Radiologic Pathologic Correlation in Renal Cell Carcinoma

BME 400 Design
December 13th, 2023

Client: Dr. Meghan Lubner
Department of Radiology
UW School of Medicine and Public Health

Advisor: Dr. Tracy Puccinelli
University of Wisconsin-Madison
Department of Biomedical Engineering

Team:
Team Leader: Ellie Steger
Communicator: Erin Schlegel
BSAC: Aleks Skutnik
BWIG: Emily Wheat
BPAG: Olivia Jaekle

ABSTRACT

Radiologic-pathologic correlation is a promising technique employing Computed Tomography Texture Analysis (CTTA) to establish connections between observed patterns in Computed Tomography (CT) images and histologic tumor patterns. This innovative technology holds the potential to enhance the accuracy and timeliness of cancer diagnosis and recurrence prediction, ultimately influencing disease-free survival (DFS) outcomes for patients [1]. However, achieving success requires further validation of pathological tissue features obtained through CTTA. Therefore, it is necessary to gather additional data to precisely correlate histologic patterns with markings identified in CT images. The current project involves taking over a previous group's device, consisting of a FormLabs coring tube and a stainless steel blade. The initial design aimed to assist pathologists in resecting kidney tumors, directly correlating findings with CT images [2]. Unfortunately, the current design proves impractical as the steel blade induces excessive tissue trauma to the surrounding site, making the remaining tumor indiscernible. In response to this challenge, our team aims to improve upon both blade design and coring device. This report outlines the team's preliminary designs for an alternative blade and coring tube, with the goal of identifying two "winning" designs through comprehensive design matrices. Subsequently, we will fabricate the selected designs and implement testing protocols to ensure the validity and effectiveness of the new blade prototype, with further plans to test the coring device in the coming semester. All together, we will work towards assembling a device to effectively resect a tissue sample with minimal damage to the surrounding renal cell carcinoma.

TABLE OF CONTENTS

I. INTRODUCTION

1.1 Motivation and Global Impact

In the United States, there are approximately 65,000 new cases and almost 15,000 deaths from renal cell carcinoma (RCC) each year [4]. Not only does it affect a wide range of individuals, but kidney cancer is almost two times more prevalent in men than it is in women [4]. Because of this, it is crucial that the diagnosis process is as efficient as possible. The only possibility of long term survival of RCC involves surgical intervention, especially when detected during early stage progression via Computed Tomography (CT) imaging. A nephrectomy of the diseased kidneys is performed and samples of the tumor are then biopsied from the resected kidney [5].

Computer tomography texture analysis (CTTA) is used to quantitatively analyze tumor heterogeneity via pixel distribution, location, and relationships [6]. This imaging technique is especially useful in diagnosing and estimating prognosis of RCC. It is a promising technology for the management of cancer metastases and predicting treatment response [7]. Due to the complex spatial heterogeneity and histologically diverse nature of renal tumors, producing an accurate image analysis is challenging for physicians. These characteristics pose complications when performing biopsies on larger tumors because of the various types of cells dispersed throughout the mass [8]. CT texture analysis allows for slice-by-slice imaging of the tumor, which may help differentiate between different types of renal cell cancers, therefore improving individualized treatment and contributing to better prognosis [7].

1.2 Existing Devices and Current Designs

The current method to collect RCC biopsies involves the CT imaging of the patient's kidney to create a spatial rendering of the kidney and tumor dimensions. The previous team produced a 3D printed acrylic box to accommodate the patient specific dimensions, which holds the kidney once it is surgically resected (Figure 1). The coring device, with a stainless steel circular blade attached, is then inserted into the top of the box to collect tissue samples (Figure 2). Though this device is effective, the stainless steel blade that is attached to the end of the coring device is too thick and not sharp enough, therefore causing substantial trauma to the surrounding tissue (Figure 3). Without precise biopsy cuts, it is difficult to keep track of the specific locations of biopsy sites. Because of this, the coring device is unusable and needs to be paired with a better suited blade.

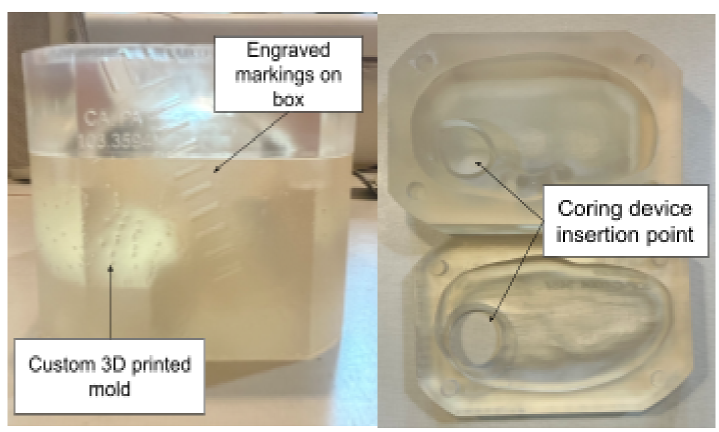


Figure 1: 3D printed acrylic box of patients kidney with tumor.

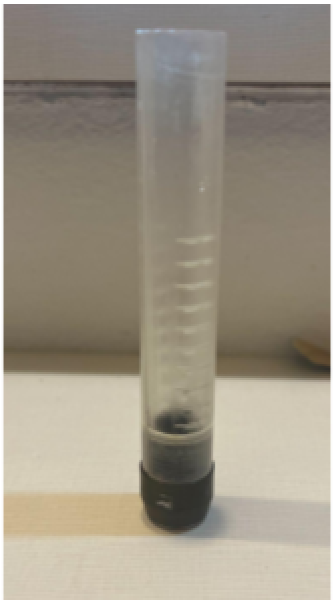


Figure 2: *Current coring device prototype with a FormLabs plastic tube 10.03cm in length and 1.74cm outer diameter with the 304 stainless steel blade attachment.*

Figure 3*: Previous group's prototype of the stainless steel blade with a 1.59cm outer diameter.*

An existing and well-known device in the realm of biopsies is the skin punch biopsy device. This device is a common tool used to conduct skin biopsies in order to diagnose various types of cancers (Figure 4) [9]. It is composed of a plastic tube and a sharp, cylindrical blade ranging from 0.5-6 mm in diameter. The device is used to collect samples of the affected tissue by pushing the cylindrical blade into the epidermis in a twisting motion, and then resending back up with the sample in the tube [10]. Though this device is extremely effective in performing skin biopsies, it is unable to penetrate deep enough into the tissue to appropriately sample RCC tumors due to the shape of its coring handle.

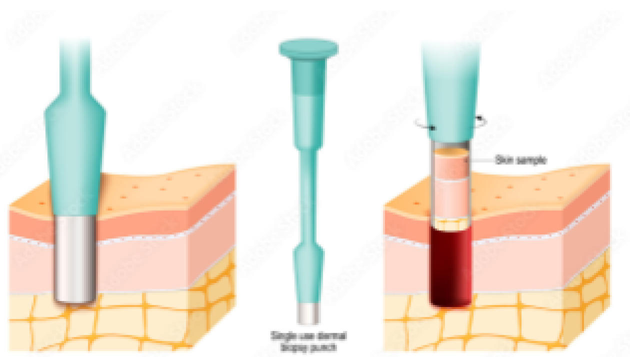


Figure 4: *An upclose depiction of a skin punch biopsy procedure. [9]*

1.3 Problem Statement

CT texture analysis is a useful tool in analyzing the heterogeneous profile of RCC tumors. The goal of this project is to validate the use of this analysis tool in the diagnosis and treatment planning of patients suffering from RCC. The patient specific, 3D printed box and coring device are advantageous at sectioning and delineating tumor samples for CT texture analysis, but the blade of the coring device is not practical to use in a clinical setting. To improve upon the previous team's successful design, this project will aim to develop a functional blade that will resect a tissue sample of 10 mm in diameter and keep the integrity of surrounding tissue by not letting any damage occur more than 3 mm away from the biopsy site. Additionally, the blade will be detachable from the coring device and will have an appropriate diameter to accommodate the large sample sizes needed to conduct RCC tumor biopsies.

II. BACKGROUND

2.1 Anatomy and physiology

Renal cell carcinoma is the most common type of kidney cancer, making up 85% of kidney cancer diagnosis [11]. Renal cell carcinomas develop inside the kidney's tubules and start off as a single group of cancer cells within one kidney. However, it can progress and later develop into multiple tumors in one or both kidneys [11]. While the risk of developing renal cell carcinomas increases with age, factors such as prior radiation exposure to the abdomen, family history, and lifestyle affect the development of kidney cancer [11].

There are more than 50 different types of renal cell carcinomas, with clear cell renal cell carcinoma (ccRCC) being the most common. These different types are classified into four different types based on their size, shape, and staining. Grades I-II are low and grades III-IV are high. High-grade tumors have increased invasive capacities and possibility of metastasis, and have a poorer prognosis [12].

CTTA is used to quantitatively analyze the spatial heterogeneity of tumors on CT images to improve the prognosis of patients [12]. Using a slice-by-slice tumor analysis technique, doctors can correlate specific tumor slices with histological findings. This more accurately depicts the gene expression and tissue types within the tumor by looking at smaller sections instead of the whole heterogeneous tumor.

Since computer tomography texture analysis is commonly used to study renal cell carcinomas, the goal of this project is to ensure the tumor samples and remaining kidney tissue remains intact with minimal damage in order to be imaged for further analysis and medical knowledge of renal cell carcinomas.

2.2 Client Information

The client for this project is Dr. Meghan Lubner, a pathologist who practices in Madison, Wisconsin. Dr. Lubner is associated with the School of Medicine and Public Health at the University of Wisconsin-Madison. Specifically, she is a professor of Radiology in the Abdominal Imaging Section and she has published many times on different oncologic imaging techniques [13].

2.3 Product Design Specifications

The blade must be reusable, easily detachable from the coring device tube, and easily sterilized in an autoclave. Since the blade will not be imaged, it does not need to be CT or magnetic resonance imaging (MRI) compatible as it will not create artifacts in the images. The client has specified the blade and coring device assembly must be able to resect a 10 mm diameter tumor sample while causing minimal tissue damage to preserve the integrity of the images. There is a tolerance for 3 mm of tissue trauma radiating from the intended cut. The final device should be ergonomically sound and comfortable for the pathologist to use. The blade should be long-lasting and able to withstand 40 resections while remaining sharp and efficient. The coring tube should form a tight seal with the blade. It should be 10-25 mm in diameter, should stay together while in use, and should create minimal tissue damage. It also must maintain a less than 3mm of tissue trauma radiating from the intended cut. Per the client's budget, the overall device should not be more than $500. The design specifications can be found in full under Appendix A: Product Design Specifications.

III. PRELIMINARY DESIGNS

3.1.1 Blade Design 1: Pineapple Corer

The team's initial design was accurately named the "Pineapple Corer" blade. The design inspiration came from household pineapple corers, which use small teeth and a twisting motion to remove the pineapple core. Similarly, the team's blade utilizes multiple rigid teeth that are 2 mm in height and line the circumference of the blade. The teeth are designed to grip and tear through multiple layers of tissue, allowing it to assume tumor depths as deep as 10cm. In tandem with the toothed edge of the blade, the design includes a rounded handle that will be 3D printed of PLA plastic to attach on the other side of the corer. The physician will use this handle to insert the assembly into the sample while simultaneously rotating the blade roughly 270 degrees through the thickness of the sample. This motion allows for the blade to effectively cut through the entirety of the tissue. The blade also employs a circular shape with a 11mm outer diameter and 10mm inner diameter. The shape of the blade intentionally allows for the cut of a 10mm diameter sample, which is the ideal size for the UW Health pathologist to observe the sample under a microscope. Finally, the blade will be made of surgical-grade stainless steel that is hardened to the Rockwell C hardness of about 46-53, as observed in the section J of the Product

Design Specifications (Appendix A).

Other notable components of the design include a lip that has a .05 cm difference in outer and inner diameters. This was designed so the blade can easily attach and detach to the previous team's FormLabs corer using a press-fit feel. This is an important function of the blade because it must be able to be sterilized in between uses in an autoclave as well as be disposed of when it becomes too dull.

