represents the theoretical thickness of the prototype needle (either 300 or 400 micrometers) and y represents which needle (1,2,3 or 4) is being tested. Two tables will be presented for each needle; the first will present the raw data itself. The second table in the set (per needle tested) will show the statistical properties associated with the raw data.

Tests (for all needles) in which no mass was removed were considered outliers. This happened twice with the Olympus EZ-Shot. These data points were removed from the data presented, as they were not meaningful in performance comparison.

Table 3-1 Needle 300-1 Test Results: This table shows the mass removed (g), removal force applied (N), and ratio of mass removed to removal force applied (g/N) for the first 300 micrometer thickness needle.

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00035	0.314	0.0011
2	0.00025	0.437	0.00057
3	0.00018	0.435	0.00041
4	0.00019	0.415	0.00046
5	0.00024	0.314	0.00076
6	0.00015	0.442	0.00034
7	0.00038	0.450	0.00084
8	0.00040	0.286	0.0014
9	0.00030	0.237	0.0013
10	0.00031	0.255	0.0012
11	0.00033	0.292	0.0011
12	0.00049	0.276	0.0018
13	0.00037	0.350	0.0011
14	0.00034	0.462	0.00074
15	0.00018	0.493	0.00037

Table 3-2 Needle 300-1 Statistics: This table shows statistical properties associated with mass removed, removal force applied, and the ratio between the two for the first 300 micrometer thickness needle.

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00030	0.364	0.00090
Median	0.00031	0.350	0.00084
Standard Deviation	0.00010	0.087	0.00043
Minimum	0.00015	0.237	0.00034
Maximum	0.00049	0.493	0.0018

Table 3-3 Needle 300-2 Test Results

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00021	0.131	0.0016
2	0.00005	0.193	0.00026
3	0.00015	0.206	0.00073
4	0.00012	0.283	0.00042
5	0.00025	0.389	0.00064
6	0.00008	0.243	0.00033
7	0.00031	0.323	0.00096
8	0.00022	0.375	0.00059
9	0.00022	0.328	0.00067
10	0.00026	0.289	0.00090
11	0.00013	0.249	0.00052
12	0.00016	0.360	0.00044
13	0.00023	0.532	0.00043
14	0.00043	0.252	0.0017
15	0.00016	0.302	0.00053

Table 3-4 Needle 300-2 Statistics

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00020	0.297	0.00072
Median	0.00021	0.289	0.00059
Standard Deviation	0.00010	0.096	0.00043
Minimum	0.00005	0.131	0.00026
Maximum	0.00043	0.532	0.0017

Table 3-5 Needle 300-3 Test Results

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00031	0.436	0.00071
2	0.00020	0.413	0.00048
3	0.00038	0.403	0.00094
4	0.00032	0.334	0.00096
5	0.00033	0.418	0.00079
6	0.00024	0.464	0.00052
7	0.00043	0.492	0.00087
8	0.00026	0.498	0.00052
9	0.00030	0.400	0.00075
10	0.00016	0.494	0.00032
11	0.00035	0.311	0.0011
12	0.00030	0.344	0.00087
13	0.00012	0.524	0.00023
14	0.00026	0.505	0.00051
15	0.00031	0.427	0.00073

Table 3-6 Needle 300-3 Statistics

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00029	0.431	0.00069
Median	0.00030	0.427	0.00073
Standard Deviation	0.00008	0.066	0.00025
Minimum	0.00012	0.311	0.00023
Maximum	0.00043	0.524	0.0011

Table 3-7 Needle 300-4 Test Results

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00039	0.260	0.0015
2	0.00032	0.295	0.0011
3	0.00030	0.316	0.00095
4	0.00040	0.311	0.0013
5	0.00022	0.185	0.0012
6	0.00030	0.314	0.00096
7	0.00043	0.291	0.0015
8	0.00020	0.327	0.00061
9	0.00034	0.439	0.00077
10	0.00037	0.242	0.0015
11	0.00026	0.371	0.00070
12	0.00018	0.344	0.00052
13	0.00025	0.430	0.00058
14	0.00018	0.222	0.00081
15	0.00038	0.467	0.00081

Table 3-8 Needle 300-4 Statistics

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00030	0.321	0.00099
Median	0.00030	0.314	0.00095
Standard Deviation	0.00008	0.080	0.00034
Minimum	0.00018	0.185	0.00052
Maximum	0.00043	0.467	0.0015

Table 3-9 Needle 400-1 Test Results

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00056	0.538	0.0010
2	0.00052	0.455	0.0011
3	0.00023	0.386	0.00060
4	0.00040	0.460	0.00087
5	0.00068	0.365	0.0019
6	0.00014	0.366	0.00038
7	0.00019	0.230	0.00083
8	0.00020	0.410	0.00049
9	0.00024	0.313	0.00077
10	0.00008	0.431	0.00019
11	0.00014	0.368	0.00038
12	0.00028	0.286	0.00098
13	0.00013	0.550	0.00024
14	0.00012	0.459	0.00026
15	0.00020	0.407	0.00049

Table 3-10 Needle 400-1 Statistics

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00027	0.402	0.00070
Median	0.00020	0.407	0.00060
Standard Deviation	0.00018	0.087	0.00044
Minimum	0.00008	0.230	0.00019
Maximum	0.00068	0.550	0.0019

