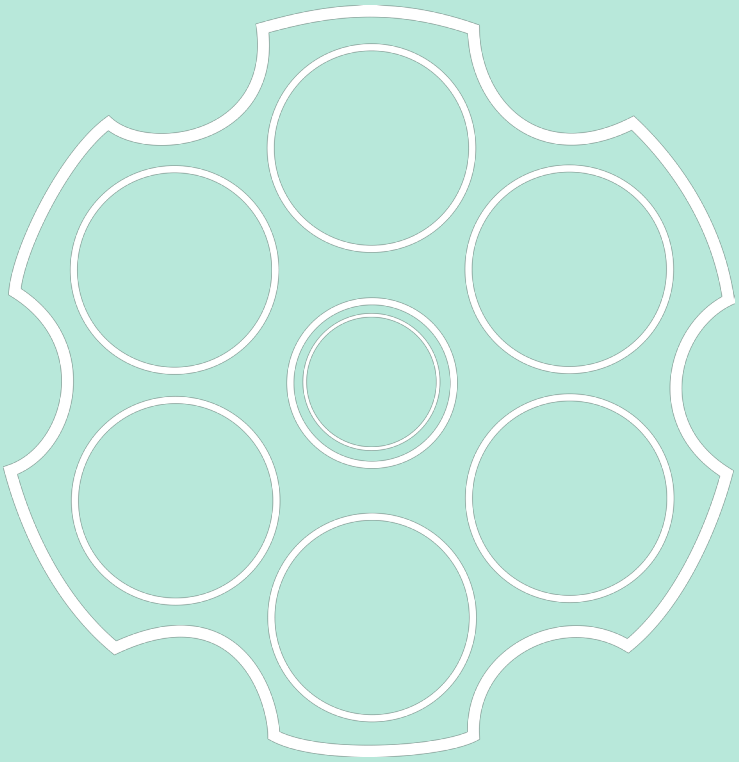
The design of a single-insertion multiple specimen biopsy instrument

The development and evaluation of a novel core-needle biopsy device



Josette Kuipéri

JOSETTE KUIPÉRI

THE DESIGN OF A SINGLE-INSERTION MULTIPLE SPECIMEN BIOPSY INSTRUMENT

THE DEVELOPMENT AND EVALUATION OF A NOVEL CORE-NEEDLE BIOPSY DEVICE

Master of Science
Delft University of Technology,
Track: BioMechanical Design (BMD)

Student number:	*4081749*
Supervisors:	*Dr. ir. A. Sakes*
	Prof. dr. ir. P. Breedveld
Graduation committee:	*Dr. ir. D. H. Plettenburg*

PREFACE

Perhaps, the shape on the cover of this thesis appears familiar to you. The shape represents the ammunition chamber of a revolver. The revolver as we know it, was first designed by Samuel Colt. He patented his design of the revolver in 1836 [1]. This design of the revolver was the first practical repeating firearm. However, the revolver is in fact a much older weapon. Its origins are unclear. Several types of early revolvers were found. The earliest revolver which is the most similar to the revolver as we know today, is the so called snaphaunce revolver. This revolver originates from the early seventeenth century [1].

Revolvers were developed because older guns or pistols had a very limiting firing speed. Instead of loading a bullet one by one, there was a need to reload the guns faster. The revolver enabled the firing of multiple bullets repeatedly one after an other. It consists of an ammunition chamber or barrel, which is able to contain five to six bullets. By triggering the revolver the chamber will rotate and fire the next bullet.

The shape of the revolver ammunition chamber has become a distinct shape, reminding of this type of gun. Even though the cover shows an ammunition chamber of a revolver, this thesis is not about firearms, but about the design of a medical instrument. The connection between these two contradictory instruments will become clear in this thesis. Hopefully after reading my thesis, the shape on the cover will remind you of a very different thing, namely my design of the novel biopsy instrument.

Josette Kuipéri

ABSTRACT

Background: When a suspicious lesion is detected, a thorough examination is essential for the diagnostics of the lesion. Information about the nature and character of the lesion is crucial for the determination of the disease and an appropriate corresponding treatment plan. Taking a biopsy plays an important role in this examination. A biopsy is the removal of a tissue sample from a living organism. The aim of the biopsy is to provide a sufficient and representative part of a lesion, which will enable a thorough examination. Unfortunately, the diagnostics of a biopsy is not always as accurate as desired. Core-needle biopsy is a commonly used minimally invasive biopsy technique. This technique uses a needle, with a varying size between 1.3 mm to 2.1 mm, to cut away a tissue sample from a lesion. Biopsies taken with core-needle instruments do not always represent the lesion sufficiently. It is often hard to determine the exact lesion site, and to know if the needle has indeed taken a biopsy from the lesion. To prevent non-diagnostic results from the biopsy, multiple samples should be taken from the lesion site. Common core-needle methods currently obtain a single biopsy sample per insertion. As multiple specimens must be obtained, multiple insertions of the biopsy instrument are required. The aim of this research is to design a single-insertion multiple specimen biopsy instrument. This design will be developed and evaluated on its performance and functionality.

Methods: A list of requirements was setup to determine the conditions which comprise the design. Next to the requirements, a functional analysis was carried out which divided the functions of the design into three main functions. A, the insertion of the device into the lesion, B, the actions required to obtain a multitude of samples, and C, the retraction of the instrument from the body. The actions to obtain a multitude of samples, are subdivided into five actions: (1) the instrument must collect a tissue sample, and (2) enclose this tissue sample into a container. (3) This container must be transported through the instrument. And subsequently stored inside the instrument, (4). Finally, (5) the instrument must be reloaded. This sequence of actions can be repeated until a number of specimens have been obtained. Using these five actions as a lead of the design process, conceptual designs were created. During the design process inspiration was found in firearms. The storing of bullets and reloading mechanisms found in guns could help find solutions to the storing and reloading functions of the biopsy instrument. For each action a conceptual design is developed, and finally these five conceptual designs are combined and elaborated, resulting into one final design. A prototype of the final design was developed and evaluated. The prototype was validated on three different aspects: the ability to obtain multiple biopsy samples through a single insertion, the ability to use the prototype in accordance to the intended use, and a comparison between the prototype and an existing biopsy instrument in terms of procedure duration. For each of these aspects the prototype was validated in three different proof of concept experiments.

Results: The prototype proved to successfully be able to take a multitude of biopsy specimens through a single insertion. Next to this initial evaluation, the intended use of the instrument is also successfully performed by the prototype. The last evaluation of the prototype, has shown that the procedure time of the prototype to take a multitude of samples is longer than the procedure time to take a multitude of samples using and existing biopsy instrument (TruCore II). The prototype took 5 minutes and 7 seconds, whereas the existing biopsy instrument took 3 minutes and 50 seconds to obtain multiple tissue samples.

Discussion and Conclusion: The fabricated prototype has proven that it is able to take multiple tissue samples through a single insertion. This multitude of samples can be used to improve the diagnosis accuracy of core-needle biopsy. The functionality of the prototype is in accordance to the intended use. This intended use provides an indication of the possibilities of use of the prototype. The procedure time of the prototype can be decreased by further improving the usability of the design. Future research can focus on a more elaborate evaluation on the accuracy of the instrument. Furthermore, future work can be carried out on decreasing the instrument length of the current design. Another research can be done on possible ways to implement a semi-, or even a fully-automatic reloading and transportation mechanism on the now manual operable instrument. With these additional future improvements, this initial proof of concept prototype has the potential to become a fully functioning biopsy instrument.

GLOSSARY

Aspirate The medical term aspirate or aspiration refers to the intake of a fluid or soft tissue through suction.

Biopsy A biopsy is the removal of a tissue specimen from a living organism. This tissue specimen is examined to determine the cause, presence or severity of a disease.

Bolt-action A mechanism found in a type of firearm which is used to transport the ammunition manually in and out of the gun shaft. The bolt-action has a handle which can be locked to enable triggering of the ammunition, and unlocked to retract the empty ammunition shells.

Cartridge A cartridge is a shell which contains a bullet and an explosive substance such as gunpowder.

Core-needle biopsy A core-needle biopsy is a type of biopsy which obtains a tissue sample through a needle. The core-needle collects the tissue sample by cutting out a part of the tissue using a mechanism in the needle.

Fine-needle aspiration Fine-needle aspiration is a type of biopsy which obtains a tissue sample through a hollow needle. The tissue is drawn into a vessel by means of suction.

Firing pin A firing pin is a part of the trigger mechanism found in guns. A hammer is used to strike the firing pin. This impact is guided via the firing pin onto the ammunition, which will detonate the explosive inside the ammunition.

Formalin Formalin is a solution of formaldehyde and water, used to conserve organic specimens.

Histology Histology is the study of the structure and architecture of tissue on a cellular level.

Invasive procedure The medical term of invasive procedure refers to the way in which the instruments are required to the enter the body. A procedure is said to be invasive when a large incision is required to be made to enable entry into the living body. The smaller the required incision, the less invasive a procedure is.

Lesion A lesion is a general term for a region of tissue of an organism which is damaged or infected by a disease.

Nucleus The nucleus is a part of the cell that is the control center of the cell. It commands the growth and reproduction of the cell. The nucleus is the part of the cell which contains the chromosomes.

Oncologist An oncologist is a clinician who specializes in the diagnostics and treatment of cancer.

Pathologist A pathologist is a clinician who studies the cause, presence, and severity of a disease found in body tissue.

Radiologist A radiologist is a clinician who uses radiographic imaging techniques to examine patients.

CONTENTS

1 Introduction

1.1. Background

1.1.1. Diagnostics and Biopsy

The examination of a suspicious lesion is crucial in the diagnostics of a disease. Identifying information about the nature and character of the lesion is essential for determining the type of disease and an appropriate treatment plan [2]. This is often done using the so-called triple-test. The triple-test is a comparison of the results of three stages of examination [3, 4].

The first stage is an examination of the patient's medical history and a physical examination [5]. A physical examination can determine the approximate lesion site. For example when pain occurs at a certain site, or when the lesion is palpable.

In the second stage, imaging techniques are used for further examination. Non-invasive imaging techniques such as UltraSound Scans (USS), Magnetic Resonance Imaging (MRI) and Computer Tomography (CT) can be used for this purpose [5]. These initial examinations can determine the location, consistency, size, and shape of a lesion.

The last stage of examination is to perform a biopsy. A biopsy is the removal of tissue from the lesion site, which can be examined to determine the cause, presence, or severity of a disease [6]. Taking biopsies is essential for achieving an accurate diagnosis [7]. The aim of the biopsy is to provide sufficient and representative tissue from the lesion, to enable thorough examination [3, 7, 8]. After the biopsy has been taken, the tissue sample is sent to a pathologist who examines the architecture and structure of the cells. The pathologist investigates whether the tissue is a tumor or not, whether it is malignant or benign, and what the margins of the lesion are [8]. With these results, the patient is diagnosed, and a treatment strategy is determined.

1.1.2. Biopsy Techniques

Categorization

A biopsy can be taken from a variety of locations on the body. Examples of biopsy sites are bones, internal organs, and the skin. As there are many different biopsy locations, a variety of biopsy techniques exist. The choice of a certain biopsy technique depends on the lesion site, the consistency of the lesion [2], and also the training and expertise of the clinician [4]. No specific biopsy technique is superior over the other, each has their own advantages and disadvantages [4]. The various techniques can be roughly categorized into three categories, shown in Figure 1.1. These categories are distinguished by their invasivity. Excisional biopsy (a) is the most invasive biopsy technique, incisional biopsy (b) is slightly less invasive, and needle biopsy (c) is the least invasive biopsy technique. Each of these categories will be discussed individually.

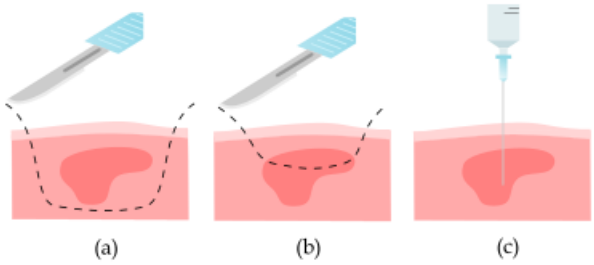


Figure 1.1: Schematic illustration of biopsy techniques on a lesion site. (a) Excisional biopsy, (b) incisional biopsy, and (c) needle biopsy.