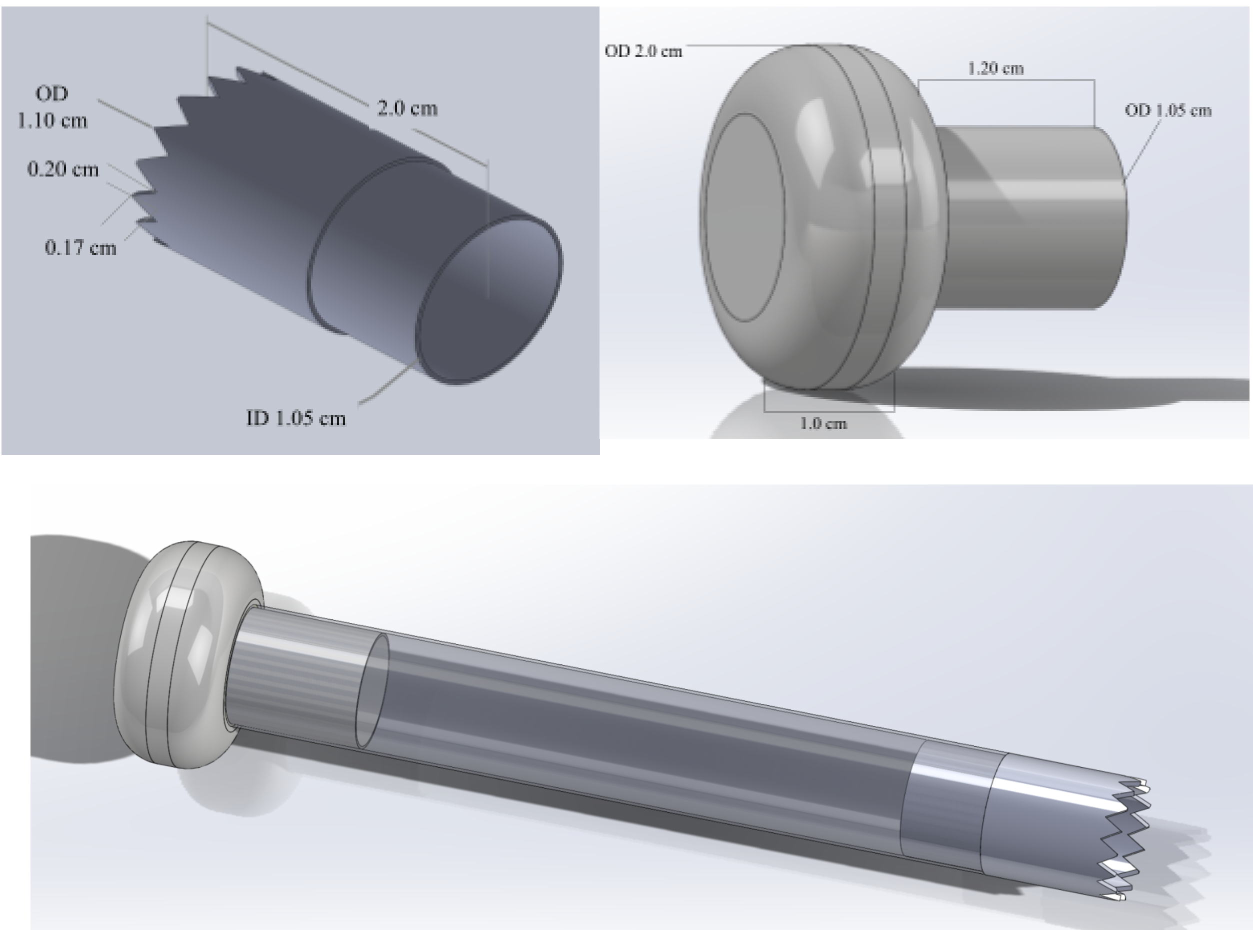


Figure 5: *SolidWorks Pineapple Corer Blade which includes toothed, rounded tip; SolidWorks of Pineapple Corer handle; Full Assembly of blade, tube, and handle.*

3.1.2 Blade Design 2: Recorder Blade

The second design the team considered was the "Recorder Blade". This idea embodied similar features to the first design, while also taking inspiration from current surgical blades. The blade included a lip with diameter of 10.5mm that would press-fit into the previous team's FormLabs corer. The blade will also be fabricated using a stainless steel material to mimic the hardness outlined by the Product Design Specifications (Appendix A).

However, the difference in this design lies in the edge of the recorder blade. The team wanted to mimic the side profile of a surgical scalpel in order to ensure a precise resection of the tissue. After much initial research, the team decided to create a concave blade with a pointed tip. This is because a pointed blade is typically used for "stabbing" and "precise" incisions [14]. Therefore this design allows for maximum pressure to be applied at the point of contact in order to effectively break the tissue and seamlessly resect a sample. Furthermore, the circular cross-section of the blade will acquire a sample within the client's size requirements of 10mm diameter.

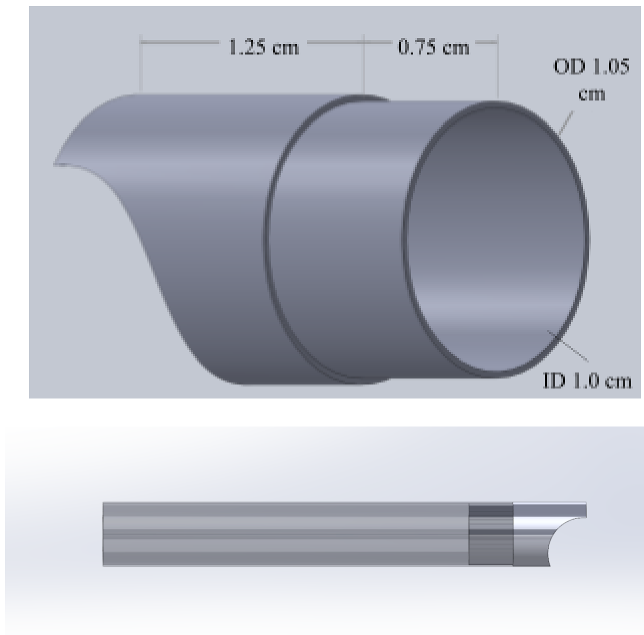
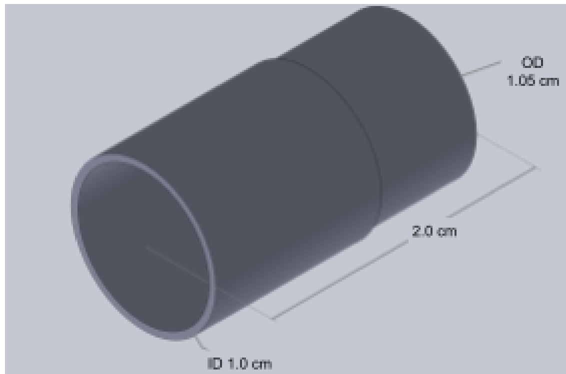


Figure 6: *SolidWorks of Recorder Blade which includes pointed pressure application at the tip; Full Assembly of blade and tube.*

3.1.3 Blade Design 3: Punch Biopsy Design

The team's third and final design was the most simplistic. The "Punch Biopsy" blade combined both the effort's of the previous team and a modern day punch biopsy. The prior group had designed a similar device, but received the feedback that the blade itself was much too blunt and caused too much damage to the tissue during sampling. To combat this, the team measured the thickness of the previous blade and reduced thickness by two-thirds in this design - effectively going from 1.651 mm to .55mm. This drastic drop in thickness will allow the blade to be much more precise in resecting a sample from the tissue. This precision will allow for less struggle during the resection and less surrounding tissue damage, maintaining the imagining integrity of the tumor.

Some components of the design are also similar to previous drawings. Characteristics such as the indent used to press-fit into the corer will utilize the same dimensions as previously mentioned (10.5mm ID and 10mm OD). The larger section of the blade will maintain a 11mm OD and 10mm ID. This blade will also be made of surgical-grade stainless steel that is hardened to the Rockwell C hardness of about 46-53, as observed in the Product Design Specifications.



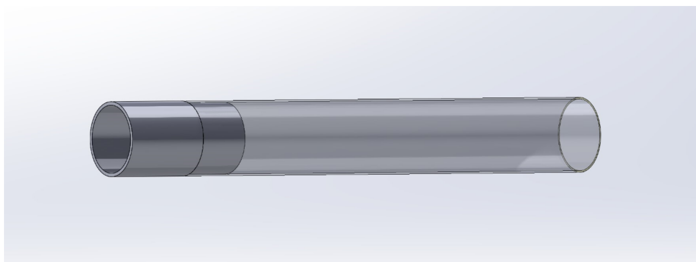


Figure 7: *SOLIDWORKS model punch biopsy which includes circular tip; Full assembly of blade and tube.*

3.2.1 Coring Device Design 1: Original Sliding Tube

The first idea analyzed was the previous team’s coring device which provides an L-shaped sliding tube design. This configuration consists of two halves that smoothly interlock, forming an L shape when viewed from above (see Figure 8). The distinctive step features on these halves, each measuring 0.15 cm in thickness, run along the side of the tube. The primary objective of this design is to facilitate the seamless integration of the two halves, allowing for the blade to effortlessly slide into the tube for a biopsy. While this tube design has proven effective in the past, a notable challenge emerged: the two halves were prone to separation when the blade was inserted.

It's worth noting that the sample tube possesses an inner diameter of 1.33cm, aligning flush with the dimensions of the previous blade. Consistent with our design approach, this tube, like all others in our project, will be 3D printed using FormLabs BioMed Clear resin, chosen for its biocompatibility and established track record in operating room applications. Ensuring consistency across our designs, each tube will maintain a length of 10cm.

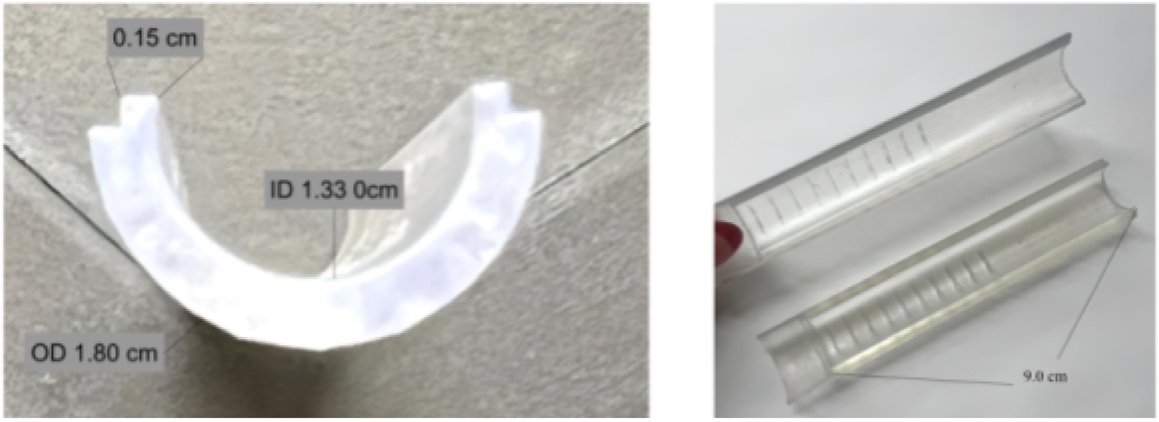


Figure 8 a-b: *Aerial view of one half of the L-Shaped Coring Biopsy Tube that was fabricated by the previous team with dimensions; Another view of the previous team's L-Shaped Coring Biopsy Tube with both halves.*

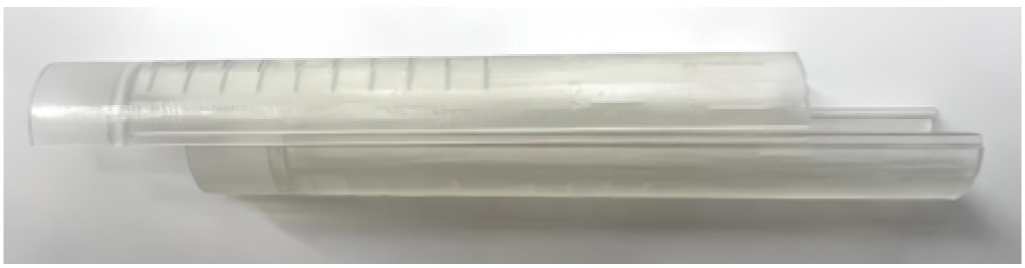


Figure 9: *The two halves of the L shaped sliding Coring Biopsy Design sliding together.*

3.2.2 Coring Device Design 2: Lego Clip Tube

The "Lego" clip coring biopsy device design is modeled after lego bricks. This design features one male and one female half. The female half has 6 holes spaced 1.25cm apart. The holes have a depth of 0.18cm and a diameter of 0.30cm. The male half of the tube has 6 corresponding pegs that fit into the female holes. These pegs have a diameter of 0.25cm and a height of 0.15cm. The pegs are .05cm smaller than the holes to account for the Stereolithography (SLA) 3D Printer tolerance and make sure that the two halves will fit together securely. The use of snaps provides a balance of stability and durability during the tube's insertion through the tumor, while also allowing for easy disassembly when removing the biopsy

The tube itself has a thickness of 0.32cm, maintaining a length of 10cm similar to the previous design. The inner diameter of 1.65cm ensures a secure attachment with the blade. Like our other designs, this lego-inspired tube will be 3D printed using FormLabs BioMed clear resin, chosen for its biocompatibility and suitability for surgical applications.