Table 3-11 Needle 400-2 Test Results

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00022	0.633	0.00035
2	0.00042	0.623	0.00067
3	0.00037	0.629	0.00059
4	0.00037	0.278	0.0013
5	0.00033	0.537	0.00061
6	0.00033	0.592	0.00056
7	0.00024	0.421	0.00057
8	0.00020	0.545	0.00037
9	0.00021	0.401	0.00052
10	0.00016	0.420	0.00038
11	0.00017	0.585	0.00029
12	0.00016	0.509	0.00031
13	0.00028	0.401	0.00070
14	0.00023	0.410	0.00056
15	0.00025	0.402	0.00062

Table 3-12 Needle 400-2 Statistics

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00026	0.492	0.00056
Median	0.00024	0.509	0.00056
Standard Deviation	0.00008	0.109	0.00025
Minimum	0.00016	0.278	0.00029
Maximum	0.00042	0.633	0.0013

Table 3-13 Needle 400-3 Test Results

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00038	0.628	0.00061
2	0.00039	0.304	0.0013
3	0.00046	0.614	0.00075
4	0.00038	0.547	0.00069
5	0.00040	0.631	0.00063
6	0.00039	0.602	0.00065
7	0.00033	0.409	0.00081
8	0.00037	0.526	0.00070
9	0.00032	0.582	0.00055
10	0.00044	0.540	0.00081
11	0.00030	0.310	0.00097
12	0.00043	0.442	0.00097
13	0.00037	0.605	0.00061
14	0.00037	0.293	0.0013
15	0.00046	0.486	0.00095

Table 3-14 Needle 400-3 Statistics

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00039	0.501	0.00082
Median	0.00038	0.54	0.00075
Standard Deviation	0.00005	0.122	0.00023
Minimum	0.00030	0.293	0.00055
Maximum	0.00046	0.631	0.0013

Table 3-15 Needle 400-4 Test Results

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00045	0.285	0.0016
2	0.00052	0.599	0.00087
3	0.00034	0.301	0.0011
4	0.00047	0.504	0.00093
5	0.00051	0.377	0.0014
6	0.00042	0.370	0.0011
7	0.00064	0.594	0.0011
8	0.00060	0.439	0.0014
9	0.00051	0.361	0.0014
10	0.00042	0.338	0.0012
11	0.00043	0.457	0.00094
12	0.00031	0.451	0.00069
13	0.00043	0.501	0.00086
14	0.00022	0.556	0.00040
15	0.00031	0.353	0.00088

Table 3-16 Needle 400-4 Statistics

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00044	0.432	0.0011
Median	0.00043	0.439	0.0011
Standard Deviation	0.00011	0.102	0.00031
Minimum	0.00022	0.285	0.00040
Maximum	0.00064	0.599	0.0016

Prototype Needle Data

To simplify comparisons between prototype needles and the Olympus EZ-Shot, the 15 measurements recorded for each 300 micrometer needle were compiled into one list of 60 measurements (4 needles*15 measurements=60 measurements) and analyzed statistically. The same was done for the 400 micrometer needles. The results are presented here in Table 3-17 and Table 3-18 (for 300 micrometer and 400 micrometer thickness prototype needles, respectively).

Table 3-17 Average Statistics for Needles of 300 micrometer Thickness

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00027	0.353	0.00082
Median	0.00026	0.339	0.00076
Standard Deviation	0.00010	0.096	0.00038
Minimum	0.00005	0.131	0.00023
Maximum	0.00049	0.532	0.0018

Table 3-18 Average Statistics for Needles of 400 micrometer Thickness

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00034	0.457	0.00078
Median	0.00036	0.447	0.00070
Standard Deviation	0.00014	0.111	0.00036
Minimum	0.00008	0.230	0.00019
Maximum	0.00068	0.633	0.0019

Olympus EZ-Shot Data

In order to evaluate the Olympus EZ-Shot, tests were completed with and without the actuating handle. Table 3-19 presents the raw data from 15 tests, including mass removed, removal force applied, and the ratio between the two. Table 3-20 provides the statistics obtained from the raw data. Table 3-21 and Table 3-22 compare the force removed test data between the Olympus EZ-Shot with and without its actuating handle. As mentioned at the beginning of this chapter, tests in which no mass was removed were considered outliers. This happened twice with the Olympus EZ-Shot.

Table 3-19 Olympus EZ-Shot (without handle) Test Results

Test #	Mass Removed (g)	Removal Force Applied (N)	Ratio of Mass Removed/Removal Force Applied (g/N)
1	0.00026	0.361	0.00072
2	0.00017	0.151	0.0011
3	0.00028	0.181	0.0015
4	0.00045	0.328	0.0014
5	0.00049	0.238	0.0021
6	0.00075	0.269	0.0028
7	0.00031	0.216	0.0014
8	0.00030	0.219	0.0014
9	0.00042	0.168	0.0025
10	0.00047	0.256	0.0018
11	0.00032	0.233	0.0014
12	0.00024	0.196	0.0012
13	0.00013	0.278	0.00047
14	0.00021	0.224	0.00094
15	0.00026	0.196	0.0013

Table 3-20 Olympus EZ-Shot (without handle) Statistics

	Mass Removed (g)	Removal Force Applied (N)	Ratio (g/N)
Mean	0.00034	0.234	0.0015
Median	0.00030	0.224	0.0014
Standard Deviation	0.00016	0.057	0.00062
Minimum	0.00013	0.151	0.00047
Maximum	0.00075	0.361	0.0028