Excisional Biopsy

Excisional biopsy is used to take the entire lesion and some of the surrounding tissue, as shown in Figure 1.1 (a) [7]. Excisional biopsy results in adequate sampling of the lesion, which makes the diagnosis easier and more accurate [4]. This biopsy method is also advantageous as it removes the entire lesion, which could serve as a treatment strategy. A disadvantage is that it is the most invasive biopsy method. The excisional biopsy procedure is time-consuming, the healing process may take long, and the procedure leaves scars. An excisional biopsy is not performed when the lesion site is too large, or when an excisional biopsy may cause threats to a vital organ [7]. In these cases an incisional biopsy is usually performed.

INCISIONAL BIOPSY

Incisional biopsy is less invasive than an excisional biopsy. During the procedure, a part of the lesion is cut away together with a small section of healthy tissue. This is illustrated in Figure 1.1 (b). Incisional biopsy has the advantage that it provides both accurate histological information of the lesion and a sample of healthy tissue which can be used for comparison. However, incisional biopsy is more invasive than a needle biopsy. Therefore, incisional biopsy is often performed when a foregoing needle biopsy was inconclusive, or when the lesion site is superficial [5, 8]. An incisional biopsy is more invasive than a needle biopsy, as it is used to take a representative section of the lesion by making an incision [5, 7]. Using incisional biopsy, larger samples of the lesion can be taken, providing a more accurate diagnosis than needle biopsy [4, 7]. Besides the advantages, incisional biopsy has some disadvantages. The first disadvantage is that an incisional biopsy is more time-consuming than taking a needle biopsy, as it is more invasive. The overall procedure time increases as well as the healing process of the patient. A second disadvantage is that the incision will leave scars, which is cosmetically undesirable [4].

NEEDLE BIOPSY

With a needle biopsy, shown in Figure 1.1 (c), the access to the lesion site is done by the puncture of a needle [5]. A needle biopsy has the advantage that it is fast and easy to perform, making it a cheap procedure [8]. A disadvantage to a needle biopsy is that it only takes a small portion of the lesion. This might cause the sample to not sufficiently represent the lesion, which could potentially cause an incorrect diagnosis [5].

A needle biopsy is a minimal invasive way to obtain tissue for diagnosis, as it does not require to make an incision into surrounding tissue. Therefore, it is often used as an initial biopsy method, making it the most commonly used method. This is why this thesis will solely focus on needle biopsy.

1.1.3. TYPES OF NEEDLE BIOPSY

FINE-NEEDLE ASPIRATION

Fine-needle aspiration obtains a small portion of a lesion through suction. Figure 1.2 shows a schematic illustration of the biopsy technique. The size of the needle used for fine-needle aspiration varies from 18 to 23 gauge needles (1.3 mm - 0.57 mm) [9]. During a fine-needle aspiration procedure, the lesion location is found by making use of a radiographic imaging technique. After confirming the lesion's location, the radiologist inserts a needle into the correct site. The sample, which is also called an aspirate, is obtained through the hollow needle by applying a vacuum [2]. At least 3 aspirates are needed from each lesion for an accurate diagnosis [2, 3].

The advantage of using the fine-needle aspiration technique, is that it is the least invasive biopsy technique causing little damage to the surrounding tissue. A disadvantage of using this technique is that it only samples a limited number of cells from the lesion, and it does not preserve the tissue structure. The tissue structure could give histological information about a disease. Therefore, fine-needle aspiration does not always guarantee sufficient representative material to diagnose [2].

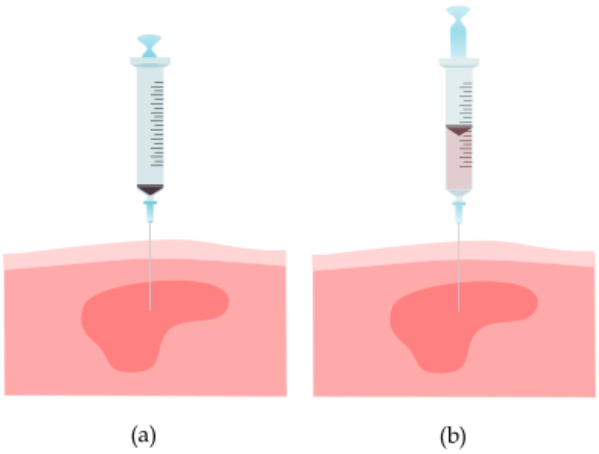


Figure 1.2: Schematic illustration of the fine-needle aspiration technique. (a) The needle is inserted into the lesion site, (b) a sample of the lesion is taken by aspiration. (Figure adapted from The National Breast Cancer Foundation [10])

CORE-NEEDLE BIOPSY

Core-needle biopsy obtains a small tissue sample that is cut away from the lesion. During a core-needle biopsy procedure, the lesion site is found using a radiographic imaging technique. When the lesion site is located, the needle is guided into the lesion [10]. A cutting mechanism in the needle subsequently obtains the biopsy sample. Three commonly used core-needle biopsy mechanisms are presented below.

The so-called BioPince mechanism [11], shown in Figure 1.3, retrieves the tissue using an inner needle which punctures the body to reach the lesion site. Subsequently a second hollow needle shaft enters the lesion site, enclosing a part of the lesion. A third shaft with a special "pincer" is used to cut off the front of the tissue from the lesion through a cavity located in the outer needle [11]. The size of the needle used for the BioPince biopsy varies from 14 to 18 gauge needles (2.1 mm - 1.3 mm) [12].

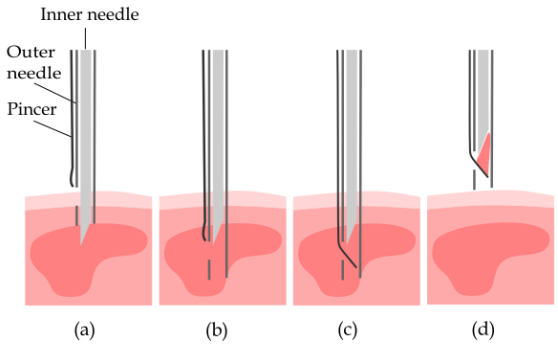


Figure 1.3: Schematic illustration of the BioPince mechanism [11]. (a) The inner needle punctures the body to reach the lesion site, (b) the second hollow needle enters the lesion site, (c) the "pincer" cuts off the front of the tissue sample, (d) the BioPince is retracted from the body, taking the biopsy specimen with it.

The second core-needle biopsy mechanism is the so-called TruCut mechanism, shown in Figure 1.4. This mechanism uses an inner needle which contains a notch on the side [13]. This inner needle is inserted in the lesion. A part of the lesion tissue will form into the side notch of the inner needle. Subsequently, a hollow outer needle cuts away and encloses the tissue sample. The size of the needle used for the TruCut biopsy varies from 14 to 18 gauge needles (2.1 mm - 1.3 mm) [12].

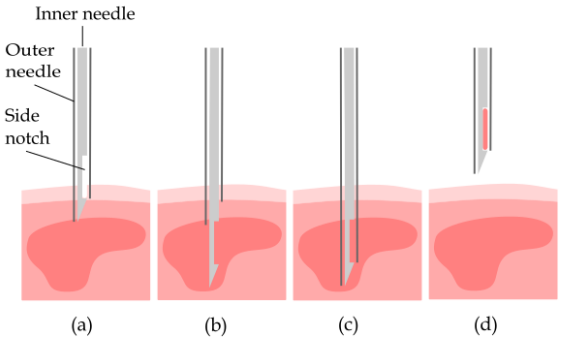


Figure 1.4: Schematic illustration of the TruCut mechanism. (a) The TruCut needle punctures the body to reach the lesion site, (b) the inner needle enters the lesion site, (c) the hollow outer needle cuts the tissue sample and encloses it in the shaft, (d) the TruCut is retracted from the body, taking the biopsy specimen with it. (Figure adapted from Edwards [13])

Vacuum-assisted biopsy is a method of obtaining a larger volume of tissue in comparison to the BioPince or TruCut mechanism. This technique is therefore mainly used when the lesion is spread over a larger area [14]. The vacuum-assisted biopsy technique is schematically shown in Figure 1.5. The size of the needle used for vacuum-assisted biopsy varies from 7 to 14 gauge needles (4.6 mm - 2.1 mm) [12]. The tissue is obtained through a side notch in the needle, assisted with a vacuum which actively draws in a tissue sample [3]. This results in a long tissue sample which is almost double in size compared to other core-needle biopsy specimens [3, 15]. Vacuum-assisted biopsy is the most invasive technique in the category of needle biopsies. The main advantage of using vacuum-assisted biopsy is that it is able to take a larger volume of tissue through one insertion of the needle [3]. Whereas for the BioPince and TruCut technique, it is often necessary to obtain a multitude of tissue samples to provide representative and sufficient tissue of the lesion.

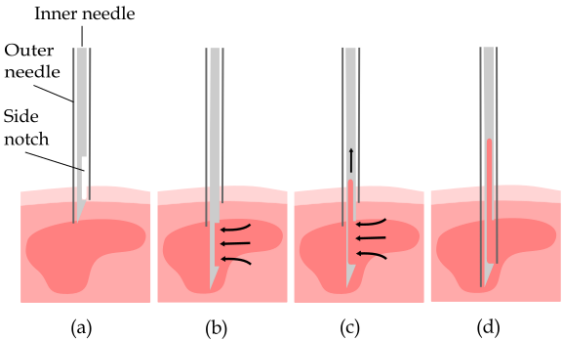


Figure 1.5: Schematic illustration of the vacuum-assisted biopsy technique. (a) The needle punctures the body to reach the lesion site, (b) the hollow inner needle enters the lesion site actively drawing in tissue by applying a vacuum, (c) The tissue is drawn into the needle shaft, (d) The outer needle cuts the attached tissue part, and encloses the sample into the shaft.

In comparison to fine-needle aspiration, core-needle biopsy is a little more invasive as it takes a larger sample of the tissue. Advantages of using core-needle biopsy over fine-needle aspiration is that the histology of the tissue sample remains intact, whereas the tissue obtained through fine-needle aspiration does not provide information about the tissue structure [3]. The accuracy of the diagnosis of the tissue sample provided by the core-needle biopsy depends on the tissue volume and the number of tissue samples sent to the pathologist [3].

1.1.4. BIOPSY SPECIMEN HANDLING

After the biopsy has been taken, the specimen of the biopsy is fixated using formalin [6, 15, 16]. This fixation prevents disintegration of the tissue sample and conserves its structure [16]. The tissue samples are contained in a container labelled with the patient's information, the biopsy site, and number of specimens. This is to prevent interchanging of the tissue specimens [6, 15]. Subsequently the tissue sample is sent to a pathologist. Before the pathologist can diagnose the specimen, the tissue has to be prepared. The biopsy samples are arranged into small containers [15]. These containers are sent to a system which replaces the moist in the tissue with paraffin wax [15]. The samples are then put

in a mold which is also filled with wax, creating a block with the tissue samples contained in them [15]. Subsequently the tissue is sliced into microscopically thin slices [15, 16]. The thin slices are put on a glass slide and dyed with pigment that attaches to certain parts of a cell, revealing the structure of the cell [15, 16]. Figure 1.6 shows an example of the result. The nucleus of the cell is dyed blue and the cell bodies are dyed pink [15, 16]. Special kinds of dyes can be used to target certain properties of the tissue. These dyes can for example target iron, pigment, or molds in the tissue [15]. This is mainly done when the pathologist suspects a certain disease and requires extra information to confirm the diagnosis [15]. With the prepared tissue, the pathologist is able to determine the diagnosis [15].

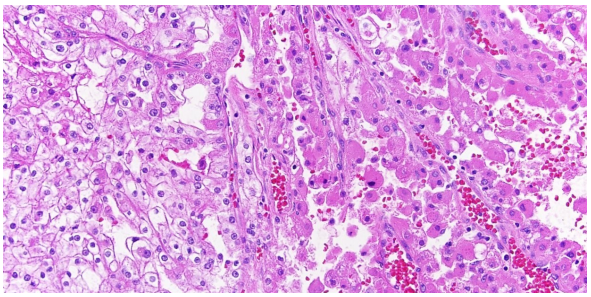


Figure 1.6: Photograph of biopsy specimen prepared for diagnosis. The blue dots indicate the nucleuses of the cells and the pink indicates the bodies of the cells. (Figure obtained from Andeen [17])

1.2. PROBLEM STATEMENT

When it is required to take a biopsy for the examination of a lesion, it is preferred to use a minimally invasive method. Therefore, incisional and excisional biopsies are only performed when absolutely necessary. The least invasive method is fine-needle aspiration. However, this technique does not provide histological information of the tissue, which is often desired for an accurate diagnosis. This is why core-needle biopsy is a commonly used biopsy technique as it both provides histological information and is minimally invasive.