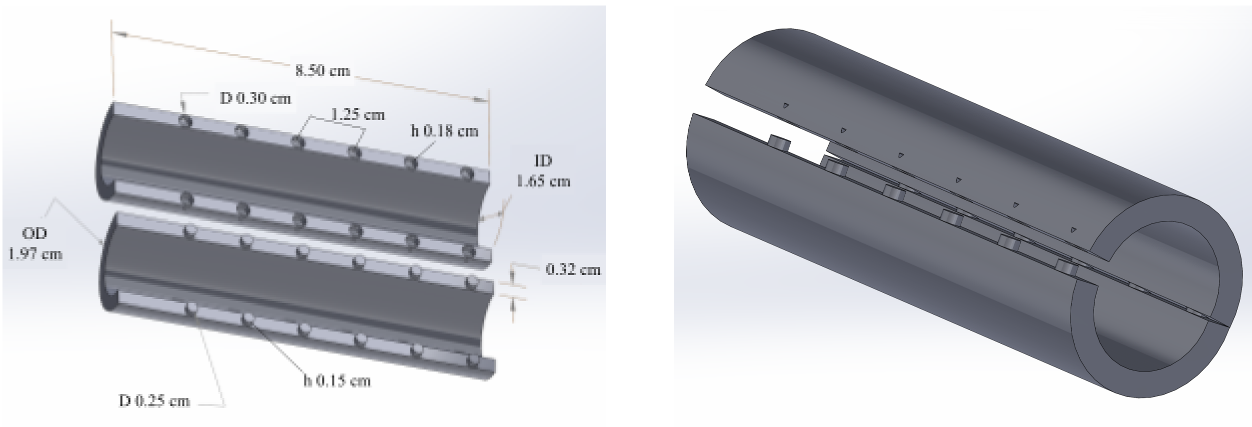


Figure 10 a-b: *SolidWorks of the male and female halves of the Lego Clip Coring Design with dimensions; Solidworks of the two halves of the Lego Design clipping together.*

3.2.3 Coring Device Design 3: Jigsaw Clip Tube

The "Jigsaw" tube design for the coring device features two cylindrical halves each with interlocking teeth. Each tooth was modeled after a cantilever snap joint which utilizes a flat side and jutted-out edge. These teeth fit into their corresponding outlines on the other half, with a .3mm tolerance gap, as is standard for most snap joints [15]. Furthermore, the corresponding length of each tooth and width was calculated using the Bayer design guide for snap-fit joints [15].

This tube has the same length as the previous design of 10cm. It also features the same inner diameter of 1.6cm for a secure attachment with the blade. This design will also be 3D printed in FormLabs BioMed clear resin.

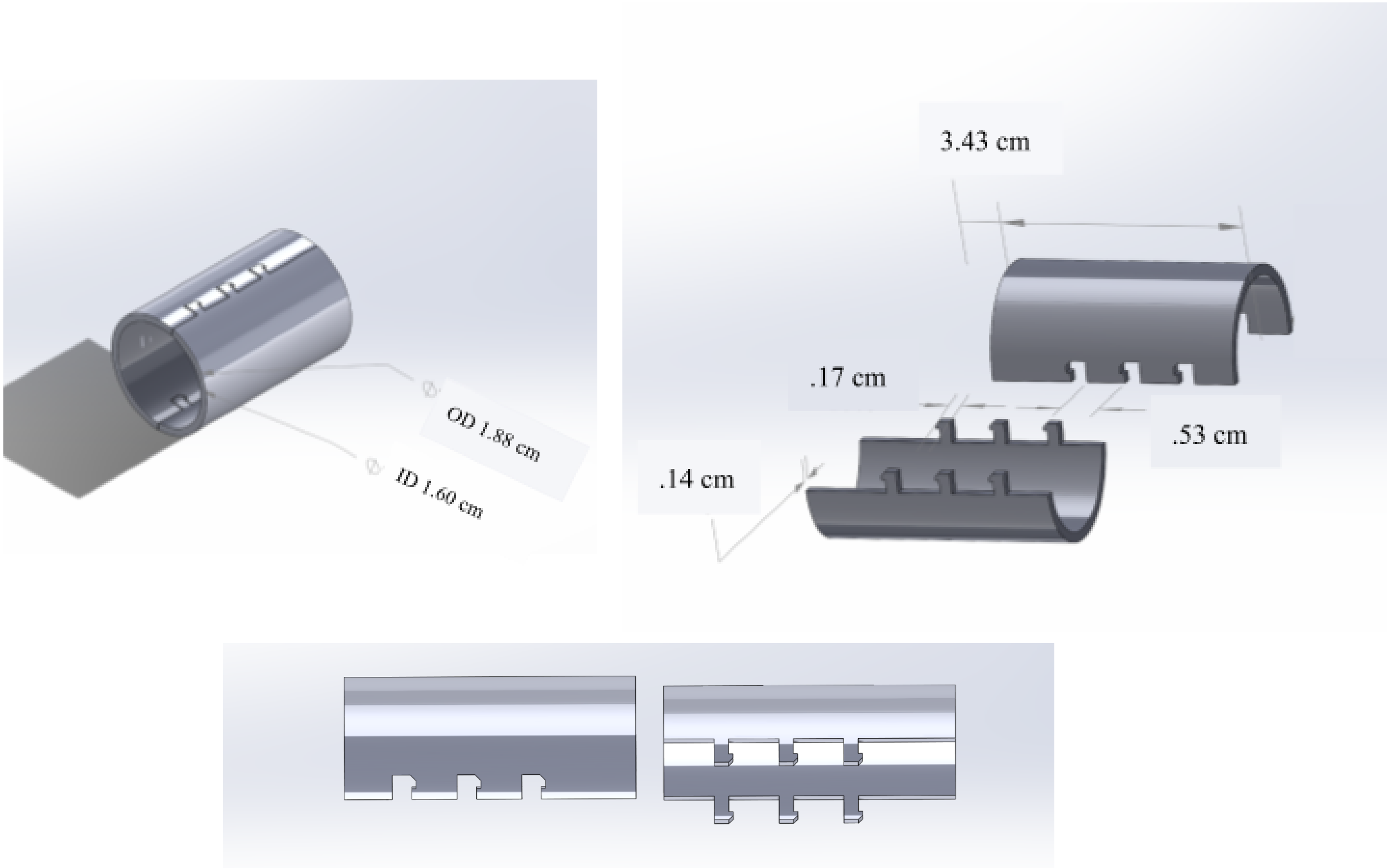
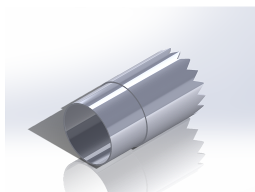
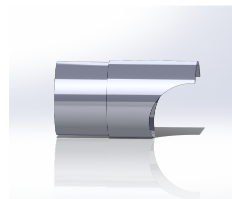
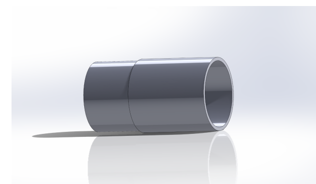


Figure 11 a-b-c: *SolidWorks of the "Lego" design as well as it's important dimensions.*

IV. PRELIMINARY DESIGN EVALUATION

4.1.1 Design Matrix for Renal Cell Carcinoma Blade

Table 1: *Design Matrix with all methods scored on precision, durability, feasibility, ease of use, and cost.*

Criteria	**Pineapple Corer**		**Recorder Blade**		**Punch Biopsy Blade**	
						
Precision (30)	2/5	12	4/5	24	5/5	30
Durability (20)	2/5	8	3/5	12	5/5	20
Feasibility (20)	3/5	12	3/5	12	4/5	16
Ease of Use (20)	5/5	20	4/5	16	4/5	16
Cost (10)	3/5	6	4/5	8	4/5	8
Score (100)	58		72		90	

4.1.2 Blade Design Matrix Scoring Criteria

Precision (30%) - Precision is a measurement of how much external tissue trauma the blade creates around the sample site. The trauma should not radiate more than 3mm in any direction off the circumference of the sample. Higher scores were assigned to designs that would cause the least amount of damage to surrounding tissue while lower scores indicate more predicted trauma.

Durability (20%) - Durability relates to how long the blade will last over the course of its lifetime. The blade must be able to effectively resect 40 samples, and be able to withstand an autoclave without losing its sharpness. Low scores were given the designs thought to dull quicker.

Feasibility (20%) - Fabrication of prototypes should not be difficult. Ideally, the prototypes should be created with resources easily accessible and not require too much finesse to manufacture. High scores are given to prototypes with more readily available resources and less complex fabrication processes.

Ease of use (20%) - Ease of use correlates to the ergonomics of the design, how easily it can detach from the core, how much pressure/strength the client needs to apply to the device, and a low procedure time (< 5 minutes). Higher scores indicate more of these requirements met than designs with lower scores.

Cost (10%) - The overall cost of fabricating the design holder prototype should be no more than $100. The team was given an overall budget of $500 but do not expect to exceed $100 for one individual prototype. Low scores indicate an expensive fabrication process , while high scores are more cost-effective designs.

4.1.3 Blade Final Design

After evaluating the "Pineapple Corer", "Recorder," and "Punch Biopsy" designs using the design matrix, the team chose to move forward with the "Punch Biopsy" blade design. This design scored the highest in four out of five criteria, including the three highest rated criteria. This is due to the simplistic cylindrical blade design.

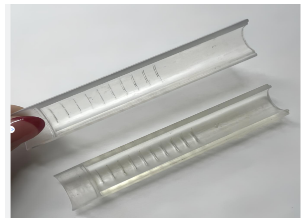
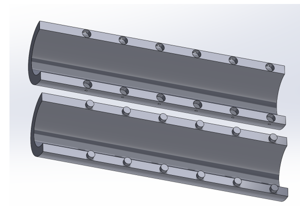
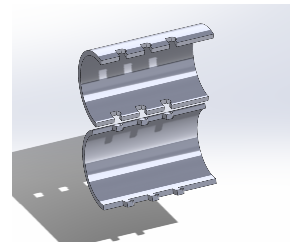
In contrast, the "Recorder Blade" and "Pineapple Corer" scored significantly lower in the Durability and Feasibility categories. This can be attributed to their more complex geometries. The teeth on the "Pineapple Corer" and arc in the "Recorder Blade" will be more difficult to fabricate due to their small intricacies. This will also cause these designs to be less durable. Additionally, their greater surface area makes them more susceptible to dulling over time and breakage.

The "Pineapple Corer" design scored highest in the ease of use category. This is due to its handle feature and bladed teeth that will grab into the tumor allowing the surgeon to easily twist through the tumor. However, this process causes excess trauma to the surrounding tumor tissue and makes the sample unusable.

Overall, the "Punch Biopsy" blade design excelled in three of the top categories: Precision, Durability, and Feasibility. Additionally, it scored the highest in terms of cost efficiency. This design is expected to offer high precision, minimizing trauma to surrounding tissue. This assumption is based on the knowledge of standard skin punch biopsy devices, which cause minimal to no trauma due to their extremely sharp-edged blades. Furthermore, the chosen design will be durable as it will be constructed from surgical-grade stainless steel, an autoclavable material widely recognized as a standard blade material. Its feasibility is also assured as cylindrical blades can be readily sourced from manufacturers, and their fabrication should not entail excessive time, effort, or production costs. Consequently, the winning design stands out as the most cost-effective option.

4.2.1 Design Matrix for Renal Cell Carcinoma Coring Device

Table 2: *Design Matrix with all methods scored on durability in the vertical direction, ease of separation, ease of fabrication, thickness, and cost.*

Criteria	**Original** 		**Lego** 		**Jigsaw** 	
Durability in Vertical Direction (30)	3/5	18	5/5	30	5/5	30
Ease of Separation (25)	4/5	20	5/5	25	2/5	10
Ease of Fabrication (20)	4/5	16	4/5	16	2/5	8
Thickness (15)	4/5	12	2/5	6	5/5	15
Cost (10)	5/5	10	4/5	8	3/5	6
Score (100)	76		85		69	

4.2.2 Coring Device Design Matrix Scoring Criteria

Durability in the Vertical Direction (30%) - This criterion emphasizes durability in the direction parallel to the vertical motion of a biopsy procedure (perpendicular to the procedure table). The paramount concern is preventing the coring device from slipping apart during biopsy operations, as observed with the previous prototype. Designs earning high scores demonstrate increased resistance to slipping, ensuring stability throughout the procedure.