Table 3-21 Olympus EZ-Shot Removal Force Comparison

Test #	Removal Force Applied (N)—without handle	Removal Force Applied (N)—with handle
1	0.361	2.353
2	0.151	2.692
3	0.181	2.522
4	0.328	2.592
5	0.238	2.868
6	0.269	2.756
7	0.216	2.947
8	0.219	2.953
9	0.168	3.141
10	0.256	2.884
11	0.233	2.949
12	0.196	2.818
13	0.278	2.874
14	0.224	2.886
15	0.196	2.830

Table 3-22 Olympus EZ-Shot Removal Force Comparison Statistics

	Removal Force Applied (N)—without handle	Removal Force Applied (N)—with handle
Mean	0.234	2.804
Median	0.224	2.868
Standard Deviation	0.057	0.197
Minimum	0.151	2.353
Maximum	0.361	3.141

The data presented in Table 3-17 through Table 3-22 of this chapter was then compiled graphically for easier comparison (Figure 3-1 to Figure 3-4). The error bars for each data set represent plus or minus one standard deviation from the mean.

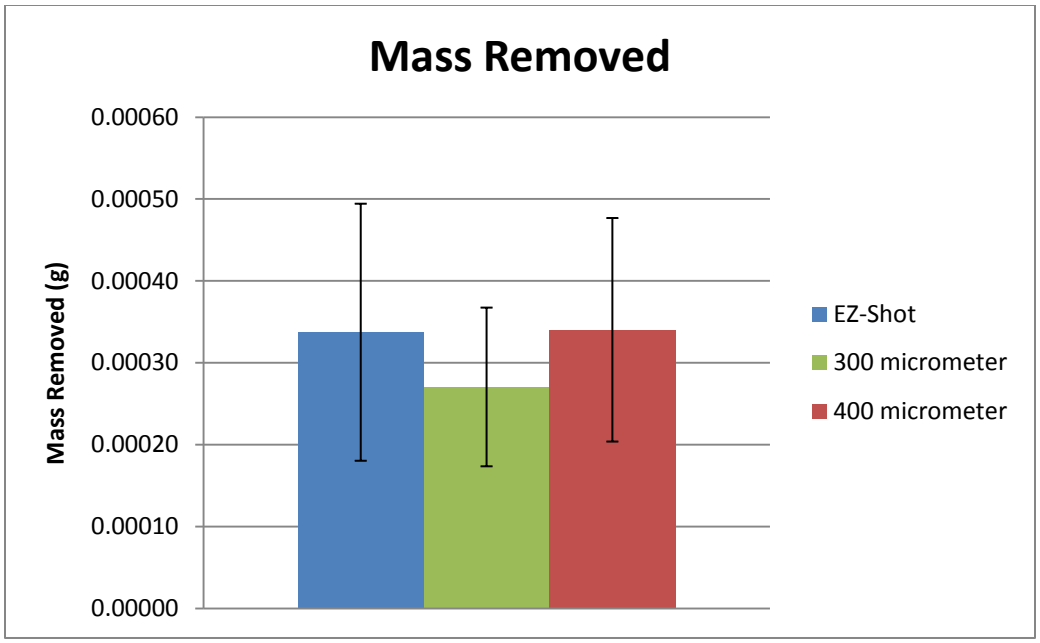

Figure 3-1 Average mass removed for EZ-Shot and meso-scale prototypes

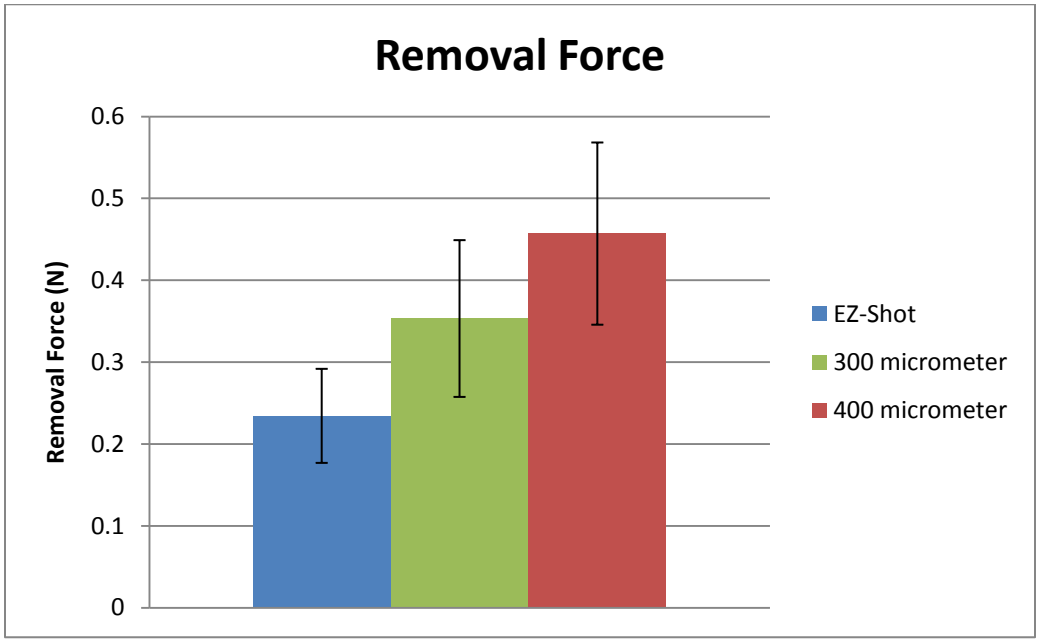

Figure 3-2 Average removal force for EZ-Shot and meso-scale prototypes