Unfortunately, the diagnostics of a core-needle biopsy is not always as accurate as desired. Biopsy samples taken with core-needle instruments do not always represent the lesion sufficiently. This is due to difficulties locating the exact biopsy site using radiographic imaging. The clinician might miss the lesion with the biopsy needle, causing the biopsy sample to be taken next to the lesion site or only a small part of the lesion site. To increase the accuracy, and to prevent non-diagnostic results from the biopsy, sufficient samples or a larger volume of tissue should be taken from the lesion site [2, 3].

A solution to this problem is the vacuum-assisted biopsy technique. This method obtains a larger volume of tissue of the lesion. However, this technique is more invasive than the BioPince and TruCut technique as the needle used for this technique is often larger than the needles used for the BioPince and TruCut. Therefore this technique is only used when the lesion site is spread over a large area [14]. The more commonly used core-needle methods such as the BioPince and TruCut techniques solve the problem by obtaining a multitude of samples. These techniques currently obtain a single biopsy sample per insertion of the needle into the lesion. As multiple specimens have to be obtained, multiple insertions of the biopsy instrument are required. To obtain a number of specimens, the biopsy instrument has to be retracted after a single sample has been taken and reinserted a couple of times during a procedure. This process may cause unnecessarily long procedures. Next to the time it takes to reinsert an instrument, the invasivity of the biopsy might increase as well. The lesion site requires to be punctured a couple of times to retrieve several biopsy samples. This causes unnecessary discomfort, and harm to the patient. Therefore, this research will look into solutions for a design of a single-insertion multiple sample core-needle biopsy device.

1.3. GOAL

The aim of this thesis is to design a single-insertion multiple sample core-needle biopsy instrument. The design will be able to obtain a multitude of biopsy specimens and store them systematically. The focus of this thesis will be on core-needle biopsy instruments, as this technique is commonly used in a large variety of biopsy locations: from internal organs to superficial spots such as the breasts or lymph nodes.

1.4. THESIS STRUCTURE

The outline of this thesis will be a description of the design process of a single-insertion multiple sample biopsy instrument. Chapter 2 describes the state of the art and its limitations. The list of requirements will be described in Chapter 3. In Chapter 4 several conceptual designs will be described. From these designs, a selection will be made of the most promising designs, and the final design will be selected and elaborated. The elaboration and final design will be described in Chapter 5. Of this final design, a prototype will be made. The process of fabrication and assembly of the prototype will be described in Chapter 6. The prototype will be evaluated with a proof of concept experiment in Chapter 7. This will be concluded with a discussion of the design in Chapter 8, followed by a conclusion in Chapter 9.

2 State of the Art

2.1. Conventional Biopsy Instrument Research

To determine the state of the art of biopsy instruments, a general search was conducted on Google. This was done to gain insights into existing biopsy instruments and to find conventional instruments which are able to obtain a multitude of biopsy samples through a single insertion. Next to the general search, an oncologist, a pathologist and a radiologist were visited to gain insights into the methods and instruments used for a biopsy [14, 15].

The general search resulted into no found existing biopsy devices which are able to obtain multiple samples. Also, the consults with the various clinicians did not result in a suggestion of the availability of such a device [14, 15]. From these findings, it can be stated that up to now there are no conventional biopsy instruments on the market which are able to obtain multiple biopsy samples through a single insertion.

2.2. Patent Research and Classification

Next to the general search, a search through available patents was conducted. There are patented designs available for multiple sample biopsy devices. It is important to look into these existing designs to identify if there is a need for redesign. An elaboration of the database search can be found in Appendix A. Two patent databases were searched for existing designs, Free Patents Online (FPO) and Espacenet. The FPO database was searched using the search query:

> *TTL/(Biopsy) AND ABST/((Instrument* OR Device* OR Tool* OR System* AND Specimen OR Sample OR Tissue AND Collect* OR Stor* OR obtain) AND (Multi* OR Dual* OR Triple* OR Variety OR Numer* OR Series OR Serial))*

This resulted in a total number of 92 patents. The Espacenet database was searched, using the search query:

> *(Biopsy) AND (Instrument* OR Device* OR System*) AND (Specimen OR Sample OR Tissue) AND (Collect* OR Stor*) AND (Multi* OR Serial)*

This resulted in a total number of 47 patents. The retrieved patents were merged giving a total number of 139 patents. From these patents, duplicates, ineligible, and inaccessible patents were removed leaving a total number of 27 patents.

These 27 patents can be categorized based on the method of transportation of the biopsy sample. Each design requires to transport the tissue sample through the instrument to make way for a new specimen. This transportation can be done in several ways. During transportation either a variety of forces act directly on the tissue sample, or no forces act on the tissue. The latter can be achieved by encasing the sample and applying forces on the container. This classification of transportation is shown in Figure 2.1.

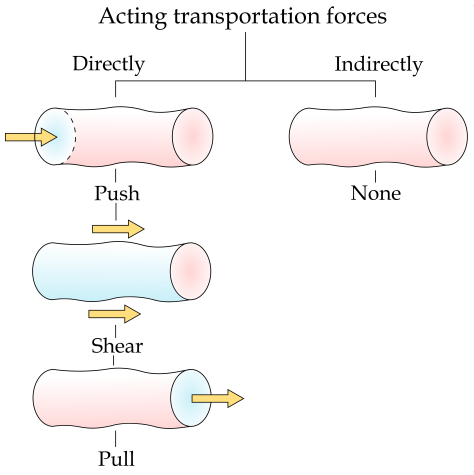


Figure 2.1: Categorization of biopsy specimen transport based on acting forces. The forces can either be applied directly onto the tissue, or indirectly via an encasement around the tissue sample.

The tissue sample is roughly cylindrically shaped due to the shape of the biopsy needle. By using this shape, a distinction can be made between a variety of locations on which the forces act. The tissue can either be transported by pushing forces acting on the front of the tissue sample, shear forces which act on the sides of the tissue sample, or pulling forces which act on the back of the tissue sample. For each category, a couple of examples of patents will be given.

2.3. TRANSPORTATION FORCES

2.3.1. PUSHING FORCES

A variety of patented designs use a pushing force to transport multiple biopsy samples. Figure 2.2 shows three examples of patents that were found using this method of transportation.

The first example, shown in Figure 2.2 (a), is designed by Taylor *et al.* (patent no. US8267868 B2) [18]. In this design, cylindrical segments connected to a cable are used to transport the biopsy sample towards the handle. The segments apply a pushing force on the tissue, which transports the sample through the instrument's shaft. The specimen can subsequently be stored in the handle, or simply be extracted from the instrument one by one.

Figure 2.2 (b) shows a push transport mechanism, by Banik *et al.* (patent no. US5471992) [19]. This biopsy grasper is able to pull a segment of the grasper tip backwards by a cable. This will push the tissue specimen into the instrument shaft. A similar design to this design was again patented four years later by Banik *et al.* (patent no. US5871453) [20].

Figure 2.2 (c) shows an example of a beak-like biopsy forceps, by Robinson *et al.* (patent no. US5573008) [21]. This design uses the force of pressing the beak into the tissue, to push previously taken samples further into the instrument's shaft.

2.3.2. SHEAR FORCES

The second category of designs found in the patents contained multiple sample biopsy devices which use shear forces on the tissue as a transportation mechanism.

Figure 2.3 (a) shows a design which uses shear forces to transport the tissue specimen. The outer needle pulls the specimens further into the needle shaft by making use of the friction force between the outer needle and the tissue. This friction force acts on the sides of the tissue sample and should be larger than the friction between the sample and the inner needle. This way, by pulling back the outer needle, the samples are transported into the instrument shaft. This design is made by Chu *et al.* (patent no. US5810744) [22]. A similar design using shear friction forces to transport the biopsy samples was developed by Banik *et al.* (patent no. 5601585) [23].

The designs shown in Figure 2.3 (b) and (c) are both designed by Coonahan *et al.* (patent no. US8282574 B2) [24]. Design (b) shows a conveyor mechanism which grabs the tissue samples and pulls them backwards using shear forces. (c) Shows a measuring tape construction which can be rolled up while retracting the specimens backwards. The specimens are held onto the mechanism by their friction force. At the end of the shaft, the specimens are dropped into a container.

Other designs which use a shear force on the tissue, not shown in a figure, create a shear transportation force by rotating a screw-like mechanism around the tissue specimen. Miller (patent no. US6530891 B2) [25], and Peliks developed such a device to transport multiple biopsy specimens (patent no. WO2016/196536 A1) [26]. A final variation of using shear transportation forces is designed by Bryan *et al.* (patent no. US6488636 B2) [27]. In this design, a shear transportation force was created by applying a vacuum on the sides of the tissue sample via a needle. This needle is subsequently transported back into the instrument.

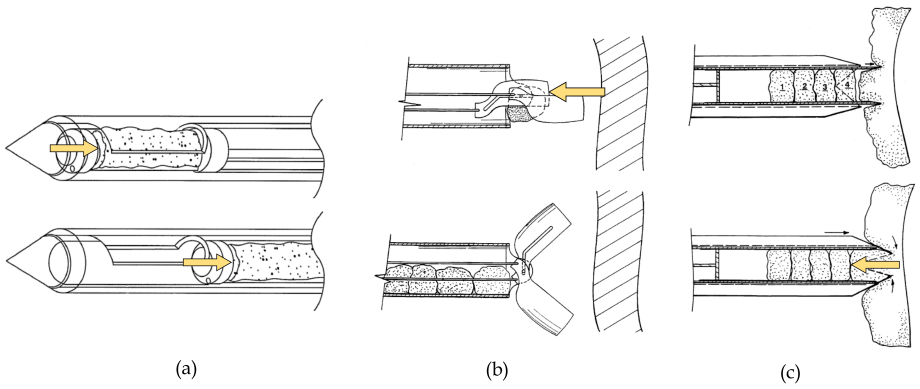


Figure 2.2: Single-insertion multiple biopsy instruments using a pushing force to transport the biopsy samples. Patents by (a) Taylor *et al.* patent number US8267868 B2 [18], (b) Banik *et al.* patent number US5471992 [19], (c) Robinson *et al.* patent number US5573008 [21]

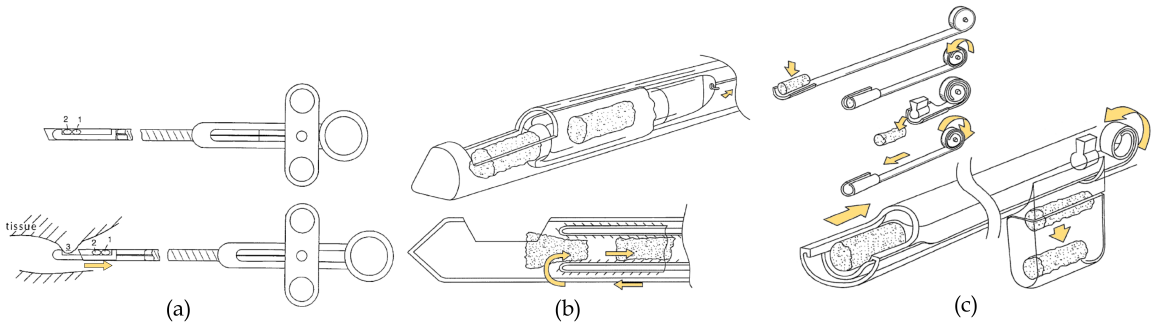


Figure 2.3: Single-insertion multiple biopsy instruments using a shear force to transport the biopsy samples. Patents by (a) Chu *et al.* patent number US5810744 [22], (b) and (c) Coonahan *et al.* patent number US8282574 B2 [24].

2.3.3. PULLING FORCES

Patents also contained a design which used a pulling force to transport the tissue samples. Figure 2.4 shows a design which uses a harpoon to pull a multitude of samples into the biopsy instrument shaft. After taking a new biopsy, the harpoon enters the tissue and stacks it onto its shaft. This design was made by Diamond *et al.* (patent no. US6142957) [28]. Similar designs to this transportation method were made by Dassa *et al.* (patent no. 5840044) [29], Gundberg *et al.* (patent no. WO2015/063071 A1) [30], Taylor (patent no. US6419640) [31], and Nakao (patent no. US7775989 B2) [32].

Other patents were found which apply a pulling force on the tissue by using a vacuum. A large variety of alternatives to this general idea were patented by Hibner *et al.* (patent no. US7740596 B2, US7867173 B2, US8118755 B2, US7753857 B2, US7867173 B2) [33–37], Treat (patent no. US6632182 B1) [38], Zimmon (patent no. 6071248) [39], Burbank *et al.* (patent no. 5928164) [40], and Farascioni (patent no. 6019733) [41].