Ease of Separation (25%) - This factor assesses how easily the sample can be extracted from the sample tube after imaging and sample resection. Maintaining the sample's integrity during removal is crucial for diagnostic accuracy. Designs receiving low scores are more likely to disturb the tissue sample during extraction, while those with high scores facilitate seamless and undisturbed sample removal.

Ease of Fabrication (20%) - Given that the coring biopsy sample tube will be reproduced for each procedure, efficient fabrication is essential. Prototypes should be easy to manufacture and replicate without requiring excessive skill. Designs with less complex geometries are favored, as they contribute to more straightforward and reliable 3D printing processes, resulting in higher scores.

Thickness (15%) - This aspect considers the thickness and dimensions of each prototype. A slim and narrow design is more cost efficient as well as reduces potential for tissue drag as the corer moves through the sample. Designs that are able to be scaled to thinner dimensions while maintaining functionality are favored and received higher scores.

Cost (10%) - The overall cost of fabricating the design holder prototype should not exceed $100. Although the team has a total budget of $500, the goal is to stay within the $100 limit for each individual prototype. Since the coring device is replaced after each use, cost-effectiveness in 3D printing is crucial. Low scores reflect expensive fabrication processes, while high scores indicate more economically viable designs.

4.2.3 Coring Device Final Design

After evaluating the "Original", "Lego", and "Jigsaw" designs, it was determined using the weighted criteria in the design matrix that the "Lego" design was the most suitable choice moving forward. This design scored highest in the top three categories, as it is an easy to print and durable model.

The alternative designs including the "Original" and "Jigsaw" had some major flaws that prevented their success. In particular, in the Durability in Vertical Direction category, the previous team's prototype, the "Original", scored the lowest score. This is because the sliding mechanism easily slips during procedural motions. Therefore, this design was not suitable. However, both the "Lego" and "Jigsaw" tubes have variations of teeth to stabilize the coring device when moving in the vertical direction, so they scored equally high.

In the second highest category, Ease of Separation, the "Original" and "Jigsaw" designs scored 4/5 and 2/5 respectively. The "Original" is easy to separate; however, it is hard to control during the separation process. Therefore, it scored less than the "Lego" which has a more controlled opening force, allowing for the pathologist to more easily protect the sample. The "Jigsaw" design scored lowest as it requires a lot of force to both open and close the device. This leaves potential to damage the sample inside the design is ill fitting.

In the next category, Ease of Fabrication, the "Jigsaw" scored the lowest with a 2/5. The "Jigsaw" design proved to be challenging to print as it required tolerance gaps as small as

0.3mm, while the SLA printers available in the UW-Makespace utilize a minimum of a 0.5mm tolerance. Therefore, this design is intricate and challenging to print.

Overall, the “Lego” design was the most simple and efficient design. It does not include any complex geometries or tolerances, allowing it to be almost universally 3D printed. It maintains durability during the biopsy procurement due to its peg and hole clasp. However, it still easily detaches to reveal the sample allowing for ease of use by the pathologist. It also maintains a relatively small budget to print, estimating around $10.00 by the UW-Makerspace. The one downside to its design is that it cannot easily be scaled down to a thinner model, as desired by the client. This is due to the pegs and holes located on the profile of each half. If the team were to make the thickness smaller, it would reduce the space for the holes and pegs to fit on. The team will have to overcome this challenge in the coming semester. However, in total, the “Lego” design prevailed as the best design to move forward with.

V. FABRICATION AND DEVELOPMENT PROCESS

5.1 Materials

The blade was fabricated out of 6ft long annealed 316 Stainless Steel tubing with an outer diameter (OD) of .625” and inner diameter (ID) of .585” (15.875mm OD x 14.859mm ID) and included a .02” wall thickness [16]. This will be a much thinner design at one-third the thickness of the previous team’s device. The chosen material is also in alignment with ASTM 269 specifications, allowing for .08% carbon content and therefore high resistance to corrosion [17]. The chosen material is also autoclavable and suitable for medical use. This steel has a Rockwell C hardness of 80, exceeding the hardness measurement specification of 46-53 as outlined in the team's Product Design Specifications (Appendix A)[18].

Furthermore, the coring device was 3D printed in FormLabs BioMed Clear Medical Resin [19]. This is a rigid, USP Class VI certified biocompatible material, with an ultimate tensile strength of 52 MPa and Young’s Modulus of 2080 MPa [19]. A strong resin was needed to uphold the durability specifications presented by the client. Full description of materials and budget can be found in Appendix B.

5.2 Methods

5.2.1 Blade Fabrication

Fabrication methods for the circular blade began with the acquisition of 316 stainless steel tubing. The exact dimensions of the tubing, as aforementioned, were determined by the specifications from our client to encompass a 10mm diameter sample from each cut. To begin, the 6ft length of tubing was cut into smaller 4 in sections using a pipe cutter. This required using a vice to clamp the tubing, being careful not to dent it. Then, the team rotated the pipe cutter in 4 full circles around the circumference of the tube until the tubing twisted off. This caused a slight lip going inwards.

After cutting a 4 inch section, a mark was made to indicate a 15 degree taper, which started at 1 inch from the edge of the tubing. In order to get this measurement, a protractor was used. Then the team used a Jet 6" x 48" Belt/12" Disc Sander and pressed the end of the blade gently against the sander, applying more pressure to the end of the tube. Once done, the blade was rotated at a constant speed 3 full times. After each group of 3, the end of the tube was dipped into a cup of water for 30 seconds to dissipate the heat created from the sander. This was continued until the taper reached the outline marked before sanding.

To account for any lips or denting to the shape of the circular blade, the team utilized a Model 100 High Speed Dremel Rotary tool. The beginning speed was 35,000 revolutions per minute and the dremel was placed on the inside of the blade for 10 second intervals until the desired shape was reached and the lip was minimized. The team repeated these steps for the desired amount of blades. For a more detailed fabrication plan please refer to the Appendix C.

5.2.2 Coring Device Fabrication

The “Lego” coring device was fabricated using 3D printing. The team modeled the device as one part in SolidWorks, measuring and dimensioning to the appropriate lengths. Once a tube was created, a reference plane was created in the middle of the tube. Then using the “Split” tool in SolidWorks, the piece was divided laterally into two equal halves which created an individual file for each half.

Then on one half, the team utilized the “Linear Pattern " tool in SolidWorks and created 6 circles, .3cm in diameter along the thickness of the tube. This process was replicated on the other side which made a total of 12 circle sketches, each 1.25 cm away from each other. Then, the team used the “Extruded Cut” tool and cut the circle sketches .18 cm into the device, which made the holes. On the other untouched half of the tube, a similar process was carried out. The team utilized the linear pattern to create and extrude .25cm diameter circles .15cm.

Each half was saved as both a .sldprt file and .stl file. Once saved, the team used Preform software to evaluate supports needed for the print. Finally, each part was 3D printed in BioMed Clear Resin on a FormLabs Form 2 SLA printer. Further procedure details can be found in Appendix D.

5.3 Final Prototype

Both the stainless steel blade and FormLabs 3D printed coring device were fabricated as final prototypes. The “Lego” coring device underwent multiple iterations of 3D printing, and while it presented some challenges, the team was able to produce a working prototype to receive initial feedback from the client in the Performance Survey(Figure 14).

Four blade prototypes were manually created utilizing the blade fabrication protocol as observed in Appendix C. To ensure the utmost quality of blade, each will partake in testing to investigate the most successful prototype and account for natural variations found when manually producing such prototypes. Further and more in depth discussion of blade testing is to follow.

Figure 12: Stainless steel "Punch Biopsy" blade made in UW TEAM Lab.

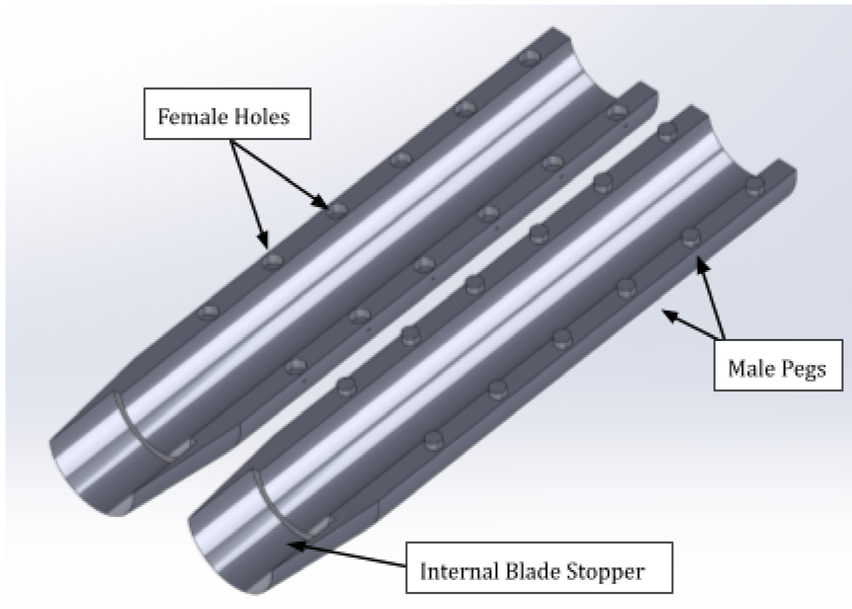


Figure 13: *SolidWorks model of final "Lego" corer device.*

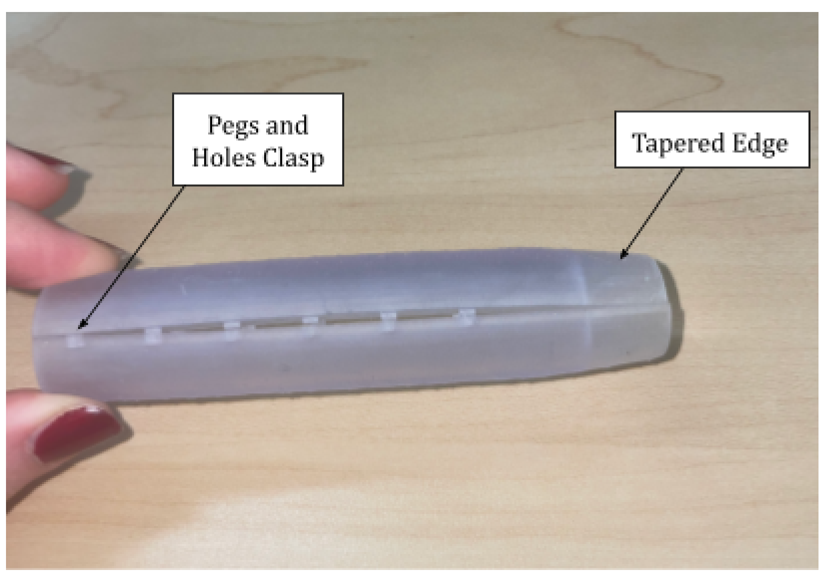


Figure 14: *Final "Lego" 3D printed prototype with some evident bowing.*

5.4 Testing

Following fabrication, the final design went through four comprehensive tests: blade integrity test, tissue damage test, autoclave test, and a performance survey. The blade integrity test confirms that the blade maintains sharpness throughout its service life. The tissue damage evaluation ensures minimal harm to surrounding tissues during live procedures. The autoclave test proves the final device can be autoclaved for multiple uses. Lastly, the performance survey serves as the final validation of the blade's readiness for clinical application. See Appendices E-H for testing protocols.