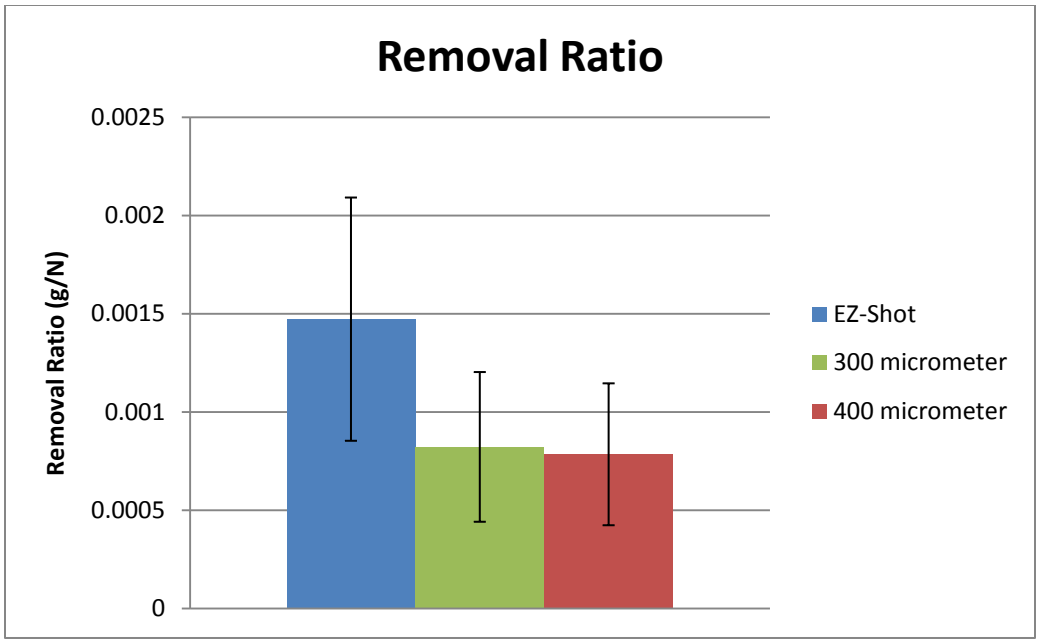

Figure 3-3 Average mass removed to removal force ratio for EZ-Shot and meso-scale prototypes

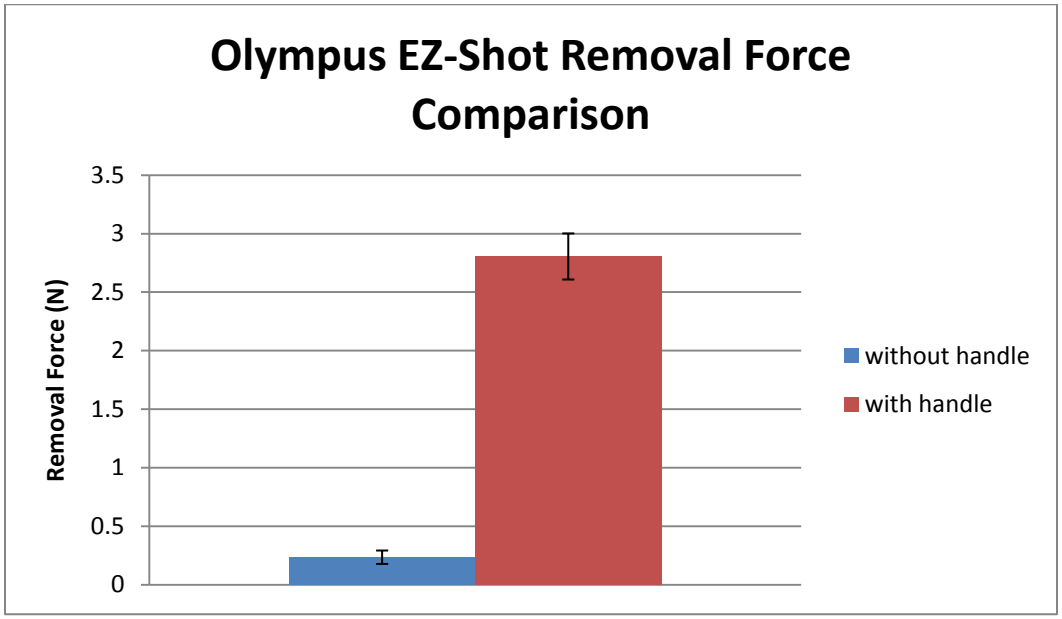

Figure 3-4 Average removal force for EZ-Shot with and without actuating handle

The data presented in this chapter will be analyzed and discussed in Chapter 4 and Chapter 5.

Chapter 4

Discussion

This chapter analyzes the results from Chapter 3. First, the Significance section discusses the meaningfulness of the results. Then, the Research Contributions section presents the deliverables of this research which help to advance the field of NOTES.

Interpretation

Interpretation of the results will begin with a comparison between the two prototype needle thicknesses and the Olympus EZ-Shot. Next, an analysis of mass removed/removal force between the 2-dimensional prototype needle thicknesses is presented. Finally, the friction force incurred through use of the actuating handle of the Olympus EZ-Shot is quantified based on the data presented in Chapter 3.