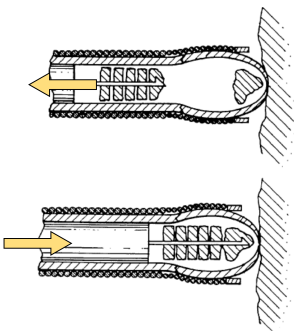


Figure 2.4: Single-insertion multiple biopsy instrument using a pulling force to transport the biopsy samples. Patent by Diamond *et al.* patent number US6142957 [28].

2.3.4. INDIRECT APPLIED FORCES

Some patents contained designs where no forces were applied directly on the tissue. The tissue samples are enclosed and subsequently transported through the instrument's shaft.

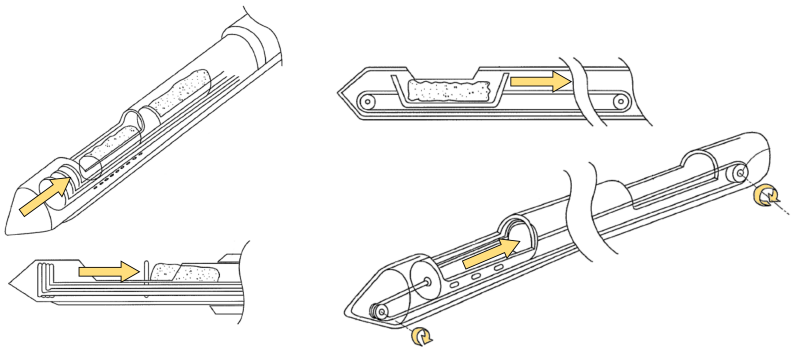
Figure 2.5 (a), by Coonahan *et al.* (patent no. US8282574 B2) [24], shows a design which contains several "drawers" in which specimen are caught. Each drawer can be pulled inside the shaft, creating space for a new biopsy sample to be taken.

The design shown in Figure 2.5 (b), is also made by Coonahan *et al.* (patent no. US8282574 B2) [24]. This design uses a conveyor-like construction in a needle, where the biopsy is stored in a container which can be pulled to the back of the shaft. At the back of the needle shaft, the biopsies can be taken out one by one. A similar design to this design was made by Thompson (patent no. US8262582 B2) [42].

Two alternative designs were found, not shown in a figure, in the patent database. Both these designs transport the samples after they have collectively been obtained. The first alternative design used a basket to catch a multitude of biopsy samples. When the procedure is finished, the basket with the multitude of specimens can be retracted from the body. This design was patented by Turkel *et al.* (patent no. 5643307) [43]. The second alternative design was developed by Damarati (patent no. US6858014 B2) [44]. This design is able to collect a multitude of samples at once using separate collecting chambers. After the procedure, the device can be retracted.

2.4. PATENT LIMITATIONS

The shown designs all have the purpose to obtain a multitude of biopsy specimens through a single insertion. This is achieved either with biopsy forceps or biopsy needles and a variety of transportation methods. Each design complies to this general purpose. However, the large variety of patented designs still come with limitations regarding the retrieval of multiple biopsies. A large number of the patents use a transportation method which apply forces on the biopsy sample. The biopsy sample is usually sketched as a cylindrical and solid tissue "block". However, this is an approximation to an actual biopsy specimen.



(a) (b)

Figure 2.5: Single-insertion multiple biopsy instruments using a pulling force to transport the biopsy samples. Patents by (a) and (b) Coonahan *et al.* patent number US8282574 B2 [24].

Figure 2.6 shows an actual biopsy sample. The biopsy specimen is usually about 1 mm thick [45, 46] and has an average length of approximately 15 mm [47]. The biopsy sample can consist of hard and solid tissue, but also of softer tissue. The size and the consistency often makes the specimen fragile. When applying large forces onto the sample, it might loose its structural architecture [15]. The sample might become compressed, entangled, clumped together, or even pulled apart. Entangled and clumped tissue samples will have to be disentangled and taken apart by a clinician after the biopsy procedure. Compressed tissue samples might lose their structural architecture, and stretched tissue might break into multiple pieces. Therefore, it is not desirable to apply forces onto the biopsy specimen.

A second limitation to some of the designs is cross contamination. This may become a problem when tissue samples touch each other directly. Diseased tissue samples might contaminate healthy tissue samples when contacting each other. This might cause wrong diagnoses.

Not all of the patented designs have these limitations. Subsection 2.3.4 describes two designs by Coonahan *et al.* [24] (Figure 2.5 (a) and (b)), which apply forces on a chamber which contains the biopsy material. This keeps the integrity of the biopsy sample and prevents cross contamination. However, these designs use a complex inner mechanism. Implementing these designs in 14 to 18 gauge needles will be very complex, as it is such a small scale. This will make the production very complicated and the mechanism fragile.

These limitations to the current state of the art cause a need for redesign. Important aspects for this redesign are the preservation of structural architecture of the tissue sample, and the prevention of cross contamination.

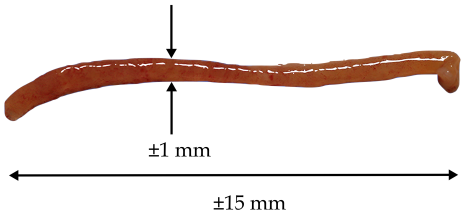


Figure 2.6: Image of a biopsy sample from a needle biopsy. (Figure adapted from RCPA [48])

3 Requirements

3.1. Area of Interest

As stated in Section 1.3, the goal of this research is to design a core-needle biopsy instrument which is able to obtain multiple samples through a single insertion. This will not include vacuum-assisted devices. For this type of core-needle biopsy multiple insertions are not necessary, as a large volume of tissue is obtained using this method. Figure 3.1 shows the intended use of the novel biopsy instrument. The biopsy samples can be retrieved from the same lesion site in different angles, from the same lesion site at the same location or with varying depths, or from a variety of lesion sites. An important aspect for this design is to look into ways to take a multitude of biopsy samples in such a way that the tissue architecture is preserved and cross contamination of the samples is prevented.

3.2. Requirements

3.2.1. Geometric Requirements

The requirements state the conditions to which the design must be in accordance with. These conditions will emphasize and comprise the design goal. The geometric requirements state the criteria to which the size and shape of the design must comply to. These requirements can be obtained by identifying important specifications of current existing core-needle biopsy instruments. For the geometric requirements, three aspects of the instrument are important to be considered. First, the needle must be minimally invasive. This means that the needle should not exceed the maximum size of current existing core-needles. Secondly, it is important for the pathologist to receive a sufficient sized biopsy sample. Therefore, geometric design requirements are set for the biopsy sample size. The sample should not be smaller than the current size of a biopsy sample. Finally, the design of the instrument itself must be within usable boundaries. This means that the instrument handle should not be unmanageable by the user. For these geometric requirements, basic ergonomic rules of instrument design are considered.

The geometric requirements are set up in a list shown in Table 3.1. The list of requirements states what specifications the design should fulfill. The acceptance criteria gives a measurable or concrete goal of when the requirement is met. Finally, a short description of the requirement will be given.

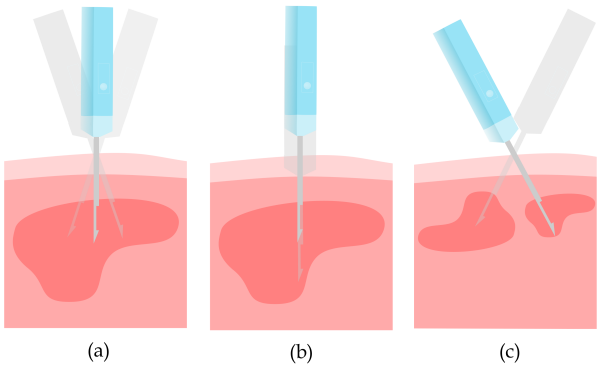


Figure 3.1: Schematic illustration of intended use of the design. (a) Shows multiple samples taken from the same lesion in different angles, (b) shows multiple samples taken from the same lesion at the same location or at different depths, and (c) shows multiple samples taken from a variety of lesions.

Table 3.1: List of geometric requirements.

1	**Needle geometry**		
#	Geometric requirements	Acceptance criteria	Description
1.1	Needle shaft length	Range of 60-200 mm	The lengths of current biopsy needles vary in a range of 60-200 mm, according to their application [9]. Therefore the instrument should be able to be made in a variety of different shaft lengths.
1.2	Needle tip and shaft diameter	Maximally 2.1 mm	To keep the biopsy instrument minimally invasive, the size of the needle should not exceed the maximum size of existing core-needles. The size of current core-needle instruments varies between 14 gauge (2.1 mm) to 18 (1.3 mm) gauge [9]. Therefore, the needle tip and shaft diameter should have a maximum diameter of 2.1 mm.
1.3	Needle shaft shape	Cylindrically shaped	The shaft of the instrument should be cylindrically shaped, as this is the standard shape of needle shafts.

2	**Biopsy specimen geometry**		
#	Geometric requirements	Acceptance criteria	Description
2.1	Biopsy length	Minimally 10 mm	Lengths of biopsy samples vary between 10 mm - 20 mm [9]. The length of the biopsy specimen should be minimally 10 mm. This is important for an accurate diagnosis of the sample [47, 49].
2.2	Biopsy diameter	Minimally 0.4 mm	Diameters of biopsy samples vary between 0.4 and 1.1 mm [50]. The sample size of the biopsy should be minimally 0.4 mm. However, to increase tissue volume, and to keep the specimen manageable during further processing [15], the diameter of the biopsy specimen should be as large as possible.

3	**Instrument geometry**		
#	Geometric requirements	Acceptance criteria	Description
3.1	Instrument grip length	Minimally 75 mm	The grip length of the instrument must have a minimum length of 75 mm. This length is a human factors standarization of NASA for a tool which is held using a palm grasp [51].
3.2	Instrument grip diameter	Maximally 75 mm	The diameter of the grip must not become larger than 75 mm. This diameter is determined by NASA's human factors standarization [51].

3.2.2. FUNCTIONAL REQUIREMENTS

To determine the functional requirements, a functional analysis is carried out. This analysis describes the main functions of the design. The functions of this design are schematically shown in Figure 3.2. The functionality of the design can be divided into three main steps; A, B, and C. Step A is the insertion of the instrument into the lesion site. Step B is the sequence of a series of actions to obtain a multitude of biopsy samples. This sequence is to be repeated until enough biopsy samples have been taken. Finally, step C is the retraction of the instrument from the body.

Function B consists out of a series of five actions. These actions are composed of functions the instrument has to perform to obtain a multitude of biopsy samples. Each of the actions are described and explained individually.

1. **Collect**: The instrument must be able to collect biopsy samples. To achieve this, the instrument must obtain and cut away tissue. This can be achieved by for example using the TruCut collecting mechanism. An important aspect of this function is that the instrument should reach the lesion site in a minimally invasive manner, and solely collect the required amount of tissue. This is to prevent unnecessary harm to the patient.

2. **Enclose**: As stated in Section 2.4, the tissue architecture must be preserved after it has been collected. Maintaining tissue integrity is important as the histological information of the tissue is necessary for the diagnosis. Therefore, it is important to enclose the specimen in a container. The container will prevent structural damage of the tissue during transportation and storage. Another important aspect of the enclosing function is the prevention of potential cross-contamination of tissue specimens. If healthy tissue samples would come in contact with diseased tissue samples, the tissue samples might contaminate each other. This may cause wrong diagnoses.