1. *Blade integrity test:* The team conducted a durability test to evaluate the blade's sharpness quality by examining the change in thickness over 40 cuts. Blade dullness is characterized by a reduction in thickness exceeding 0.04mm during the 40 cuts. This assessment was carried out using chicken breast as the tissue source. Blade thickness was measured every 5 cuts during the test. Success in this test was defined as blade thickness changes remained below 0.04mm after making 40 cuts and by adhering to the specifications detailed in Appendix A, the PDS.
2. *Tissue Damage test:* Conducted simultaneously with the blade integrity test, the team employed the same experimental setup to assess tissue damage. Using the blade, 40 incisions were made in chicken breast, and the team ensured that any observable tissue damage surrounding the site does not exceed 3 mm from the circumference. This was monitored through visual examination, checking for any external tissue damage every 5 cuts and documenting these observations. The test considered the test successful when the external tissue damage for any of the 40 cuts were less than 3 mm.
3. *Autoclave test:* To assess the autoclavability of the final designs, an autoclave was utilized in the biochemistry building. This examination is crucial as the design is intended for multiple reuses, needing a sanitation process. In this evaluation, the 4 blades underwent 3D scanning before and after autoclaving to identify any observable differences resulting from the autoclave procedure. Additionally, caliper measurements were taken before and after to determine if there were any changes in blade thickness due to autoclaving. The test would be considered successful if no observable differences were detected in the 3D scanned images of each blade, and if there were no alterations in blade thickness. The autoclave operated for 1.5 hours on system 7, reaching a maximum temperature of 121°C.
4. *Performance survey:* Following the completion of all other tests, the final examination will serve as a conclusive assessment of the blade's ability to produce clear and accurate tissue samples for CT scans. In this test, the client and her team were able to use the 4 final design blades on human and pig kidney. When using the blades they were asked to fill out a survey to state how well each of the blades performed. The six categories on the survey were: minimal pressure needed to cut through the specimen; low number of cuts needed to puncture the specimen all the way through; limited tension in wrist when using

blade; sharpness was marinated over the multiple cuts made during the survey; no observable tissue damage found after cutting specimen with blade; overall satisfied with the cut each blade made. Each category was ranked on a 1 to 5 scale by the user. A score of 1 indicated strongly disagree, a score of 2 indicated disagree, a score of 3 indicated neutral, a score of 4 indicated agree, and a score of 5 indicated strongly agree. A successful test was defined as a score of 4/5 or higher in all categories, for each of the 4 blades.

VI. RESULTS

Blade Integrity Test

The examination of blade integrity took place in the ECB teaching lab, utilizing raw chicken breasts as the testing material for the blades. Each of the four blades underwent 40 cuts into raw chicken breasts. Blade thickness measurements were documented before the test and after every 5 cuts, resulting in a total of 9 recorded thickness measurements (mm) for each blade in this specific test. From this test, it was found that the change of thickness ranged from 0.01-0.03mm (Figure 15). Subsequently, an ANOVA statistical test was applied to these measurements, yielding a p-value of 4.42e-32 and an f-value of 1058.6. Consequently, the blade thickness measurements demonstrated statistical significance and exhibited considerable variability among the four blades. In summary, the blades successfully passed this integrity test. All graphs and statistical analysis were created and performed in Matlab, see Appendix J for Matlab code.

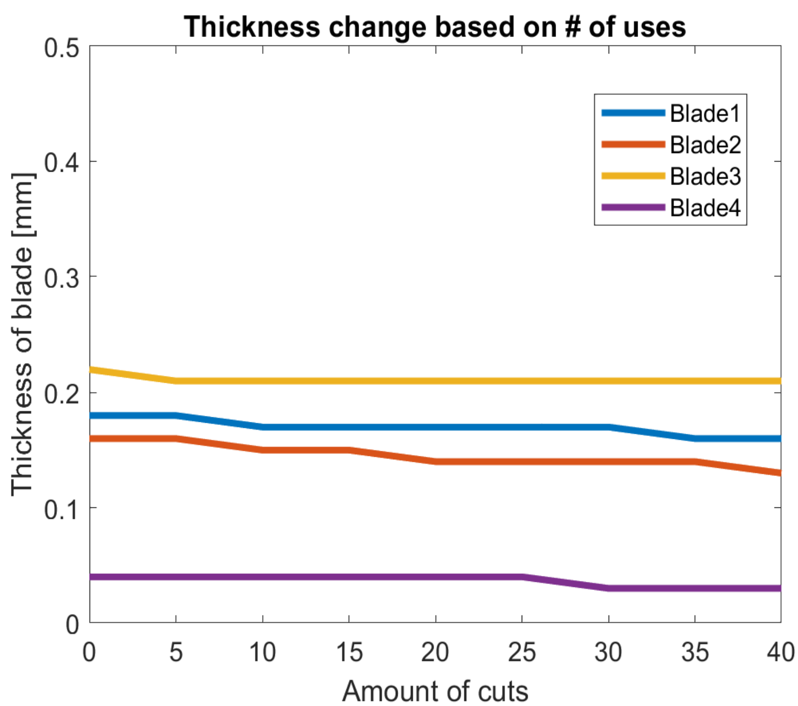


Figure 15: *Plot of 4 different blade's thickness in increments of 5 cuts (40 total).*

Tissue Damage Test

Conducted concurrently with the blade integrity test, the tissue damage examination involved the team observing the cuts made in the chicken breasts after every 5 repetitions. Observations regarding tissue damage within the chicken breast due to the cuts were recorded. Across all four blades and a total of 40 cuts, no observable damage was identified (Figure 16). Consequently, the tissue damage test was deemed successful.

Figure 16: *Test biopsy on a chicken breast showing minimal surrounding tissue trauma.*

Autoclave Test

The autoclave test was carried out on four blades to assess their autoclavability using a combination of a 3D scanner, caliper measurements, and an autoclave. Thickness measurements were taken with a caliper before and after autoclaving to calculate the percentage change in thickness resulting from the autoclave process. Additionally, each blade underwent 3D scanning before and after autoclaving to detect any observable differences. The caliper measurements indicated a .001% difference in thickness before and after autoclaving. In terms of the 3D scanned images, there was no noticeable alteration in the shape of the blades before and after autoclaving (Figure 17a-b). Therefore, the autoclave test demonstrated that the blades are autoclavable, and they successfully passed this evaluation.

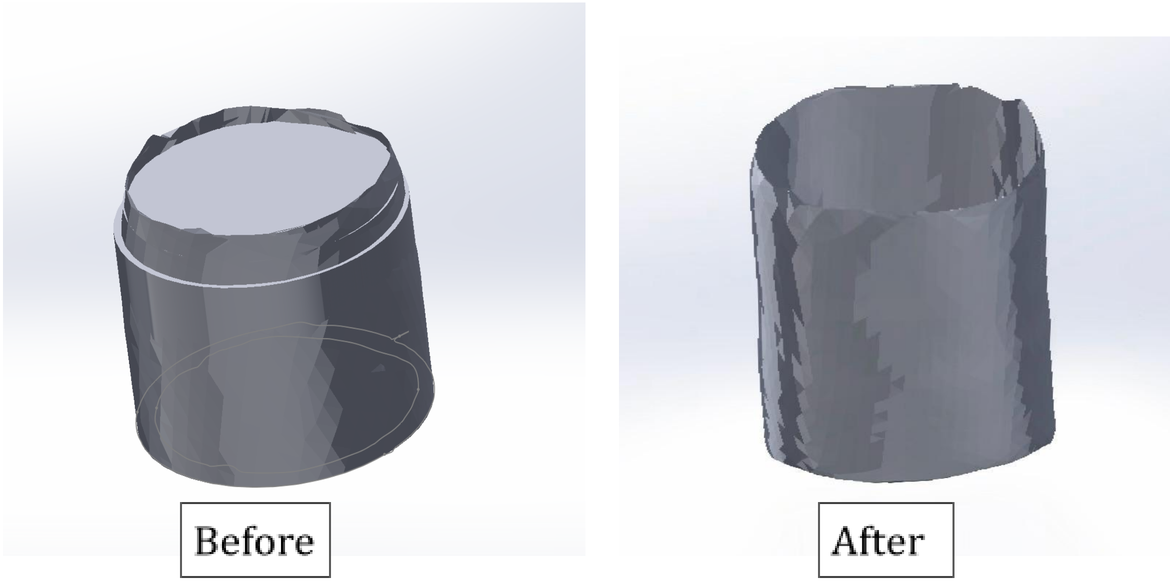


Figure 17a-b: *(Left to Right) Image of Blade #1 3D scanned before Autoclave; Image of Blade #1 3D scanned after Autoclave.*

Performance Survey

The performance evaluation took place within the WIMR radiology department lab, involving four different users who conducted the test on each of the four blades. The survey took into account two distinct types of materials: human kidney and pig kidney. While both materials shared similar consistencies, the human kidney featured an additional layer of fat. Upon completion of all surveys, the team compiled the responses into a graph, categorizing them into the six categories from the survey (Figure 18). The answers for all four blades were combined within each category, considering that they were manufactured using the same protocol and intended to represent the same product.

The results revealed that the overall average of the survey was 3.19 +/- 1.053. The test criteria stipulated that each category should achieve an average score of at least 4 out of 5. Unfortunately, only three out of the six categories scored 4 or higher, leading to the conclusion that the test did not pass. Specifically, the three categories falling below a score of 4 were minimal pressure needed to cut the blade, limited tension caused by pushing the blade into the specimen, and sharpness of the blade maintained over the survey duration.

Additionally, it was observed that all blades caused internal "staircase" damage. This phenomenon occurs when the blade is used to cut through the specimen, resulting in the cut tissue within the blade being compressed, creating stretch marks in the shape of a staircase (Figure 19).

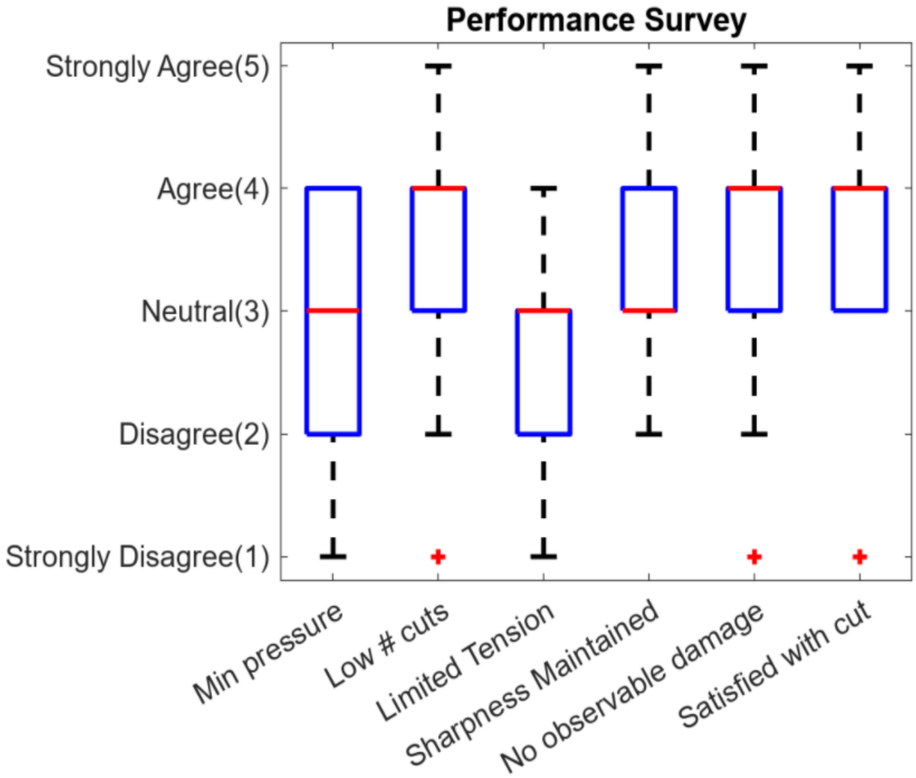


Figure 18: *Box plot of the performance survey results.*

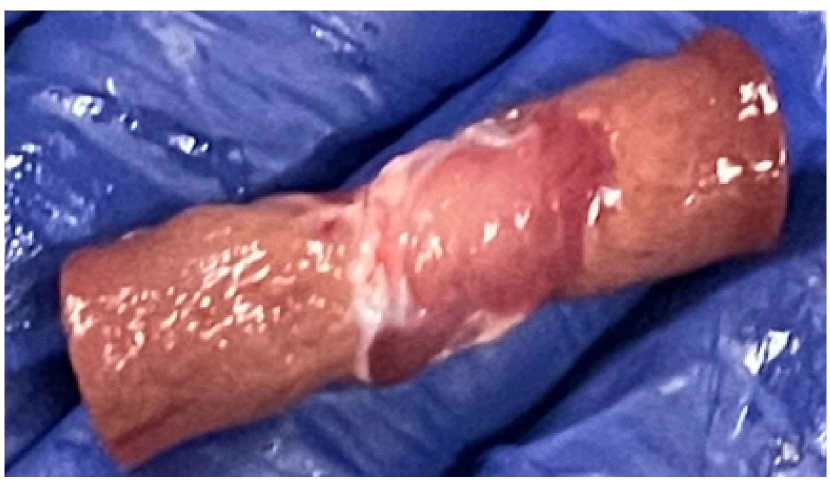


Figure 19: *Image of staircase damage within internal tissue caused by Blade #3.*

VII. DISCUSSION

6.1 Implications of Results

The results of the blade integrity test show that all blades had less than a 0.03mm change in blade thickness after performing 40 biopsy incisions on tissue. This shows that the blades sustain structural integrity for long periods of time and may be reused for multiple biopsy procedures.