Figure 3-1 shows that the Olympus EZ-Shot and the 400 micrometer thickness needle removed a similar average mass which was larger than the average mass removed by the 300 micrometer thickness needle. However, Figure 3-2 shows that the EZ-Shot required the lowest average removal force, making it appear to be the preferred design. However, the error bars show significant scatter in the data. As a result, even though the EZ-Shot appears to be the "better" choice, this cannot be said definitively based on the results presented in this thesis.

It should also be noted that two of the fifteen test trials completed with the Olympus EZ-Shot returned no mass. These tests were omitted from the results as outliers in order to provide a more meaningful performance comparison between the EZ-Shot and the prototype needles, but they certainly demonstrate the potential unreliability of the current instrumentation and the

strong need for improvement. Tests with no mass removal were not an issue for the 2-dimensional prototype needle at either tested thickness.

Additionally, it was observed that the Olympus EZ-Shot removed fairly large volumes of liquid mass from the apple in addition to pulp mass by use of its aspiration mechanism. Though attempts were made to remove this excess liquid manually using absorbent cloth, it was impossible to remove it in its entirety without altering the pulp mass. In the testing of the prototype needles, excessive liquid mass removal was not observed. As a result, the mass removed data using the EZ-Shot could be skewed higher than actual mass removed due to this extraneous liquid mass.

Statistical analysis using a t-test showed that the 400 micrometer thick needle required a significantly greater removal force than the 300 micrometer needle (p value=1.30E-7). However, the 400 micrometer thick needle also removed significantly more mass than the 300 micrometer needle (p value=8.22E-4). Interestingly, the mass removed to removal force applied ratio between the two needles was determined to be not statistically different (p value=0.290).

The average mass removed for both prototype thicknesses was not statistically significant compared to the EZ-Shot (p value=0.067 and 0.473 for 300 and 400 micrometer thickness needles, respectively), but both required a significantly larger removal force (p value=1.381E-18 and 9.627E-19 for 300 and 400 micrometer thickness needles, respectively). As a result of these larger average removal forces, the mass removed to removal force ratio was also significantly lower for both prototype needle thicknesses (p value=1.348E-10 and 1.345E-10 for 300 and 400 micrometer thickness needles, respectively).

Niebel et al showed that the EZ-Shot removed more mass than the prototype needle but required a much higher removal force (the mass removed to force applied ratio for the prototype

needle was actually slightly higher) [25]. The only meaningful discrepancy between these results and the results presented in this thesis is in the EZ-Shot removal force data, which Niebel et al found to be much larger than presented in this research. This is likely due to the suggested explanation by Niebel et al that the suction required to operate the EZ-Shot could be responsible for an increase in removal force [25]. In contrast, the test protocol presented in Chapter 2 of this thesis removes the suction before the needle is removed from the sample in order to prevent mass from being suctioned higher up into the needle length. Therefore, any increases in removal force due to suction are eliminated.

One explanation of the lower mass removal measurements for the prototype needles is error in experimentation and modeling. Because the apple testing sample chosen has a high liquid content, the Olympus EZ-Shot aspirates liquid mass into the hollow needle in addition to solid mass. It was observed that this liquid more than doubled the "mass removal" measurement, so efforts were made to remove as much of the excess liquid as possible. However, it is still possible that EZ-Shot mass removal measurements are higher than they should be. Another possible explanation is the previously mentioned omission of two EZ-Shot tests that did not remove any mass at all and would certainly lower the average mass removed if included in the EZ-Shot data.

The quantification of the friction force in the actuating handle of the EZ-Shot was more definitive. Standard deviations, as shown in Figure 3-4, were much smaller. As reported in Table 3-22, the average removal force required without use of the actuating handle was 0.234 +/- 0.057 N and the average removal force required with use of the actuating handle was 2.804 +/- 0.197 N (mean plus or minus one standard deviation). This can also be seen graphically in

Figure 3-4. If the friction force, F_f, is defined as F_{handle}-$F_{nohandle}$, the following can be used to quantify the friction force through propagation of error technique:

$$F_f = (F_{handle} - F_{nohandle}) \pm \sigma_{F_f}$$

$$\sigma_{F_f} = \sqrt{\left(\frac{\delta F_f}{\delta F_{handle}}\right)^2 {\sigma_{F_{handle}}}^2 + \left(\frac{\delta F_f}{\delta F_{nohandle}}\right)^2 {\sigma_{F_{nohandle}}}^2}$$

$$\sigma_{F_f} = \sqrt{{\sigma_{F_{handle}}}^2 + {\sigma_{F_{nohandle}}}^2} = \sqrt{0.197^2 + 0.057^2} = 0.205\ N$$

Therefore, the average friction force can be quantified as 2.570 +/- 0.205 N.

Research Contributions

Each of the three objectives completed through the research documented in this thesis makes a contribution to the field of device design for NOTES. First, the developed test protocol for the Olympus EZ-Shot can serve as a starting point for further comparison testing between the EZ-Shot and current or future needle prototypes. It provides a baseline upon which future testing can be built and a superior endoscopic biopsy needle can emerge.

The second completed objective, application of the developed test protocol to compare the performance of the EZ-Shot to the performance of the 2-dimensional prototype needles, shows that, although some results were not significant, there is viability in the 2-dimensional endoscopic biopsy needle design presented in Chapter 2 of this thesis if a lower moisture, more uniform sample is chosen and further testing is performed in which the excess liquid mass removed using the EZ-Shot is eliminated. Though the removal force required by both prototype needles was significantly larger than the removal force required by the Olympus EZ-Shot, a

sample change with more accurate test results could "justify" this increase in force with a larger and more consistent removed mass than the EZ-Shot can provide.