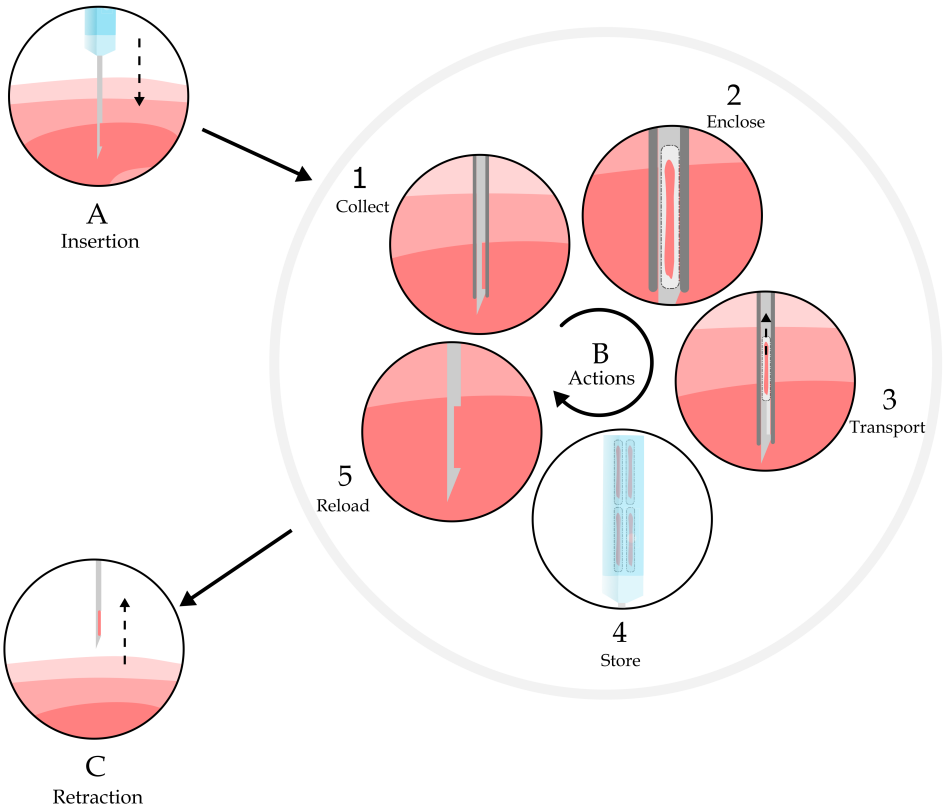


Figure 3.2: Schematic illustration of functional analysis of the design. Step A is to insert the needle into the lesion site. Step B is to start the action sequence with which a multitude of biopsy samples can be taken. This action sequence consists out of: 1. collecting the tissue sample, 2. enclosing it in a container, 3. transporting this container towards the instrument's handle, 4. storing the containers inside the handle, and 5. reloading the instrument so that the sequence can be repeated. Finally, when a multitude of biopsies are taken, step C is to retract the instrument from the body.

3. **Transport**: The instrument should be able to transport the tissue samples. This is required to make way for a new tissue sample. An important aspect of this function is the traceability of tissue specimens. Keeping track of the specimens is important as clinicians might want to trace back the biopsy sequence for each sample after the procedure.

4. **Store**: The instrument should be able to store the biopsy samples. After the procedure, the clinician will be able to retrieve these stored specimens from the instrument. Again, an important aspect in the storing function is that the biopsy samples should remain traceable. Finally, it is important for the stored biopsy samples to be easily accessible after the procedure.

5. **Reload:** The final action is the reloading of the instrument. After the previous actions, the instrument must be reloaded to be able to take a new biopsy. This reloading mechanism must reset the instrument so that it can continue the sequence of actions. This way the instrument will be able to take a multitude of specimens.

The functional analysis will form a set of design requirements, provided in Table 3.2 and Table 3.3, which can be used as individual quantitative and concrete goals. The list of functional requirements is divided into categories based on the main functions of the design, with their associated requirements.

Table 3.2: List of functional requirements.

A	**Insertion**		
#	Functional requirements	Acceptance criteria	Description
A	Insert and reach	Needle tip	To insert and reach the lesion site the instrument must have a needle tip.

B	Actions		
1	**Collect**		
#	Functional requirements	Acceptance criteria	Description
1.1	Biopsy retrieval number	Minimally 3 biopsy samples	The instrument should be able to deliver a minimum of 3 biopsy samples. This requirement is set to 3 based on the current number of samples averagely taken during a biopsy (1-6 biopsies) [15].
2	**Enclose**		
#	Functional requirements	Acceptance criteria	Description
2.1	Integrity	No loss of structural architecture of tissue samples	Throughout the entire biopsy procedure the obtained specimens should be kept intact and its structural integrity should be maintained.
2.2	Sanitation	No direct contact between tissue samples	The biopsy samples should be kept clean to prevent cross-contamination. Therefore the samples should not come into direct contact with each other.

Table 3.3: List of functional requirements.

3	**Transport**		
#	Functional requirements	Acceptance criteria	Description
3.1	Integrity	No loss of structural architecture of tissue samples during transport	Throughout the entire biopsy procedure the obtained specimens should be kept intact and its structural integrity should be maintained.
3.2	Traceability	Each specimen should be traceable in the retrieval sequence of the biopsy samples	To prevent interchanging and loss of biopsy specimens, it is important for the instrument to be able to keep the specimens traceable and ordered during transportation.

4	**Store**		
#	Functional requirements	Acceptance criteria	Description
4.1	Traceability	Each specimen should be traceable in the retrieval sequence of the biopsy samples	To prevent interchanging and loss of biopsy specimens, it is important for the instrument to be able to keep the specimens traceable and ordered in the storage.

5	**Reload**		
#	Functional requirements	Acceptance criteria	Description
5.1	Intuitive	Intuitive reloading	The user must be aware of when the instrument is reloaded. This prevents the user to try to take a biopsy with an unloaded instrument.

C	**Retraction**		
#	Functional requirements	Acceptance criteria	Description
C	Accessibility	Easy removal of biopsy	The biopsy specimen should be able to be removed easily from the instrument after the biopsy procedure is done.

4 Conceptual Design

4.1. Inspiration

The functional analysis resulted into five main actions which the instrument has to be able to execute. The instrument must be designed to be able to collect, enclose, transport, store, and reload itself in order to obtain multiple biopsy samples. Inspiration of this general design idea was found in the weapons department. Similarities can be found in the working principles of a gun. But instead of firing a bullet into a target, the instrument must work in an inverted way. This is shown schematically in Figure 4.1. The "bullet" enters the body and collects and encloses a biopsy specimen (1 and 2). Subsequently, the bullet must go in a reverse direction through the shaft, towards the ammunition chamber (3). It is then stored systematically into the ammunition chamber (4). Finally, the instrument must be reloaded to be able to take a new specimen (5).

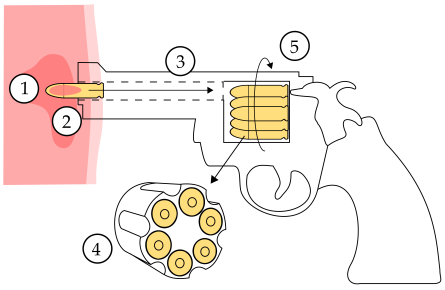


Figure 4.1: Schematic illustration of the design inspiration. 1. The inverted gun is able to collect a tissue sample, 2. enclose it in a bullet, 3. transport it back into the instrument and 4. store it systematically. Finally, 5. the instrument is reloaded to be able to take a new biopsy sample.

The five main actions of the instrument will form the backbone of the conceptual design process. Each action will describe a different design step. Three of these actions have common ground with the working principles of guns. Inspiration for this part of the design can be found in a large variety of guns, which are able to shoot, store and reload their munition in diverse manners. This gives insights into how to store and capture multiple biopsy samples. This chapter will first describe the working principles of a variety of guns. Subsequently, the conceptual design process will be described step by step, based on the functional analysis.

4.2. Guns

4.2.1. Shooting a Bullet

In this section a closer look will be taken at the working principles and mechanisms behind a gun. A large variety of guns exist. However, for each type of modern-day gun the firing of the bullet is done using the same working principle. Figure 4.2 shows the firing mechanism of a standard handgun. The gun uses a trigger (a) to release a hammer (b) at the back of the gun. The released hammer will hit the back of the ammunition via a so called firing pin [52]. The firing pin will give an impulse at the back of the ammunition. The ammunition, or cartridge, consists out of a shell which contains gunpowder, and a bullet. By releasing the hammer onto the back of the shell, the gunpowder explodes (c). This explosion causes a rapid expansion of gas, causing the bullet to shoot out of the shell, through the gun shaft, and into the target (d) [52].

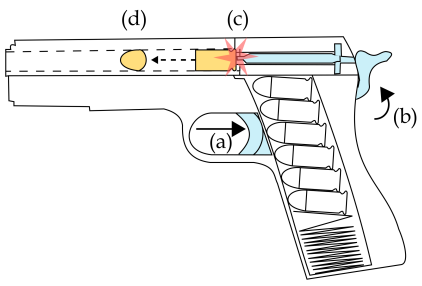


Figure 4.2: Schematic illustration of firing mechanism of a handgun. (a) By pulling a trigger, a hammer (b) will be released, causing an explosion inside the cartridge (c) which will shoot the bullet through the shaft (d).

4.2.2. GUN TYPES

CATEGORIZATION

The shooting mechanism as described is implemented in a large variety of guns. A division can be made between these guns based on their loading mechanism. The loading mechanisms of guns can be categorized into non-automatic, semi-automatic, and fully-automatic. A gun is said to be automatic when the bullets are reloaded by making use of the energy released by the firing of the bullet, the recoil [53].

NON-AUTOMATIC GUNS

An example of a non-automatic gun is the revolver, shown in Figure 4.3. The revolver uses a barrel-like ammunition chamber in which the bullets can be stored in a tangential direction, shown in Figure 4.3 (a). To load the gun, the ammunition chamber can be rotated by pulling the trigger. This is shown in Figure 4.3 (b). The barrel is rotated by a ratchet mechanism (indicated in yellow), which is connected to the trigger. By pulling the trigger, the ratchet rotates the barrel [54]. This way, a new bullet is aligned with the gun shaft. At the same time, the hammer (indicated in blue) is cocked which puts tension on a spring located inside the revolver's handle. By pulling the trigger the tension on the spring will be released, discharging the hammer and firing the gun.

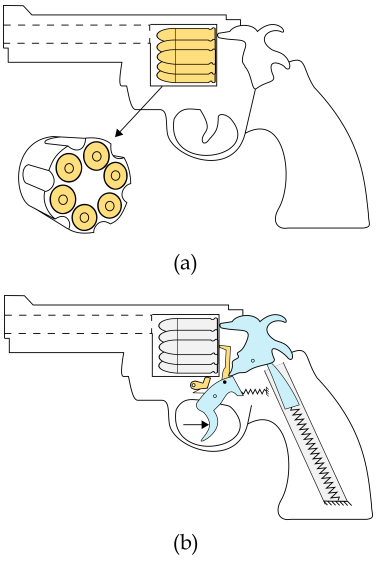


Figure 4.3: Schematic illustration of a revolver. (a) Shows the storage of bullets inside the revolver. The bullets are stored in a tangential manner inside a barrel. (b) Shows the trigger mechanism, which both fires the gun and rotates the ammunition chamber. The trigger and the hammer are indicated in blue. The ratchet mechanism which rotates the chamber is indicated in yellow.

SEMI-AUTOMATIC GUNS

An illustration of a semi-automatic handgun is shown in Figure 4.4. The handgun has an ammunition chamber in the handle, shown in Figure 4.4 (a). The bullets are stacked in a radial direction inside the handle of the gun. The reloading of these bullets happens in a semi-automatic manner. This is shown in Figure 4.4 (b). When the bullet is fired, the energy of the explosion causes the upper part of the gun to recoil. This way, a gap is opened between the ammunition chamber and the gun shaft [52]. The new bullet is pushed up into the gun shaft by a spring located underneath the stack of bullets. The new bullet pushes the remaining empty shell out of the top of the gun.

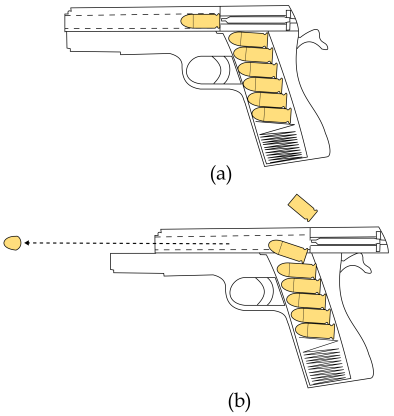


Figure 4.4: Schematic illustration of a semi-automatic handgun. (a) Shows the method of storage of the bullets inside the gun's handle, in a radial direction. (b) Shows the reloading mechanism of the handgun.

FULLY-AUTOMATIC GUNS

A fully-automatic gun, also known as a machine gun, is shown in Figure 4.5. A machine gun has a strip of bullets which are attached parallel to each other, and stored outside of the gun, as shown in Figure 4.5 (a). The fully-automatic gun is able to fire its bullets rapidly. The gun will keep firing bullets while the trigger is being held. The reloading mechanism of the fully-automatic gun is quite complex, therefore a simplification is shown in Figure 4.5 (b). The firing of a bullet causes a part of the gun to recoil (shown in blue). Due to the recoil, a spring will be compressed behind this part. In turn, the spring will push back the recoiling part, making it reciprocate [55]. A mechanism shown in orange is attached to the blue arm, and moves with this reciprocating part. This orange part will push the bullet into the gun shaft and fire the bullet via a firing pin [55]. A green arm continuously grabs the next bullet from the ammunition-strip [55]. This arm moves from side to side due to the reciprocating motion made by the blue part. This is all done very rapidly, enabling the gun to vigorously fire many bullets.