A primary goal of this project was to minimize tissue trauma, with criteria aiming for <3mm of localized damage. After performing the blade integrity test along with the tissue damage test, it was noted that the blades had no quantifiable surrounding tissue damage, deeming the blades to be successful in minimizing tissue trauma.

The autoclave test was performed successfully and showed insignificant amounts of material deformation after being placed in an autoclave. This means that the blade can withstand the conditions of an autoclave and can be safely sterilized without sacrificing the structural characteristics of the blade.

Lastly, the blade prototypes scored an average of 3/5 on the performance survey given to the client and her team. The blade prototypes were deemed unsuccessful in this area of testing. Lower scores in categories of discomfort levels and amount of pressure applied needed to puncture the tissue may have been due to the consecutive cutting that the client and her team were performing during a short period of time. This likely caused strain and made it more difficult to use the blades during the later stages of testing.

Nonetheless, the blade and coring collection tube designed by the team surpasses the capabilities of the previous design and holds the potential to become a functional biopsy unit in the future. The improved abilities of the blade and the controlled closure of the collection tube are promising steps toward a successful biopsy device.

6.2 Ethical and Safety Concerns

An ethical concern that may arise from this project is the use of animal tissue during testing. During our testing trials, chicken breasts and pig kidneys were used to test the effectiveness of the blade design. This animal tissue was sourced locally from the UW butcher shop and was necessary for evaluating the blade before using it on human kidney samples.

Using human kidneys for testing may also have ethical considerations that were evaluated by the team. The human kidney used in the third cutting test was a kidney that was no longer clinically needed as was to be discarded. The human kidney was professionally evaluated and tested thoroughly by physicians at the UW Department of Radiology before blade testing was performed on it.

The primary safety concern of this project is the uncovered, sharpened blade. Since the team was not tasked to create a blade cap, the blade is exposed and may pose a safety hazard if used improperly. To mediate this issue, the team may add a blade cap to a future design to minimize this safety risk and keep the blade sterile.

Another safety concern of this project is the sterilization process. In order for the blade to be reusable, it must be able to withstand autoclave sanitization between biopsies. An autoclave uses high pressure and high heat steam to kill bacteria and viruses on the blade [20]. The material chosen for this project, 316 stainless steel, can withstand such conditions, as noted in the conducted autoclave test results.

6.3 Evaluation of Testing

When evaluating the testing and results of this project, the team noted a few possible areas in need of improvement. A phantom tissue type will be chosen to better simulate human kidney tissue when conducting future blade integrity testing. Human kidney tissue has a fibrous surface layer that is thicker and more difficult to penetrate than the animal tissue that the team was using to conduct tests on. This discrepancy may be remedied by increasing blade sharpness even further to avoid the application of extra pressure necessary to pierce the initial tissue layer.

When conducting future performance surveys, the team should ask the client to perform less cuts in a given time period to avoid strain in the hand and wrist from consecutive cutting with minimal rest in between trials. This would likely improve the scores assigned to the blades as wrist fatigue would be minimized, ensuring a fair and accurate scoring of the blade.

6.4 Sources of Error

The team noted some sources of error during the fabrication process and testing procedures. When fabricating the blades, the team did not measure the extent to which the blades were sanded down, meaning that there was inconsistency in fabricating the blades. This means that some blades may have undergone more sanding than others, which may have contributed to the differing blade ratings when conducting cutting tests and the ergonomic survey.

Another source of error may have occurred during testing procedures. During the chicken breast cutting test, the thickness of the blade was measured every five cuts into the chicken breast using calipers. Due to the tapered nature of a blade, it was difficult to re-measure the thickness of the blades after every trial. Therefore, the change in blade thickness during this test may not have been due to the blade wearing down, but rather an inaccurate measurement.

When conducting the series of cutting experiments, the team did one experiment using chicken breasts, one experiment using pig kidneys, and one experiment using a human kidney. As the client mentioned during the human kidney testing trial, human kidneys have a surface layer of connective tissue and fat that is hard to initially penetrate using the blade. The experiments using chicken breasts and pig kidneys did not have this fibrous layer. Differing physiological components between the test organs and human tissue makes the evaluation of the blade during experimentation slightly inaccurate and can cause differences in performance when used in a clinical setting. This can be remedied by making the blade even sharper to make cutting through the fibrous layer easier.

VIII. CONCLUSIONS

7.1 Conclusion

Renal cell carcinoma is spatially heterogeneous and histologically diverse, making it difficult for physicians to accurately analyze images of the mass. In addition to this, these characteristics also pose complications when performing tumor biopsies due to the heterogeneous nature of the tumor [8]. CT textural analysis is a growing approach to rendering accurate images of renal cell carcinoma tumors to better understand the heterogeneous nature of tumors and create patient specific treatment plans. Developing a functional biopsy device to correlate extracted tissue samples with images taken on CT is a vital step towards improving the diagnosis, treatment, and management of renal cell carcinoma.

The blade and coring tube established by a previous team on this project were unsuccessful in harvesting useful biopsies of the renal tumors. The blade proved to be too dull and the coring tube easily fell apart when pressure was applied. The team aimed to improve the design to enhance the abilities of this biopsy device in order for it to be used in a clinical setting

The guidelines established by the client were used to create a blade that harvests cored biopsies of resected renal cell carcinoma tumors. The design that best fit the criteria was a punch biopsy inspired removable blade that securely attaches to the FormLabs Biomed resin collection tube when taking samples. The prototype's performance was evaluated by its ability to cut through the tumor mass while causing minimal trauma to surrounding tissue. In addition to the blade, a coring device was 3D printed that utilizes a peg and hole fit, similar to a Lego. Though the device is still undergoing updates, the team collected valuable feedback from Dr.Lubner's team regarding performance of the tube. As the project progresses, the tube and blade will come together to effectively perform renal cell carcinoma biopsies in order to advance scientific discovery.

7.2 Future Work

In the future, the team will work on integrating the blade and the coring tube into a functional, detachable unit. The blade and tube must stay together while minimizing drag and trauma to the surrounding tissue when taking the biopsy. It is imperative that the blade can also be easily detached, facilitating imaging without disrupting the tube's position within the tumor. The team's current final prototype features a lip to stop the blade from going too far into the tube and a taper to ensure a smooth transition from the blade to the collection tube. However, challenges have arisen during the 3D printing process, specifically in terms of material bowing during the 3D printing process. The team will continue to fine tune the SolidWorks modeling and printing orientation. The team's goal is to achieve a reliable printing outcome, allowing for easy reproduction before each procedure.

In addition, the team will be fabricating a silicone thumb cap for both stability and ergonomic purposes. The team received feedback during the performance survey that the device began to irritate the palm of the user's hand and caused excess tension in the wrist after repeated uses. A silicone cap would provide cushioning for the user's palm and allow for a better grip when twisting the blade through the tumor. The cap would also provide more stability between the two halves of the coring device.

The team will implement better manufacturing processes when fabricating the blade portion of the design. This will include consistent blade angles and widths with a set fabrication process in place. However, even with strict fabrication protocols, there are limitations to the team's manufacturing capabilities both in the sharpness and consistency of the blades. The team is looking into purchasing pre-fabricated 10 mm diameter punch biopsy blades that the blade design is based on. These blades are biocompatible, autoclavable, and proven to be sharp enough to easily cut through skin and adipose tissue [21]. The team would then modify the prefabricated blade to fit securely into the coring biopsy tube, providing more consistent and accurate biopsied tissue samples for imaging.

During the client's testing on the preserved human kidney, the team observed a substantial layer of perirenal fat enveloping the resected kidney, as illustrated in Figure 20. Notably, this adipose tissue presented a formidable challenge in terms of cutting, emphasizing its significance in blade testing scenarios. To replicate this particular tissue challenge, the team is exploring the development of a phantom that accurately mimics the properties of perirenal fat. Additionally, we recognize the importance of virtual simulations and are actively investigating methods to simulate this specific tissue virtually. Integrating both physical and virtual simulations will contribute to a comprehensive understanding of the blade's performance, ensuring its effectiveness in real-world scenarios where cutting through perirenal fat is a critical factor.

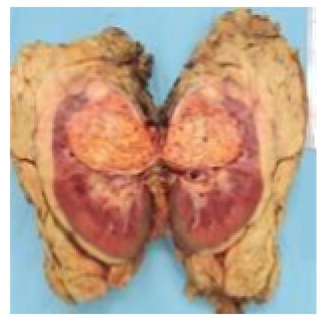


Figure 20: *Resected kidney with RCC surrounded by the layer of perirenal fat [22].*

The existing design is compatible with CT scans but lacks compatibility with MRI scans. To address this limitation, modifications will be made to the coring tube, introducing a mechanism for marking slits to enhance sample location visualization during MRI imaging. The envisioned solution involves incorporating embossed icon shapes along the coring tube, aligning with the laser cut slits on the coring device, as seen in Figure 21. These uniformly placed indentations will cast shadows on the MRI images, providing physicians with improved tracking and identification of biopsy areas and depths. This approach enhances the overall utility of the device in MRI settings, contributing to more accurate and precise biopsy procedures.

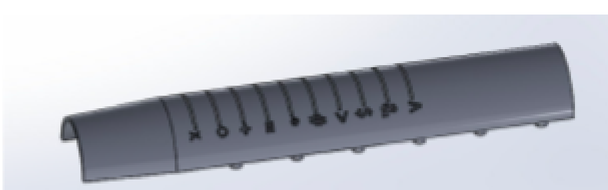


Figure 21: *SolidWorks model of the tube with icon markers: 10 slits 1.5cm each, 0.5cm apart with accompanying icons.*

The current prototype poses a safety hazard as the blade is currently exposed. To resolve the blade sharpness hazard, the team may develop a blade cap to minimize safety risks, improve the lifespan of the blade and to keep the blade shielded from potential environmental contaminants.

7.3 Acknowledgements

The team would like to extend their appreciation for Dr. Lubner, Dr. Shapiro, Dr. Abel, Dr. Hu, and Dr. Puccinelli for their continued guidance and support throughout this project. Additionally, the team would like to thank the members of the TEAM Lab and UW Makerspace for their assistance in the fabrication process.

IX. REFERENCES

[1] J. Oh et al., "Hepatocellular carcinoma: Texture analysis of preoperative computed tomography images can provide markers of tumor grade and disease-free survival," Korean Journal of Radiology, vol. 20, no. 4, p. 569, Apr. 2019. doi:10.3348/kjr.2018.0501

[2] "Precision device for evaluation of radiologic-pathologic features in heterogeneous tumors." Available: https://bmedesign.engr.wisc.edu/projects/f18/ct_correlation. [Accessed: Oct. 3, 2023]

[3] M. Deborah A Baumgarten, "Renal cell carcinoma imaging," Practice Essentials, Radiography, Computed Tomography, https://emedicine.medscape.com/article/380543-overview?form=fpf (accessed Oct. 11, 2023).

[4] "Key statistics about Kidney Cancer," American Cancer Society, https://www.cancer.org/cancer/types/kidney-cancer/about/key-statistics.html (accessed Oct. 11, 2023).

[5] L.-M. Krabbe, A. Bagrodia, V. Margulis, and C. Wood, "Surgical management of renal cell carcinoma," Seminars in Interventional Radiology, vol. 31, no. 01, pp. 027–032, 2014. doi:10.1055/s-0033-1363840

[6] M. G. Lubner, A. D. Smith, K. Sandrasegaran, D. V. Sahani, and P. J. Pickhardt, "CT texture analysis: Definitions, applications, biologic correlates, and challenges," RadioGraphics, vol. 37, no. 5, pp. 1483–1503, Sep. 2017. doi:10.1148/rg.2017170056

[7] Y. Deng et al., "CT texture analysis in the differentiation of major renal cell carcinoma subtypes and correlation with Fuhrman grade," European Radiology, vol. 29, no. 12, pp. 6922–6929, May 2019. doi:10.1007/s00330-019-06260-2

[8] D. Zhang et al., "Spatial heterogeneity of tumor microenvironment influences the prognosis of clear cell renal cell carcinoma," Journal of Translational Medicine, vol. 21, no. 1, 2023. doi:10.1186/s12967-023-04336-8

[9] S. Rostami. Rostami. and M. L. Ramsey, "Skin biopsy - statpearls - NCBI bookshelf," Skin Biopsy, https://www.ncbi.nlm.nih.gov/books/NBK470457/ (accessed Oct. 11, 2023).