If another test sample with less free liquid is used instead of an apple, it is possible that the average mass removed by the Olympus EZ-Shot will decrease significantly and show that the larger removal force for the prototypes is "justified" by more mass removed. Testing with another, lower moisture sample would provide a much better comparison between the Olympus EZ-Shot and the prototype needles because it would make the EZ-Shot data more representative of actual mass removed as opposed to solid mass removed plus liquid mass removed. To test this idea, preliminary tests were done on a raw chicken breast, as shown in Table 4-1.

Table 4-1 Mass Removal Tests on a Raw Chicken Breast

Test #	Mass Removed— Olympus EZ-Shot (g)	Starting Mass— 300/400 micrometer needle (g)	Final Mass— 300/400 micrometer needle (g)	Mass Removed— 300/400 micrometer needle (g)
1	0.00011	3.62575/3.82601	3.62584/3.82622	0.00009/0.00021
2	0.00015	3.62575/3.82601	3.62585/3.82625	0.00010/0.00024
3	0.00017	3.62575/3.82603	3.62589/3.82621	0.00014/0.00018
4	0.00011	3.62576/3.82601	3.62584/3.82624	0.00008/0.00023
5	0.00016	3.62576/3.82601	3.62592/3.82621	0.00016/0.00020
AVG	0.00014	--	--	0.00011/0.00021

Small amounts of extra liquid were still observed when the EZ-Shot was used to test on the raw chicken breasts, but the liquid was in the form of small droplets instead of "pools" and seemed to have much less effect on the mass removed measurement. More tests should be completed in the future to verify these results, but preliminary analysis shows that the 400 micrometer needle removed a 33% higher average mass than the EZ-Shot, presenting the possibility for a highly effective design if the larger removal force is medically acceptable.

It was also determined after testing that the needle manufacturing process is unable to make needles of exactly 300 and 400 micrometers due to shrinking during cooling and slightly non-uniform mold shapes; this may have also contributed to the error in the data. Therefore, actual needle thicknesses were measured and compared to the average mass removed measurements to see if a stronger correlation could be observed based on actual as opposed to theoretical needle thicknesses (Table 4-2). The data is plotted graphically in Figure 4-1 and shows that the data exhibits an 84% fit to an increasing linear relationship, proving that larger needle thicknesses do indeed remove more mass.

Table 4-2 Average Mass Removed vs. Actual Needle Thickness Data

Needle	Average Mass Removed (g)	Actual Needle Thickness (micrometers)
300-1	0.00030	290
300-2	0.00020	220
300-3	0.00029	260
300-4	0.00030	240
400-1	0.00027	350
400-2	0.00026	310
400-3	0.00039	390
400-4	0.00044	420

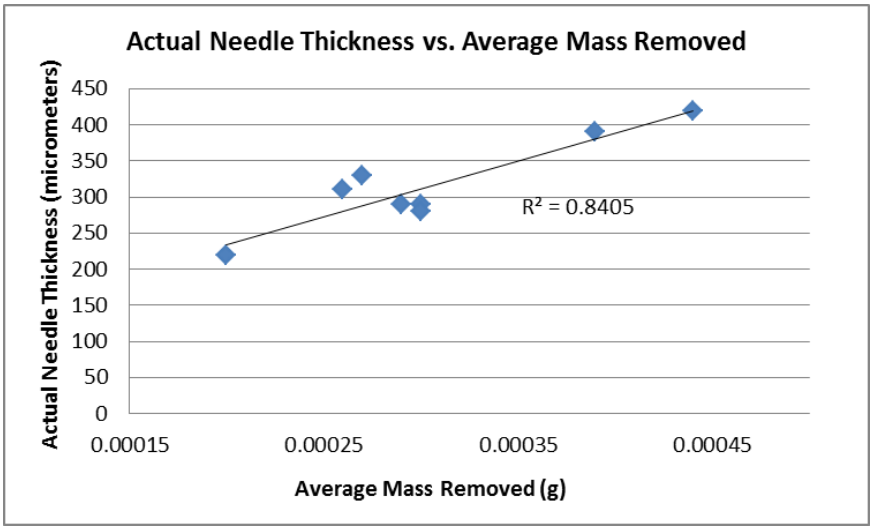

Figure 4-1 Average needle thickness plotted against average mass removed

The third objective to determine the effect of needle thickness on removal force and average mass removed showed that the 400 micrometer thickness needle removes a significantly larger mass than the 300 micrometer thickness needle, but at the price of a significantly larger removal force. Interestingly, the mass removed to removal force ratios for both thicknesses were unable to be categorized as statistically different. Therefore, across these small differences in needle thickness, the trend shows that an incremental change in needle thickness leads to proportional gains in both removal force and mass removed. Since the prototype needle removes mass over the area exposed to the sample, it makes sense that an even thicker needle would continue the trend of removing more mass with a higher force, as suggested by the data in this chapter. If a maximum allowable removal force during endoscopic biopsy procedures could be determined and agreed upon by medical doctors, the value could be used as a design constraint and the needle thickness could be designed to remove the most mass at the highest allowable force.

Success within each of these objectives will bring NOTES biopsy procedures closer to widespread implementation. If these remaining needs are addressed in the future, this 2-dimensional needle design could potentially fill the medical need for a superior endoscopic biopsy needle. A 3-dimensional design would likely be more effective than the 2-dimensional design if manufacturability limitations on such a small scale could be overcome. However, one possible compromise between a full 3-dimensional needle and the 2-dimensional needle tested in this research would be a 2-dimensional needle similar to the one tested in this thesis only bent slightly over its length to allow for a supplemental “scooping” mechanism.