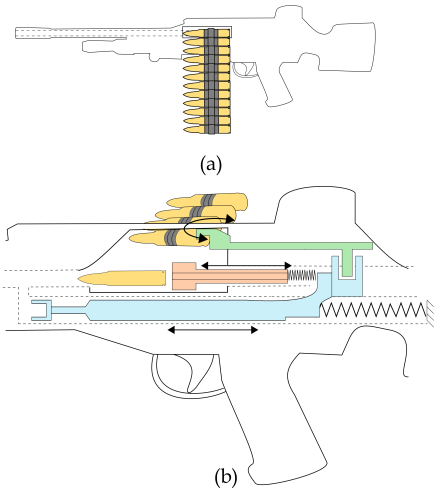


Figure 4.5: Schematic illustration of a machine gun. (a) Shows the storing of the bullets. The bullets are stored parallel to each other in a strip. (b) Shows a simplified representation of the reloading mechanism. Due to the firing of the bullet, a part of the gun, indicated in blue, recoils. Attached to this part is an orange part which pushes the bullet into the gun shaft and subsequently fires it. The arm indicated in green grabs the next bullet in the strip and moves it into the gun due to the reciprocating motion caused by the recoil.

4.3. CONCEPTUAL DESIGN

4.3.1. COLLECT

The overall idea of the design is shown in Figure 4.1. For each function of this design idea, a conceptual design will be made. The full brainstorm, and its elaboration can be found in Appendix B. This section will provide a summary of the brainstorm. The first function is the collecting of the biopsy samples. For this function, conceptual design ideas are generated based on designs of existing biopsy devices. In order to collect a biopsy specimen, a tissue sample of the lesion has to be cut away. Devices as presented in Section 1.1.3, such as the BioPince and the TruCut, both use a different method for achieving this. Based on their working principle, a couple of additional concepts are generated. The needles of the BioPince and TruCut use either the top or the side to collect the tissue. Other concepts can be generated based on this categorization. This is done to explore the possibilities of tissue collecting methods.

A selection of the concepts generated in the brainstorm are shown in Figure 4.6. The existing BioPince mechanism (a) collects the biopsy sample using the top of the needle. By puncturing the lesion, a tissue sample enters the hollow needle. To loosen the tissue sample from the lesion, a pincer is used to cut the front of the tissue sample. An alternative design for this concept is shown in (b). The pincer can be inside the hollow needle instead of outside. (c) Shows a conceptual design which uses double pincers outside the needle to cut the tissue from the lesion.

Another option is to collect the tissue specimen using a notch as the side of the needle. (d) Shows the existing TruCut mechanism. The sample is collected in a notch on the side of the inner needle. A hollow outer needle slides over this side notch, cutting the tissue loose from the body. An alternative, shown in (e), is similar to the existing TruCut design. This concept uses an inner needle instead of an outer needle to cut the tissue. Finally (f) shows a design with which the outer needle is twisted around the inner needle to cut the tissue.

The selection of the final concept for the collecting function of the design is based on two selection criteria. The first criterion is the invasivity of the design. The invasivity criterion entails the amount in which the mechanism will damage the surrounding tissue unnecessarily. The second selection criterion is the complexity of the mechanism. Complex mechanisms might not be able to fit inside a small needle shaft, or will make the mechanism fragile or hard to produce.

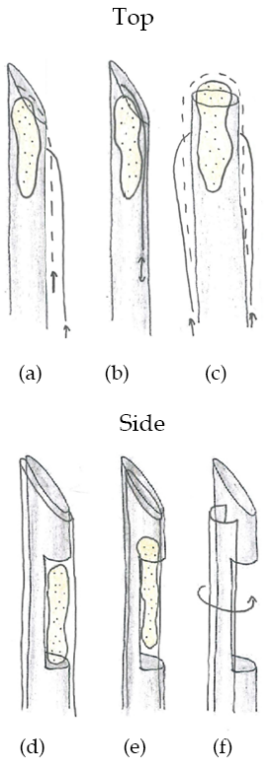


Figure 4.6: Conceptual designs of the collecting function of the instrument. (a) The existing BioPince mechanism. (b) Alternative design of the BioPince, with a pincer inside the needle shaft. (c) Concept which uses two pincers outside the needle shaft to cut the tissue at the front. (d) The existing TruCut mechanism. (e) Alternative of the TruCut mechanism with an inner needle that cuts the tissue sample. (f) A concept with an outer needle that twists around the inner needle to cut the tissue sample.

Based on these criteria it is decided to use the existing TruCut design (d) for the novel biopsy instrument. The top collecting mechanisms (a), (b), and (c) are more complex compared to the TruCut mechanism. This is because each top collecting mechanism requires an additional third needle which is only used to puncture the lesion site. Without this needle, the hollow needle would collect tissue all the way from the skin to the lesion site. The alternative designs which collect the tissue using a side notch, (e) and (f), achieve the same result in terms of collecting tissue compared to the existing TruCut mechanism. These designs are not selected because the TruCut design has been used in a large variety of biopsy instruments already. Developing a novel method of collecting tissue samples would be more complex to achieve than using an existing collecting method. As the alternative designs do not provide any advantages, it is decided to use the existing TruCut design for collecting the tissue. This mechanism is simple, minimally invasive, and has proven its worth in practice.

4.3.2. ENCLOSE

To prevent the tissue from being damaged or contaminated by other tissue samples, it has to be enclosed in some kind of bullet or container. A variety of conceptual designs are made for the enclosing function, of which a couple are shown in Figure 4.7. The biopsy specimen can either be fully captured, or partly captured by the container. To fully capture the tissue sample, the compartment has to be closed off entirely.

(a) Shows a container which partly encloses the biopsy sample. This concept is a small hollow tube, which can slide over the tissue sample to capture it. Concept (b) is a similar conceptual design to the tube. In this design one side is closed at the back of the container, like a barrel. (c) Shows a container which fully encloses the tissue sample. A hollow barrel can slide over the tissue sample, capturing it, and a lid at the front closes the container. (d) Shows another container which can be fully closed. The lid on the side of the container slides over the sample to fully enclose the tissue sample.

The selection of the conceptual design for the enclosing function is based on the complexity criteria. For this conceptual design it is chosen to stick to the most simple design: the barrel shaped container (b). This concept is able to be made and used on a small scale, and it also provides enough protection for the tissue sample.

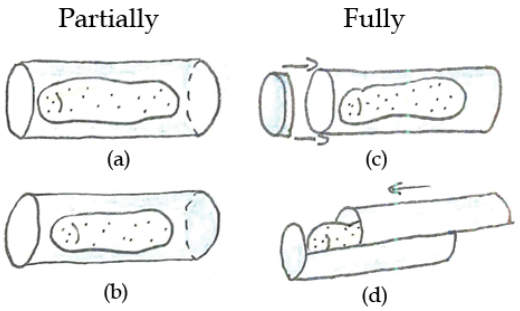


Figure 4.7: Conceptual designs of the enclosing function of the instrument. (a) A tube which can enclose the tissue sample by sliding over it. (b) A concept similar to the tube, but with one end of the tube closed off, like a barrel. (c) A barrel container which can be fully closed off using a lid at the top. (d) A container which can fully close with a lid that slides over the side of the sample.

4.3.3. TRANSPORT

The transportation of a bullet through a gun shaft is done using the explosion of gunpowder. This explosion causes a rapid expansion of gas behind the bullet, which transports the bullet out of the gun shaft. The biopsy instrument however, must transport the "bullet", or container, back into the instrument's shaft and towards the storage. This can be achieved in a large variety of ways. Transportation can be categorized into the forces acting on the container with the tissue enclosed in it. As stated in Section 2.2, the acting forces can be pushing forces, shear forces, and pulling forces.

Figure 4.8 shows a selection of the design ideas for the transportation method. (a) Transporting the tissue container can be done by using segments which push the container back to the instrument. The outer needle grabs one segments after obtaining the tissue. By retracting the outer needle, the segment pushes the container back through the needle shaft. (b) Another way of transporting the container using a pushing force, is to load a spring at the front of the container, which shoots the sample back to the instrument handle, like a bullet.

(c) Shows an idea which uses shear friction forces on the container applied by the outer needle. The sides of the outer needle will be in contact with the container. If this contact surface provides a larger friction force than the contact surface of the inner needle with the container, the container will move along with the outer needle. This way if the outer needle is retracted, the container will move with it. Conceptual design (d) shows a peristaltic motion of the outer needle, which will transport the container back into the needle shaft.

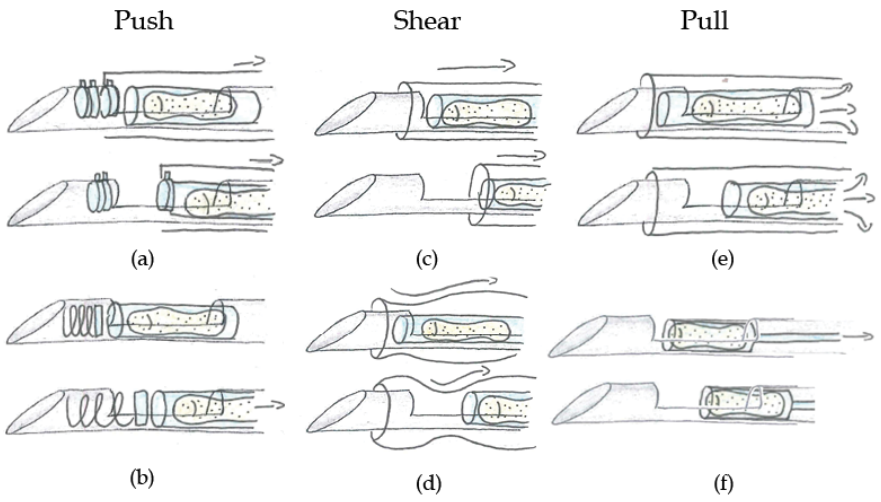


Figure 4.8: Conceptual designs of the transportation function of the instrument. (a) Concept which pushes the container through the instrument shaft by using segments. (b) Pushes the container back to the instrument by using a loaded spring. (c) Uses a shear friction force to transport the container. (d) Uses a peristaltic motion of the outer needle to transport the container. (e) Concept which transports the tissue container by applying a vacuum. (f) Concept which pulls the container through the shaft using a pulling rod.

(e) and (f) show concepts which use a pulling force. Concept (e) pulls the container through the needle shaft by applying a vacuum. Concept (f) shows a conceptual idea which uses a pulling rod. This rod can be attached to the container to pull out the container.

The selected transportation concept is the pulling rod concept (f). When solely looking at the method of applying forces, one can eliminate the force application based on a complexity criteria. Pushing the container out of the needle will require some mechanism to act in front of the container. This becomes complex as pushing parts have to be implemented into the tip of the needle itself. Applying shear forces on the container is also complex as the outer needle is required to be adjusted to be able to apply those forces. In the case of the shear friction concept, the outer needle will require a coating to be able to apply larger friction forces. The peristaltic concept would require a flexible outer needle. Pulling the container out of the needle is the least complex mechanism as the space for a transportation mechanism lies behind the container. The vacuum pulling concept is a possible mean of transporting the container. However, applying a vacuum in a needle which is not fully sealed may cause leaking problems. Therefore it is easier to pull the container using a pulling rod. This concept is simple and applicable on a small scale.

4.3.4. FROM BULLET TO NEEDLE

So far, it is decided to collect the tissue specimen using the TruCut mechanism, enclose it in a barrel shaped bullet or container, and transport it using a pulling rod. These functions have to be combined into one working mechanism. By combining these functions, the mechanism will consists out of a loose container with a separate pulling rod and a cutting mechanism, as shown in Figure 4.9 (a). This combination of functions however can be simplified, making sure less parts are necessary to achieve the same goal. To reduce the required parts, the concept can be simplified by combining the pulling rod and the container parts into one single part, as shown in Figure 4.9 (b). Instead of enclosing the tissue in a bullet, a third needle, shown in green, is able to both serve as an enclosure of the tissue specimen, and a pulling rod.