[10] D. Hurkudli, S. Sarvajnamurthy, S. Suryanarayan, and V. Chugh, "Novel uses of skin biopsy punches in dermatosurgery," Indian Journal of Dermatology, vol. 60, no. 2, p. 170, 2015.

[11] C. C. medical professional, “Renal cell carcinoma: Symptoms, treatment & prognosis,” Cleveland Clinic, https://my.clevelandclinic.org/health/diseases/24906-renal-cell-carcinoma (accessed Oct. 10, 2023).

[12] Z. Feng, Q. Shen, Y. Li, and Z. Hu, “CT texture analysis: A potential tool for predicting the Fuhrman grade of clear-cell renal carcinoma - cancer imaging,” BioMed Central, https://cancerimagingjournal.biomedcentral.com/articles/10.1186/s40644-019-0195-7#:~:text=Computer%20tomography%20texture%20features%20can%20predict%20the%20Fuhrman,the%20most%20important%20imaging%20marker%20for%20clinical%20application. (accessed Oct. 11, 2023).

[13] “Profile,” Department of Radiology, https://radiology.wisc.edu/profile/meghan-lubner-460/ (accessed Oct. 11, 2023).

[14] “Surgical blades: Which scalpels are right for your operating room?,” USA Medical and Surgical Supplies, https://www.usamedicalsurgical.com/blog/surgical-blades-which-scalpel-is-right-for-your-operating-room (accessed Oct. 11, 2023).

[15]“Snap-fit book final 11-05 - Massachusetts Institute of Technology,” Snap Fit Joints for Plastics, https://fab.cba.mit.edu/classes/S62.12/people/vernelle.noel/Plastic_Snap_fit_design.pdf (accessed Nov. 29, 2023).

[15] “12 in x 12 in nominal size (WXL), 0.022 in thick, stainless steel sheet 304,” Grainger, https://www.grainger.com/product/GRAINGER-APPROVED-Stainless-Steel-Sheet-304-796XT3 (accessed Oct. 11, 2023).

[16] “Welded, 316 stainless steel, tubing,” Grainger, https://www.grainger.com/product/APPROVED-VENDOR-Tubing-Welded-3ADN7?opr=ILOF (accessed Dec. 13, 2023).

[17] “Standard specification for seamless and welded austenitic stainless steel tubing for General Service,” A269/A269M, https://www.astm.org/a0269_a0269m-22.html (accessed Dec. 13, 2023).

[18] “3/8 in outside DIA, 4 ft overall LG, stainless steel round tube 316,” Grainger, https://www.grainger.com/product/APPROVED-VENDOR-Stainless-Steel-Round-Tube-786H92 (accessed Dec. 13, 2023).

[19] Medical resin biomed clear - formlabs, https://formlabs-media.formlabs.com/datasheets/2001432-TDS-ENUS-0.pdf (accessed Dec. 14, 2023).

[20] “Everything About Autoclaves,” Autoclave Machine: Uses, Guidelines & Cost | Knowledge Center, https://www.steris.com/healthcare/knowledge-center/sterile-processing/everything-about-autoclaves#:~:text=An%20autoclave%20is%20a%20machine,a%20given%20amount%20of%20time. (accessed Dec. 3, 2023).
Show less

[21]“Limited reuse biopsy punch, various sizes,” World Precision Instruments, https://www.wpiinc.com/var-949-reusable-biopsy-punch-various-sizes.html (accessed Dec. 12, 2023).

[22] M. M, “Kidney cancer,” Flickr, h4tps://www.flickr.com/photos/58937697@N00/309704909 (accessed Dec. 4, 2023).

X. APPENDIX

Appendix A: Product Design Specification

Function :

The goal of this project is to develop a blade and coring device for tumor resection. The blade should be able to effectively resect a cross-section from an ex-vivo kidney tumor without causing damage to the overall tissue sample. Currently, the resection device used is too blunt and thick to effectively extract tissue without causing surrounding areas to be damaged and un-imageable on CT. The coring device should stay in tact during the biopsy while also easily revealing the sample inside for analysis. By creating a new blade and coring tube designs, the pathologist can preserve the extracted tumor during the biopsy. In maintaining the integrity of the tumor, the pathologist will be able to accurately correlate CT image markings and findings with their location in the patient sample.

Client requirements:

- Timeline: All final deliverables must be completed by December 13th, 2023
- A device is needed to allow for radiologic-pathologic correlation of resected renal cell carcinoma
- The device must accommodate ex vivo tumors of large size, approximately 20 x 7 x 7 cm
- Tissue samples should be cleanly cored without damaging the integrity of the tissue
- The device should be easily sterilized and cleaned between uses
- The device should be reusable and long-lasting
- The blade must be easily detachable from the cylindrical corer
- The team has a budget of $500 for one device

Design requirements:

1. Physical and Operational Characteristics

a. *Performance requirement*s: The coring blade must be able to resect a single tissue sample from the kidney, roughly 7-10mm in size in order to fit on a microscope slide. The cut must be sharp enough to minimize the trauma to the surrounding tissue. The blade must be reusable and therefore must be able to withstand sterilization in an autoclave at 121 degrees Celsius. The blade must be easily detachable in order to be removed before imaging. The sample collection coring tube must preserve the integrity of the biopsied tissue, minimizing tissue trauma on the samples. The tube must also minimize drag and surrounding tissue trauma, meaning it must have a smooth finish. It must also stay closed during the biopsy collection process but be easy to open to retrieve the biopsy samples.

b. *Safety*: To ensure the safety of the pathologist, the blade should be round and smooth on the sides while remaining sharp at the point of incision. A cover will be made to cover the blade when not in use to protect the pathologist.

c. *Accuracy and Reliability*: The device must be effective enough so that it takes only one cut to insert into the tumor. The extent of trauma to the surrounding tissue should be no more than 3mm in diameter.

d. *Life in Service*: The blade portion of the coring device should be reusable and able to perform at least 40 resections of tissue samples without becoming dull. Therefore, it should compare to the hardness of sterile surgical blades which are outlined in BS 2982:1992 and BS EN ISO 7153 Part 1 [1]. The coring tube is a single use device that is 3D printed using FormLabs BioMed Clear resin on a case to case basis, therefore has a one case life in service.

e. *Shelf Life*: The blade must have a minimum shelf life of 50 years [2]. When not being used, the device should be stored in sealed packaging in dry, room-temperature conditions (<50% humidity, 27 ℃) [3]. The coring device must adhere to the FDA 1991 shelf life regulations for medical devices [4].

f. *Operating Environment*: The coring device should only be used in a clinical pathology lab. This laboratory should be compliant with the ISO 15189 standard [5]. This standard outlines quality and competence standards for medical laboratories. It's designed for labs to develop their management systems, assess their competency, and gain recognition from users, regulators, and accreditation bodies.

g. *Ergonomics*: The blade and coring tube should be comfortable and easy for the pathologist to use. Therefore, it will be lightweight (< .453 kg), have no rough edges, and be balanced so that it only takes one attempt to successfully collect a sample in less than 5 minutes [6].

h. *Size*: The coring device must produce samples that can be accurately observed on microscope slides. Therefore, the diameter of the circular blade must be between 7 to 10 mm according to Dr. Jason Abel. The core blade must resect a tumor that is 10 cm in depth. The tissue collection tube varies between patients based on the dimensions of the kidney and tumor. The diameter of the tube must be the same as the blade, 10 mm, to properly harvest tissue samples.

i. *Weight*: The design should be as simple as possible, minimizing unnecessary bulkiness. The coring aspect of the device should be less than .453 kg to not put any strain on the pathologist's hands when collecting a sample.

j. *Materials*: The blade of the coring aspect should be made of surgical-grade stainless steel that is hardened to the Rockwell C hardness of about 46-53 [7]. The material of the blade must be able to withstand high temperatures in order to be sterilized in an autoclave. The material of the coring tube should be biocompatible so that it does not interfere with the surrounding tissue integrity.

k. *Aesthetics, Appearance, and Finish*: The device should be smooth and simple. There are no appearance or finish specifications required by the client.

2. Production Characteristics

a. *Quantity*: There is only a requirement for one device, however considering the possibility of mass production, the number of devices may need to meet market demands. The coring tube is 3D printed within the client's facility based on patient specific data.

b. *Target Product Cost*: The target product cost for this device is $500. It will be paid for via UW Health research funds.

3. Miscellaneous

a. *Standards and Specifications*: The device would need to adhere to the ISO 13485:2016 regulation which outlines requirements for regulatory purposes of medical devices. Regarding the blade for a tumor resection coring device, this standard specifies that a technical support device must consistently meet customer and applicable regulatory requirements [7]. In addition, the device must follow ISO 15189:2022 so that it meets the quality and competence requirements to be used in a medical laboratory [6]. Because the blade may need to be detachable, the device should also adhere to ISO 7740:2018 which states the dimensions and features needed to be a detachable blade used in a laboratory [8]. Lastly, the model would also need to follow the FDA's Code of Federal Regulations Title 21, Volume 8 which outlines the requirements for medical devices [9].

b. *Customer*: Dr. Meg Lubner is a professor (CHS) in the Abdominal Imaging Section at the University of Wisconsin School of Medicine and Public Health. She is asking for a blade that would be compatible with the tumor resection coring device that was fabricated by the previous group. Dr. Daniel Shapiro and Dr. Jason Aebl will act as alternate contacts for this project as well. Both doctors have specialties in minimally invasive surgery and urologic oncology, giving the team specialized knowledge about RCC.

c. *Patient-related concerns*: The device will not interact directly with the patient, only with the kidney tumor after it has been fully surgically removed. However, it is crucial that the coring device takes an accurate and interpretable biopsy of the tumor. Minimizing the tissue trauma caused to the kidney tumor when taking a core biopsy is critical to conclude an accurate diagnosis and to collect data from the procedure.

d. *Competition:* Currently, there is a lack of available devices in the market designed for core biopsies of kidney tumors. The existing method involves excising square sections around markers within the tumor. However, this approach falls short of providing comprehensive insights into the depth of specific areas of interest. A device sharing a similar underlying principle already present in the market is the punch biopsy tool employed for skin graft procedures. In a punch biopsy, a circular-tipped cutting instrument is utilized to extract deeper layers of skin for diagnostic purposes [10]. This tool is rotated into the skin and then withdrawn to generate a columnar biopsy of the skin's deeper layers. However, these devices cannot be used to create a core biopsy of a kidney tumor because they do not cut deep enough.

References:

[1] “ISO 7153-1:2016 - Surgical instruments - Materials - Part 1: Metals.” https://webstore.ansi.org/standards/iso/iso71532016?gad_source=1&gclid=CjwKCAjwyNSoBhA9EiwA5aYlb6QOZJk1WsQh60pnvlbu12DcnrgfUrEscKmUyMdjTL5-pCZ6FudwEhoCH7gQAvD_BwE (accessed Sep. 28, 2023).

[2]“The Lifespan & Recyclability Of Aluminium And Steel,” Metals Warehouse, Apr. 09, 2021. Available:https://www.metalswarehouse.co.uk/lifespan-recyclability-aluminium-steel/. [Accessed: Dec. 04, 2023]

[3] "Humidity control of steel for world's largest independent steel trader." Munters. https://www.munters.com/en/munters/cases/stemcor-steel-storage/. [Accessed on: September 20, 2023].

[4] Center for Devices and Radiological Health, “Shelf life of Medical Devices,” U.S. Food and Drug Administration, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/shelf-life-medical-devices (accessed Dec. 13, 2023).

[5]14:00-17:00, “ISO 15189:2012,” ISO, Jan. 26, 2021. https://www.iso.org/standard/56115.html (accessed Sep. 27, 2023)

[6] C. C. for O. H. and S. Government of Canada, “CCOHS: Hand Tool Ergonomics - Tool Design,” Jun. 13, 2023. https://www.ccohs.ca/oshanswers/ergonomics/handtools/tooldesign.html (accessed Sep. 28, 2023).

[7] N. K. Meckel, “Scalpel blade having high sharpness and toughness,” Sep. 20, 2001

[8]14:00-17:00, “ISO 15189:2012,” ISO, Jan. 26, 2021. https://www.iso.org/standard/56115.html (accessed Sep. 27, 2023).

[9]“CFR - Code of Federal Regulations Title 21.” https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPartFrom=800&CFRPartTo=1299 (accessed Sep. 21, 2023).