Chapter 5

Conclusions

This chapter first reflects upon this thesis research in its entirety with a Summary section. Next, the Additional Research section presents possible realms for research in the future based on the results presented in this thesis.

The relatively recent development of minimally invasive surgery (MIS) has shown significant reductions in risk of infection, heavy bleeding, tissue damage, and healing times post-surgery in comparison to traditional open surgical techniques. Because of these advantages of MIS over open surgery, research focused on MIS procedures across a broader range of medical procedures has increased in recent years.

One development of MIS in progress is that of natural orifice transluminal endoscopic surgery, or NOTES. NOTES procedures are conducted through the use of a flexible endoscope, which is inserted through natural orifices. Various accessories, such as forceps, lights, biopsy needles, cauterizing tools, scissors, and cameras assist the surgeon during surgical procedures through endoscopic accessory channels.

Research in the field of NOTES has expanded future possibilities for MIS, but improvements need to be made to accessory instruments in order to make NOTES easier and more reliable in the operating room. Endoscopic biopsy needles are no exception to these instrumental limitations. There remains a need for a superior biopsy needle that can be used through an endoscope to perform non-invasive biopsy procedures. The Olympus EZ-Shot Test Protocol developed in this thesis can be used to benchmark future designs against a commercially available product.

In addition to developing the Olympus EZ-Shot test protocol, this research also involved testing a new 2-dimensional endoscopic biopsy needle being developed at The Pennsylvania State University. This was accomplished by using an apple as a testing sample and recording 15 trials for each prototype (four prototype needles at both 300 and 400 micrometer thickness—a total of 60 trials per thickness) and 15 trials for the Olympus EZ-Shot. In each trial, mass removed and removal force required were measured and used to calculate the mass removed to removal force required ratio. This data can be used to improve future testing procedures or future 2-dimensional endoscopic biopsy needle prototype designs.

Summary

Overall, the research and testing presented in this thesis could be beneficial in propelling the field of NOTES forward. The development of an Olympus EZ-Shot Test Protocol will improve further comparison testing objectives by providing a strict baseline upon which additional comparisons can be built. As such, this task, noted in this thesis as the first objective, was successful and should require few to no alterations in the future.

In relation to the second and third objectives of comparing the 2-dimensional prototype needles to the EZ-Shot and determining the effect of needle thickness on removal force and mass removed, some changes should be made to the testing materials and methods in order to obtain more accurate data. While the results presented in this thesis do show potential for the prototype needle design, there was significant scatter in the data. The scatter is likely due to varying density and/or moisture levels in different areas of the apple testing sample and could be reduced by choosing another, more uniform testing sample with a lower moisture content. The scatter

could also be due to non-uniform needle thickness. Uniformity of needle thickness would help eliminate variations across the thickness range, and a lower moisture content sample would prevent the EZ-Shot data from being skewed due to aspiration of liquid mass in addition to solid pulp mass.

It would be helpful for prototype instrument design purposes if a maximum allowable removal force design parameter was developed either through further testing or expert opinion from medical professionals. Prototype testing between 300 and 400 micrometer thickness needles demonstrated a relationship in which increases in thickness led to proportional increases in both mass removed and removal force applied, keeping the ratio between the two nearly constant. If further testing could verify that this relationship occurs over larger ranges of prototype needle thicknesses, a maximum removal force design parameter would allow the design team to create a prototype needle that can remove the maximum mass while remaining within design constraints.

Though the scatter in the current data prevents the prototype needle from being defined as "better" or "worse" than the EZ-Shot, the relative success of the prototype needles certainly supports further testing. If the changes presented in this section are made, the prototype needle could prove to be very useful during NOTES biopsies by removing more mass than commercially available needles and maximizing the chances that a single biopsy attempt would be sufficient to confirm or disprove the presence of cancer.

Additional Research

The research presented in this thesis presents definite opportunities for additional research. In relation to the first and second objectives, one such opportunity would be to use the test protocol and methods presented in Chapter 2 to carry out further comparative testing using a different testing sample. The preliminary tests from Chapter 4 of this thesis suggest a sample with lower moisture and more uniform structure, such as raw meat. Possible design alterations for the prototype might also be worth considering. Perhaps a similar needle design that could also perform a "scooping" mechanism to remove mass would be more effective in removing larger masses. Ideally, a 3-dimensional design should also be tested, but manufacturing constraints on such a small scale may make that difficult.

Further research related to the third objective of determining the effect of needle thickness on removal force and mass removed was introduced in the Research Contributions section. As mentioned, testing of 2-dimensional prototype needles over a wider range of thicknesses could be done to see if the mass removed to removal force ratio remains relatively constant over a larger range of needle thicknesses than tested in this thesis for design purposes. If this could be determined, a design constraint for the maximum allowable removal force of the 2-dimensional biopsy needle could be dictated.

As previously mentioned in Chapter 1, NOTES procedures (including the endoscopic biopsy procedures at the center of this research) offer significant gains over traditional surgical techniques, including reduced scarring, recovery time, patient discomfort, and bleeding. If this research is continued and completed, current instrumental limitations in the area of endoscopic biopsy needles will be greatly reduced. More importantly, NOTES will be one step closer to replacing traditional, more risky surgical options and improving the lives of patients everywhere.