Considering this new concept, the inner TruCut needle (indicated in purple) will require to be made hollow. By making the inner needle hollow, the needle will become more fragile and prone to plastic bending. This is because the side notch will eliminate the coherence of the hollow needle, causing it to easily bend at this part of the needle. Instead of making the inner needle of the TruCut hollow, it is both easier and safer to keep the inner needle solid. Therefore, the inner TruCut needle should be the most inner needle in the collecting mechanism. This can be achieved by moving the green pulling rod needle to the outside of the TruCut needles. This way, instead of serving as a container, the green needle can serve as a cannula, as shown in Figure 4.9 (c). The two TruCut needles (purple and yellow) can be transported through the cannula (green) to the storage system. The cannula will stay at the desired location in the lesion, while the TruCut mechanism can be refreshed after each biopsy specimen has been taken. An advantage to this conceptual idea is that the tissue sample is automatically enclosed by

the TruCut collecting mechanism. As a conclusion, it is decided to change the previous made ideas into this combined collect, enclose, and transport concept, shown in Figure 4.9 (c).

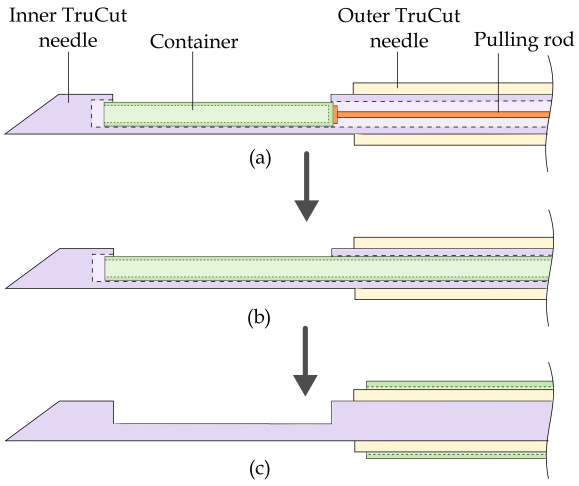


Figure 4.9: The combination process of the collecting, enclosing and transportation function of the instrument. (a) The initial conceptual design with an inner needle indicated in purple, and outer needle indicated in yellow, a container indicated in green, and a pulling rod indicated in orange. (b) The simplification of the initial concept. The container and the pulling rod can combine into one part. This part will become a third needle which can be pulled to transport the specimen. (c) A further elaboration of the concept. The two TruCut needles can be transported instead of the third, green needle. The green needle can serve as an outer cannula which stays in the right position while switching needles.

4.3.5. STORE

The main function from which the inspiration of the working principles of guns could be taken, is the storing and reloading of the bullets of a gun. When looking at the variety of types of gun, the storage of the ammunition is done in either axial, radial, tangential, or parallel direction, as shown in Figure 4.10. (a) The axial storage direction is a rare method of ammunition storage in guns. This storing method can be found in a Winchester 1873. (b) The radial storage of the bullets is a more common storage method in guns. It can be found in many types of gun such as regular handguns. Storage method (c) is a well known storage mechanism of the revolver, which stores its bullets in a tangential manner. Finally, the machine gun storage of bullets in a parallel direction (d), where the bullets are stored in a long strip outside of the gun.

Instead of bullets, the biopsy instrument will store needles. Therefore, axial storage (a) would require a long instrument if all the needles were to be stored into an axial direction. (b) The radial direction is an efficient way of storing the needles. However, this mechanism is prone to jamming during the reloading. Each new needle must be properly aligned with the instrument shaft. If this is not done appropriately, the mechanism will jam. (d) The parallel way of storing is complex to implement for long and thin needles. A simple and reliable storage method is the tangential storing method (c), the revolver. It was decided to use this concept for the storing function of the instrument.

4.3.6. RELOAD

The last function of the instrument is the reloading function. The reloading of the instrument must be done by refreshing the used needle with a new needle. In essence the reloading is a combination of transporting the needle to the storage, retrieving a fresh needle from the storage and transporting this fresh needle back through the cannula. Retrieving the unused needle can be done using a separate storage, and a separate mean of transportation. This means that the storage of the unused needles would be a different storage than the storage part of the used needles. This would allow the system to reload the new needles right after the used needle has been transported. However, this will require double storage systems and a separate transportation method, making the mechanism complex. To keep the system simple and easy in use it is decided to use the same storage and transportation method for new and used needles.

The reloading of the instrument can be done in a fully-automatic, a semi-automatic, or in a non-automatic manner, similar to guns. Guns are able to reload the mechanism after firing the bullet. For the biopsy instrument, this is different. Before a new needle can be reloaded, the used needle must be back in the revolver storage. It will be complex to achieve this in a semi-, and a fully-automatic way. This is because to be able to make the reloading automatic, an external energy source would be required. It is therefore decided to keep the reloading of the instrument non-automatic. The reloading will be done by manually rotating the revolver barrel.

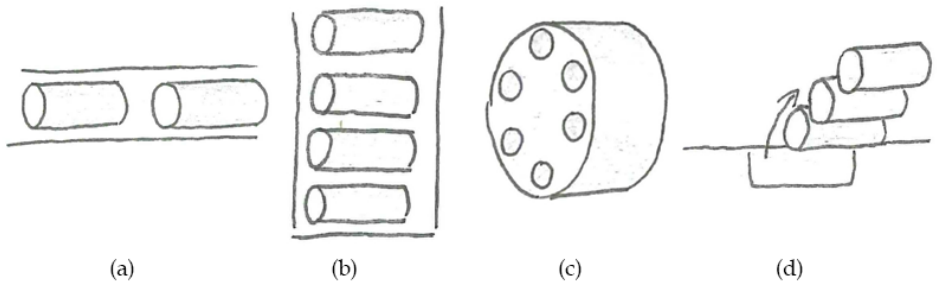


Figure 4.10: Conceptual designs of the storing and reloading function of the instrument. (a) Shows an axial manner of storing, (b) shows storage in a radial direction, (c) shows a revolver storage in tangential direction, and (d) shows the storage in parallel direction.

4.4. COMBINING THE CONCEPTS

A conceptual design has been chosen for each function. These concepts must be combined to form a single instrument. Figure 4.11 shows a schematic illustration of all the concepts combined. The collecting (1) and enclosing (2) will both be carried out by TruCut needles. The inner needle, indicated in purple, will obtain a tissue specimen in the side notch. Subsequently the outer needle, indicated in yellow, will cut the specimen from the body and enclose it in the side notch of the inner needle. After collecting and enclosing the biopsy sample, the two TruCut needles will be transported (3) through the shaft of a third needle, the cannula (indicated in green). The used TruCut needles will be stored inside a revolver chamber (4), and reloaded by rotating the chamber (5). This way a new needle can be transported through the cannula and collect another biopsy sample. After the procedure, the entire instrument can be retracted and all the biopsy samples can be extracted from the revolver chamber.

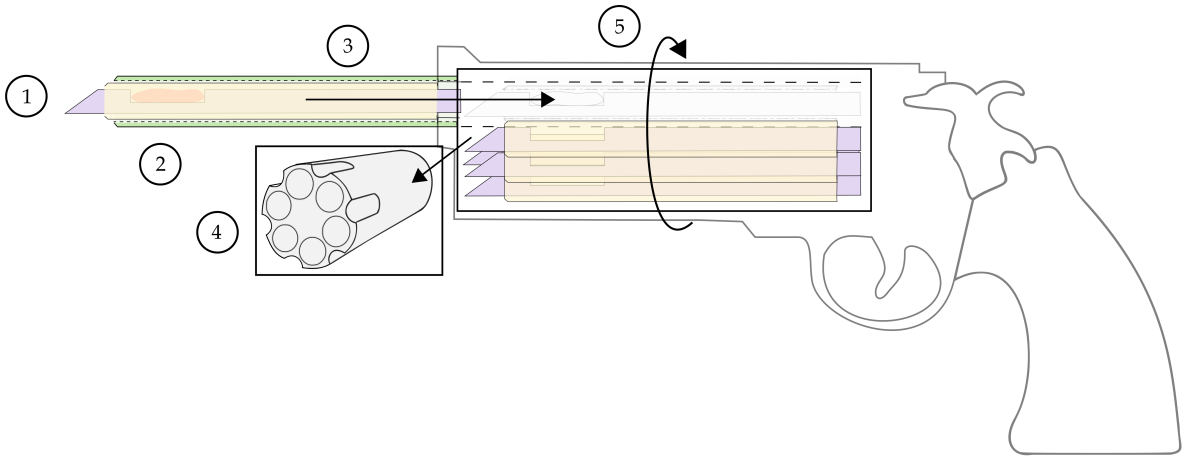


Figure 4.11: Schematic illustration of overall conceptual design of the single-insertion multiple specimen biopsy instrument. Function 1. and 2. are the collecting and enclosing of the biopsy specimens. This is done using the TruCut needles (purple and yellow). Function 3. is the transportation function. The TruCut needles are transported through a cannula (green), and 4. subsequently stored into a revolver chamber. Finally, 5. the instrument can be reloaded to be able to obtain a new biopsy sample.

5 Final Design

5.1. Design Elaboration

5.1.1. Collect

TruCut Collecting Mechanism

The conceptual design as presented in Section 4.4 does not yet describe a fully functioning design. Therefore, the conceptual design will be further elaborated in this section. This elaboration will again be categorized based on the five actions as presented in Section 3.2.2. The collecting of the tissue sample will be done with an existing TruCut mechanism. Existing TruCut biopsy instruments vary from very simple instruments to more advanced instruments, shown in Figure 5.1. The simple instrument (a) consists only out of the two TruCut needles and a plastic handle. To collect a tissue specimen, the outer needle is manually driven over the side notch of the inner needle. The more advanced biopsy instruments (b) contain a single spring inside the instrument. This spring can be loaded to shoot the outer needle over the inner needle to cut the tissue. The advantage of using this spring-loaded shooting mechanism is that the cutting speed is the same for every use. This provides the same biopsy sample quality with every use. Cutting the sample manually does not provide this guarantee. Therefore, it is decided to implement this spring-loaded shooting mechanism into the novel biopsy instrument.

Figure 5.2 shows the mechanism behind these more advanced TruCut devices. To load the instrument, the outer TruCut needle (indicated in yellow) is held in place. By pressing the inner needle (indicated in purple) through the outer needle, both the spring is loaded and the side notch of the inner needle is pushed into the lesion site. Subsequently, the outer needle can be released to cut the tissue. For this, the inner needle is held in place and the outer needle is released to cut the tissue.

For the elaboration of the collecting mechanism of the design, the specifications of the spring, the loading mechanism, and the trigger mechanism must be determined. Each will be described individually.

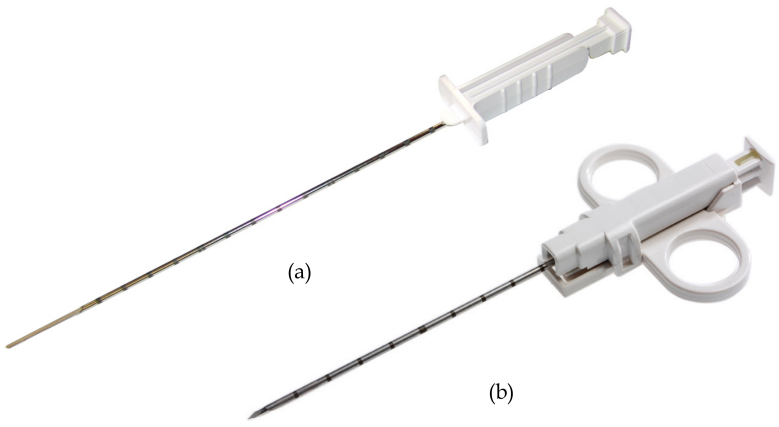


Figure 5.1: Photos of existing TruCut instruments. (a) Shows the simplest version of a TruCut biopsy device. To collect the tissue, the outer TruCut needle is manually driven over the sidenotch of the inner needle. (b) Shows a more advanced biopsy instrument. This instrument uses a spring loaded mechanism to collect the tissue. (Photos retrieved from Picswe [56])

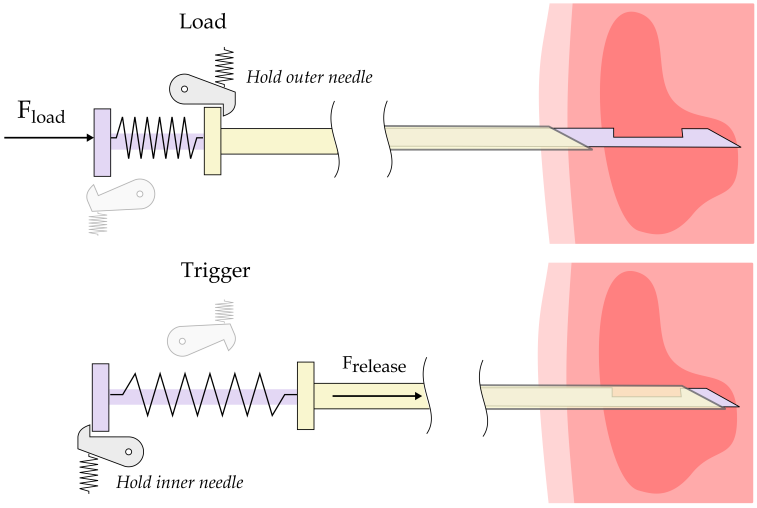


Figure 5.2: Schematic illustration of the loading and triggering of a TruCut spring-loaded mechanism. The inner TruCut needle is indicated in purple, and the outer TruCut needle in yellow. To load the device, the inner needle is pressed into the lesion, while the outer needle is held in place. To trigger the mechanism, the inner needle is held in place, and the outer needle is released to cut the tissue.