[10]“Punch biopsy,”MayoClinic, https://www.mayoclinic.org/tests-procedures/skin-biopsy/multimedia/punch-biopsy/img-20005764 (accessed Sep. 27, 2023).

Appendix B: Expense Spreadsheet

Item	Description	Manufacturer	Part Number	Date	QTY	Cost Each	Total	Link
Component 1								
	Tubing: Welded, 316 Stainless Steel, 5/8 in Outside Dia, 0.585 in Inside Dia, 6 ft Overall Lg	Grainger	3ADN7	10/10/23	1		22.01	link
Component 2								
	3D printed tube	Makerspace		11/01/23	1		5.80	
Component 3								
	Chicken Breast	Animal & Dairy Science Dept		11/05/23	8	2.00	16.00	link
Component 4								
	Lego and Puzzle Piece Tube 3D printing	Makerspace		11/10/23	1		25.87	
Component 5								
	Pig Kidney	Animal & Dairy Science Dept		11/20/23	4	10.59	42.36	link
Component 6								
	Reprint- Lego and Puzzle Piece Tube 3D printing	Makerspace		11/30/23	1		23.06	
Component 7								
TOTAL:								**135.1**

Appendix C: Blade Fabrication Procedure

Materials:

- 1-316 stainless steel tube
- Mini tube cutter
- Sanding Belt machine
- Dremel
- 1 cup of water

Procedure:

1. Retrieve 316 stainless steel tube
2. Make marks every 4 in with black sharpie
3. Clamp tube to table
4. Align mini tube cutter blade with black mark
5. Tighten the tube cutter just enough that it doesn't fall off the tube
6. Rotate tube cutter in 4 circles towards you until tube splits into two
7. Continue steps 4-6 until the tube is cut into the right amount of sections
8. Take each subsection of the tube and put them all together
9. Take one and turn on the sanding belt machine
10. Press the tip of the cut tube into the sanding belt
11. Rotate the tip to evenly sand down the tube
12. After making 2 full revolutions, remove the tube and dip it into a cup of water for 30 seconds
13. Repeat 10-12 until the outside of the tube looks even and sanded down
14. Take the same piece of tubing and clamp it to the table
15. Plug in the dremel and find a top piece that fits inside the tube
16. Turn on the dremel and sand the inside the tube by pressing force around the inner surface
17. Stop after two revolutions and place the tube into a cup of water for 30 seconds.
18. Repeat steps 16-17 until thickness of the tip is less than .25 mm
19. Repeat whole process for all cut sub sections of the tube

Appendix D: Coring Tube Fabrication Procedure

Materials:

- BioMed Clear Resin
- SolidWorks 2023 software
- FormLabs Form 2 SLA 3D Printer
- File

Procedure:

1. Open SolidWorks
2. Sketch a circle with a diameter of 1.97 cm
3. Sketch a concentric circle with a diameter of 1.65 cm
4. Extrude the outer circle 8.50 cm
5. Create an extruded cut at the inner circle diameter for a length also of 8.50 cm
6. Create an asymmetrical chamfer starting 1.905 cm (.75in) from the edge
7. Create a 1.3335 cm concentric circle and cut extrude it 1.27 cm to create a lip to stop the blade
8. Make a reference plane going through the center plane of the tube
9. Use the split tool to create two halves of this tube.
10. One one half, use the “Linear Pattern " tool in SolidWorks and created 6 circles, .3cm in diameter along the thickness of the tube
11. Repeat this process on the other side to make a total of 12 circle sketches, each 1.25 cm away from each other
12. Use the “Extruded Cut” tool and cut the circle sketches .18 cm into the device to make holes
13. On the other half use the linear pattern tool to create and extrude .25cm diameter circles .15cm.
14. Save each .sldprt file into an STL file
15. Use Preform software to model the supports needed to 3D print as well as receive a cost estimate
16. Select BioMed Clear Resin as the material
17. Print parts on a FormLabs Form 2 SLA 3D printer
18. Once printing is finished, use a file to take off supports and smooth the surface

Appendix E: Blade Integrity Testing Protocol

<u>Materials:</u>

- 8 chicken breasts
- Final prototype of the blades
- Ethanol
- Scissors
- Caliper
- Gloves
- A large, square, polystyrene dish
- Paper towels

<u>Procedure:</u>

1. Prepare the area by layering the polystyrene dish with multiple paper towels
2. Put on gloves
3. Using the scissors, cut open the packages of chicken breasts and drain the liquid
4. Place the chicken breasts in the polystyrene dish, making sure no chicken breasts overlap
5. Measure the thickness of the blade with the caliper and record the measurement in millimeters
6. If more than one person is testing the different blades, ensure that the same person tests the same blade throughout all cuts
7. Cut the chicken breast by holding the blade in your hand with your thumb pointing down and rotating your wrist
    a. You can rotate your wrist multiple times to cut all the way through the chicken breast, but do not take the blade out and put in back in the chicken to make the cut
8. Once the blade is through the entire chicken, lift the blade up and remove the specimen from the inside
9. Repeat this process four more times for a total of five individual cuts
10. After 5 cuts, measure the thickness of the blade using the caliper and record the measurement in millimeters
11. Repeat steps 7-10 seven more times for a total of 40 individual cuts
    a. Ensure you record the blade thickness after every 5 cuts for a total of 9 measurements
12. Repeat steps 5-11 for all blades being tested
13. Bag all of the chicken, packaging, gloves, and paper towels and dispose of in the trash
14. Using ethanol, wipe down the table, polystyrene dish, scissors, calipers, and all blades
15. Put back all materials once dry

Appendix F: Tissue Damage Testing Protocol

<u>Materials:</u>

- 8 chicken breasts
- Final prototype of the blades
- Ethanol
- Scissors
- Caliper
- Gloves
- A large, square, polystyrene dish
- Paper towels

<u>Procedure:</u>

1. Prepare the area by layering the polystyrene dish with multiple paper towels
2. Put on gloves
3. Using the scissors, cut open the packages of chicken breasts and drain the liquid
4. Place the chicken breasts in the polystyrene dish, making sure no chicken breasts overlap
5. Cut the chicken breast by holding the blade in your hand with your thumb pointing down and rotating your wrist
    a. You can rotate your wrist multiple times to cut all the way through the chicken breast, but do not take the blade out and put in back in the chicken to make the cut
6. Once the blade is through the entire chicken, lift the blade up and remove the specimen from the inside
7. Using the calipers, measure the amount of tissue damage the cut created and record this distance in millimeters
    a. This is the distance from the edge of the circle of the intended to the furthest sign of tissue trauma, either a tear in the chicken or a larger than 10mm diameter circle
    b. If no visual damage is seen, record this observation
8. Repeat steps 5-7 for a total of 40 cuts
9. Bag all of the chicken, packaging, and paper towels and dispose of in the trash
10. Using ethanol, wipe down the table, polystyrene dish, scissors, and all blades
11. Put back all materials once dry

Appendix G: Autoclave Testing Protocol

<u>Materials:</u>

- Final prototype of blades
- Certification in autoclave use

<u>Procedure:</u>

1. Schedule an appointment with the UW Makerspace to 3D scan
2. Go to the scheduled appointment and meet with the worker
3. Have the certified worker 3D scan the blades using their machinery
    a. You are unable to perform this yourself, it has to be done by a worker
4. Export the 3D scan image as a SolidWorks (sldprt) file
5. Get the dimensions of the inner and outer diameter of the blade from a caliper and record these dimensions in millimeters
6. Repeat steps 3-5 for all blades being tested
7. Schedule an appointment to autoclave at the Biochem Building
8. Go to the scheduled appointment
    a. Ensure that you are autoclave certified by completing the online training
9. Place the blade into the autoclave and follow the steps to autoclave i
10. Remove the blade from the autoclave
11. Repeat steps 9-10 for all blades being tested
12. Schedule an appointment with the UW Makerspace to 3D scan
13. Go to the scheduled appointment and meet with the worker
14. Have the certified worker 3D scan the post-autoclaved blades using their machinery
15. Export the 3D scan image as a SolidWorks (sldprt) file
16. Get the dimensions of the inner and outer diameter of the blade from a caliper and record these dimensions in millimeters
17. Repeat steps 14-16 for all blades that were autoclaved

Appendix H: Performance Survey Testing Protocol

<u>Materials:</u>

- 16 copies of the performance survey found in Appendix I
- Pencil
- Final prototype of blades
- 4 pig kidneys
- Scissors
- Caliper
- A large, square, polystyrene dish
- Gloves
- Paper towels
- Ethanol

<u>Procedure:</u>

1. Prepare the area by layering the polystyrene dish with multiple paper towels
2. Put on gloves
3. Using the scissors cut open the packages of pig kidneys and drain any liquid
4. Place the pig kidney in the polystyrene dish
5. Have the client cut into the pig kidney using one blade
6. Once the blade is through the entire pig kidney, lift up the blade and remove the tissue specimen
7. Have the client note the integrity of the tissue specimen and the overall pig kidney
8. Ask the client the questions of the performance survey and write down their answers
9. If there is noticeable tissue damage, use the calipers to measure how much damage there is in millimeters
10. Repeat steps 5-9 with 3 other clients
11. Place all pig kidney waste, paper towels, and gloves in a bag and dispose of in the trash
12. Using the ethanol, wipe down the calipers, scissors, blades, polystyrene dish, and table
13. Put all materials back where they belong

Appendix I: Performance Survey

Name:

Blade #:

1. Cutting the tissue required minimal pressure using the blade.

   (1) Strongly Disagree (2) Disagree (3) Neutral (4) Agree (5) Strongly Agree

2. It took a limited number of attempts to cut the kidney (<2).

   (1) Strongly Disagree (2) Disagree (3) Neutral (4) Agree (5) Strongly Agree

3. I did not feel any tension in my wrist or hand when using the blade.

   (1) Strongly Disagree (2) Disagree (3) Neutral (4) Agree (5) Strongly Agree

4. The blade quality did not decrease over time.

   (1) Strongly Disagree (2) Disagree (3) Neutral (4) Agree (5) Strongly Agree

5. The blade did not cause any observable tissue damage.

   (1) Strongly Disagree (2) Disagree (3) Neutral (4) Agree (5) Strongly Agree

6. I am satisfied with the cut of the blade.

   (1) Strongly Disagree (2) Disagree (3) Neutral (4) Agree (5) Strongly Agree

7. The coring tube opens and closes easily.

   (1) Strongly Disagree (2) Disagree (3) Neutral (4) Agree (5) Strongly Agree

8. The coring tube will stay intact when I need it to.

(1) Strongly Disagree (2) Disagree (3) Neutral (4) Agree (5) Strongly Agree

9. If there was any tissue damage, how widespread was the damage from the cut? Please give an answer in mm.

10. Please provide any other feedback on blade design

Appendix J: Matlab code

```
%name= ["Blade 1", "Blade 2","Blade 3","Blade 4"]
Blade1 = [0.18; 0.18; 0.17; 0.17; 0.17; 0.17; 0.17; 0.16; 0.16];
Blade2 = [0.16; 0.16; 0.15; 0.15; 0.14; 0.14; 0.14; 0.14; 0.13];
Blade3 = [0.22; 0.21; 0.21; 0.21; 0.21; 0.21; 0.21; 0.21; 0.21];
Blade4 = [0.04; 0.04; 0.04; 0.04; 0.04; 0.04; 0.03; 0.03; 0.03];
tbl = table(Blade1, Blade2, Blade3, Blade4)
matrix = [Blade1(:), Blade2(:), Blade3(:), Blade4(:)]
anova(matrix)
cuts= [0 5 10 15 20 25 30 35 40];
figure (1)
plot (cuts, matrix, 'LineWidth', 3)
title("Thickness change based on # of uses")
xlabel("Amount of cuts")
ylabel("Thickness of blade [mm]")
legend(["Blade1","Blade2","Blade3","Blade4"])
set(gca,'FontSize',12);

matrix=table2array(ErgonomicDataSheet13)
x= ["Min pressure", "Low # cuts", "Limited Tension", "Sharpness Maintained", "No observable
damage", "Satisfied with cut"];
y=["Strongly Disagree(1)", "Disagree(2)", "Neutral(3)", "Agree(4)", "Strongly Agree(5)"]

figure (2)
bh= boxplot(matrix)
set(gca,'xtick',[1:6],'xticklabel',x)
set(gca,'ytick',[1:6],'yticklabel',y)
set(gca,'FontSize',12);
set(bh,'LineWidth', 2);
title("Performance Survey")

M= mean(matrix, 'all')
st=std(matrix(:))
```