Appendix

Table A-1 Needle 300-1 Starting and Final Mass Measurements

Test #	Starting Mass (g)	Final Mass (g)
1	3.62575	3.62610
2	3.62575	3.62600
3	3.62577	3.62595
4	3.62575	3.62594
5	3.62577	3.62601
6	3.62555	3.62570
7	3.62575	3.62613
8	3.62562	3.62602
9	3.62574	3.62604
10	3.62566	3.62597
11	3.62572	3.62605
12	3.62567	3.62616
13	3.62582	3.62619
14	3.62579	3.62613
15	3.62579	3.62597

Table A-2 Needle 300-2 Starting and Final Mass Measurements

Test #	Starting Mass (g)	Final Mass (g)
1	3.76843	3.76864
2	3.76865	3.76870
3	3.76850	3.76865
4	3.76855	3.76867
5	3.76838	3.76863
6	3.76845	3.76853
7	3.76836	3.76867
8	3.76833	3.76855
9	3.76831	3.76853
10	3.76851	3.76877
11	3.76850	3.76863
12	3.76860	3.76876
13	3.76849	3.76872
14	3.76837	3.76880
15	3.76866	3.76882

Table A-3 Needle 300-3 Starting and Final Mass Measurements

Test #	Starting Mass (g)	Final Mass (g)
1	3.71735	3.71766
2	3.71741	3.71761
3	3.71742	3.71780
4	3.71742	3.71774
5	3.71742	3.71775
6	3.71744	3.71768
7	3.71758	3.71801
8	3.71750	3.71776
9	3.71736	3.71766
10	3.71740	3.71756
11	3.71742	3.71777
12	3.71751	3.71781
13	3.71751	3.71763
14	3.71746	3.71772
15	3.71754	3.71785

Table A-4 Needle 300-4 Starting and Final Mass Measurements

Test #	Starting Mass (g)	Final Mass (g)
1	3.61862	3.61901
2	3.61869	3.61901
3	3.61882	3.61912
4	3.61912	3.61952
5	3.61912	3.61934
6	3.61914	3.61944
7	3.61893	3.61936
8	3.61898	3.61918
9	3.61892	3.61926
10	3.61897	3.61934
11	3.61907	3.61933
12	3.61914	3.61932
13	3.61911	3.61936
14	3.61909	3.61927
15	3.61899	3.61937

Table A-5 Needle 400-1 Starting and Final Mass Measurements

Test #	Starting Mass (g)	Final Mass (g)
1	3.82606	3.82662
2	3.82630	3.82682
3	3.82624	3.82647
4	3.82613	3.82653
5	3.82625	3.82693
6	3.82630	3.82644
7	3.82608	3.82627
8	3.82602	3.82622
9	3.82598	3.82622
10	3.82594	3.82602
11	3.82601	3.82615
12	3.82594	3.82622
13	3.82594	3.82607
14	3.82594	3.82606
15	3.82594	3.82614

Table A-6 Needle 400-2 Starting and Final Mass Measurements

Test #	Starting Mass (g)	Final Mass (g)
1	3.59248	3.59270
2	3.59242	3.59284
3	3.59252	3.59289
4	3.59254	3.59291
5	3.59254	3.59287
6	3.59251	3.59284
7	3.59252	3.59276
8	3.59260	3.59280
9	3.59251	3.59272
10	3.59256	3.59272
11	3.59255	3.59272
12	3.59255	3.59271
13	3.59254	3.59282
14	3.59256	3.59279
15	3.59254	3.59279

Table A-7 Needle 400-3 Starting and Final Mass Measurements

Test #	Starting Mass (g)	Final Mass (g)
1	3.67735	3.67773
2	3.67756	3.67795
3	3.67710	3.67756
4	3.67784	3.67822
5	3.67788	3.67828
6	3.67786	3.67825
7	3.67754	3.67787
8	3.67751	3.67788
9	3.67733	3.67765
10	3.67720	3.67764
11	3.67729	3.67759
12	3.67731	3.67774
13	3.67750	3.67787
14	3.67733	3.67770
15	3.67737	3.67783

Table A-8 Needle 400-4 Starting and Final Mass Measurements

Test #	Starting Mass (g)	Final Mass (g)
1	3.65034	3.65079
2	3.65042	3.65094
3	3.65054	3.65088
4	3.65027	3.65074
5	3.65026	3.65077
6	3.65046	3.65088
7	3.65012	3.65076
8	3.65004	3.65064
9	3.65004	3.65055
10	3.65036	3.65078
11	3.65058	3.65101
12	3.65054	3.65085
13	3.65024	3.65067
14	3.65014	3.65036
15	3.65027	3.65058

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ACADEMIC VITA

Melissa C. Buydash

Melissa C. Buydash
516 Pinkerton Run Road
Oakdale, PA 15071
mcb5175@gmail.com

Education: Bachelor of Science Degree in Mechanical Engineering, Penn State University, Spring 2011
Minor in Bioengineering
Honors in Mechanical Engineering
Thesis Title: Evaluation of a Novel NOTES Endoscopic Biopsy Needle
Thesis Supervisor: Dr. Mary Frecker

Awards: President's Freshman Award
President Sparks Award
Dean's List (All Enrolled Semesters)
Miller G Mechanical Engineering Scholarship
Wilcox Arthur Memorial Award in Mechanical Engineering
NSF GRFP Fellow
FE/EIT Certification

Activities: American Society of Mechanical Engineers (Student Chapter)
Penn State University Campus Band
Engineering House Mentor
Tutor (Mathematics) at State College High School