SPRING SPECIFICATIONS

The loading of the biopsy instrument is done using a single spring. The specifications of the spring used in current biopsy instruments vary between instruments. No clear information was found about the specifications of the spring in commonly used TruCut devices. A single research, done by Wendt *et al.*, was found in which the cutting velocity of various TruCut devices are compared to the sample quality [57]. Also, an available spring of an existing TruCut instrument can be measured to find out its specifications.

The research done by Wendt *et al.* compares the cutting velocities of five different TruCut instruments and their sample quality [57]. The quality of the sample was determined by the relative weight of the sample, which is a quotient of the measured weight of a sample and the reservoir volume of the needle. With the information found in this research an estimation could be made of the spring constants used in existing TruCut instruments. The elaboration of this estimation can be found in Appendix B.

The estimation of the spring constants of the five biopsy instruments discussed in the research, varies between 0.16 N/mm to 1.33 N/mm. This is according to the spring constant measured on the available existing TruCut instrument, of which the spring has a spring constant of 1.13 N/mm. These spring specifications can be compared to the quality of the biopsy samples obtained by the associated instruments.

The higher cutting velocities, and the therefore higher spring constants, do not necessarily provide the best sample quality. It is for that reason decided to use a spring with a lower spring constant in the design. Implementing a lighter spring is also a safety measurement for the first prototype. A lower spring constant will put less stress on the collecting mechanism, making the prototype more reliable and less prone to malfunctioning. It is decided to use a spring with a spring constant similar to the spring as used in a biopsy instrument which obtained a good tissue quality. This spring constant is around the 0.35 N/mm. With this spring constant, the TruCut mechanism will reach a cutting velocity of about 11 m/s through air. This velocity is able to provide a sufficient quality biopsy sample. The design will be made in such a way that, if desired, in a later stage a spring with another spring constant can be implemented.

LOADING

The loading of existing TruCut instruments is currently done by using a loading force applied directly onto the inner needle. This is schematically shown in Figure 5.3 (a). For now, the biopsy instrument will be figuratively shown as a revolver. The loading force applied to the inner needle puts tension on the spring between the inner needle and the outer needle. This loading force, shown as F_{load}, will be counteracted by the hand holding the instrument, F_{hand}. The combination of these two forces cause a moment M_{load} on the instrument. This moment must also be counteracted by the hand and wrist of the instrument's user. This counter moment will act around a pivot point indicated as a red dot. The hand must keep the instrument steady because it is not desirable for the tip of the biopsy needle to move within the body. This is for the purpose of the biopsy: a biopsy needs to be taken from the exact lesion location. And for the patient: moving the needle inside the body will cause discomfort and unnecessary damage to the patient.

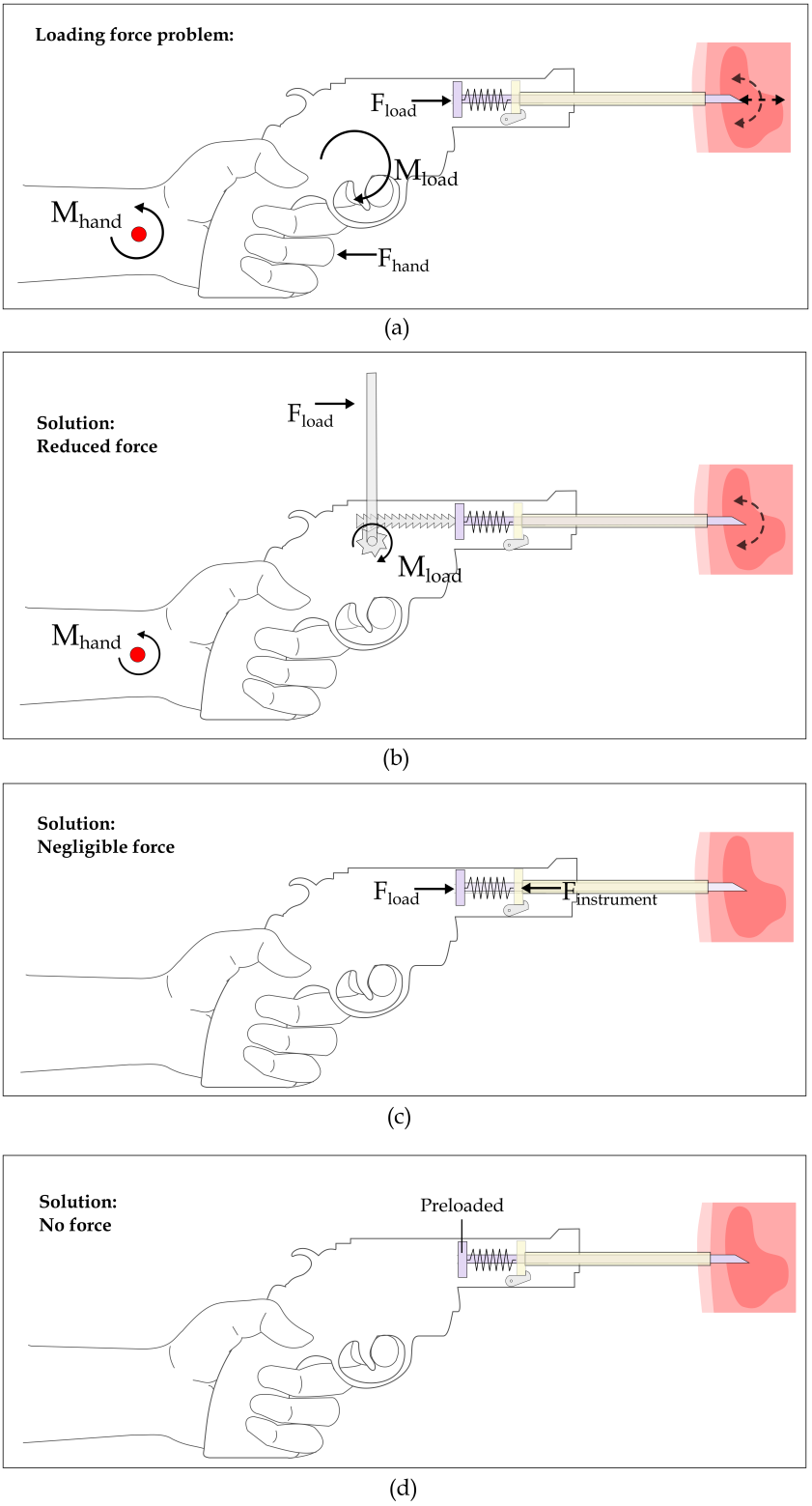


Figure 5.3: Schematic illustration of the forces acting on the biopsy instrument when loading the spring. In the figure, the inner TruCut needle is indicated in purple, and the outer TruCut needle is indicated in yellow. Between these two needles is a spring which is required to be loaded to be able to collect a tissue sample. (a) The loading of the spring done by directly applying a loading force on the spring, causing motion in the tip of the instrument. (b) An example where mechanical advantage is used to reduce the force applied on the instrument to load the spring. (c) Shows a solution in which he instrument counteracts the loading force, by for example attaching the instrument to a large object. This way, the loading force may be reduced to a negligible amount. (d) By preloading the TruCut needles before the use of the instrument, no loading forces are required during the biopsy procedure.

To prevent the needle tip from moving inside the body, the hand is required to perfectly counteract the loading force and moment. Unfortunately, this will never be the case. The current loading mechanism will always cause the needle tip to move inside the body. To avoid this problem, another loading mechanism of the spring should be designed.

One solution to reduce the movement of the needle tip inside the body, is to reduce the loading force. Reducing the loading force causes the counter force to be reduced as well. This force reduction can be achieved by applying a mechanical advantage on the loading mechanism. Figure 5.3 (b) shows an example of this solution. By making a long lever on the instrument, the loading force will be reduced due to the elongated moment arm. This force reduction will cause less displacement of the needle tip, as it will be easier to counteract the loading force with the hand. However, this will not fully eliminate the motion of the needle tip inside the body.

A second option is to counteract the force using the instrument. This solution would keep the acting forces within the instrument, as shown in Figure 5.3 (c). This could be achieved by for example attaching the instrument to a fixed environment. This way, the fixed instrument will counter act the loading force. This would make the loading force negligible. However, this solution will still cause the user to apply a force on the instrument, while it is inside the patients body.

A final solution would be to preload the TruCut needles. The preloading of the spring can be done in advance of the biopsy procedure. This way, the needles will not require to be loaded when the needle tip is inside the body. This is schematically shown in Figure 5.3 (d). This solution will eliminate the problem of the motion of the tip instrument. It is therefore decided to use the solution of the preloaded needle for the final design. The preloaded mechanism can be compared to the cartridge around a bullet. This cartridge contains the explosive gunpowder inside, and it is only required to be triggered to fire the bullet.

The final design of the preloaded needle cartridge is shown in Figure 5.4. This cartridge will consist out of the two TruCut needles, two tubes and a spring. The inner TruCut needle (purple) will be attached to an outer tube (indicated in blue). The outer TruCut needle will be attached to an inner tube (both indicated in yellow). Between these tubes a spring is inserted. By pushing the inner tube in the outer tube, the spring between the tubes will be compressed. The inner tube contains a slot at the front, in which snap-fits which surround the front of the outer tube, can lock onto. This way, the spring will be preloaded inside the needle cartridge.

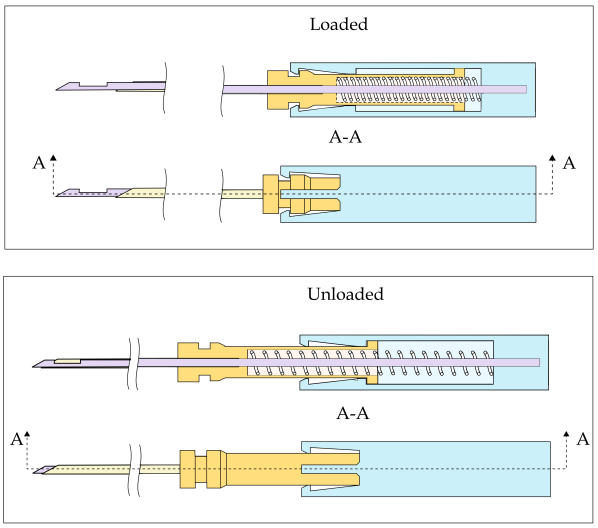


Figure 5.4: Schematic illustration of the needle cartridge. The top two illustrations show the loaded state of the cartridge. The lower figures show the unloaded state of the needle cartridge. The outer needle is indicated in blue, attached to the outer tube is the inner TruCut needle indicated in purple. The inner tube is attached to the outer TruCut needle, both are indicated in yellow.

TRIGGERING

Figure 5.4 shows the design of the preloaded needle cartridge. When the spring is loaded, the snap-fits of the outer tube (blue) are locked with the inner tube (yellow). To fire the mechanism, the snap-fits should be released. For this, a trigger is designed. The trigger is a hollow tube which is able to go around the inner tube and will lift the snap-fits of the outer tube from the slot of the inner tube. This is schematically shown in Figure 5.5. The trigger, indicated in orange, is a hollow tube with a narrowed tip at the end which ends in a bevel. By pushing the tip of the trigger and its bevel onto the snap-fits of the outer tube, the snap-fits will be lifted from the slot of the inner tube. At the same time, the inner tube is released and fired by the spring. The inner tube will travel through the hollow trigger. This way, the outer needle, which is attached to the inner tube, is fired over the side notch of the inner needle, collecting a tissue sample.

For safety reasons, the needle cartridge will be stored into a duct with the same diameter as the cartridge. This way, the snap-fits will not be able to be released until the cartridge moves out of the storage duct. The duct in which the trigger is located will be broader than the storage duct. This will enable the snap-fits to be opened only proximate to the trigger. During triggering the needle cartridge must be locked in place. This locking mechanism will be described in the transportation section.

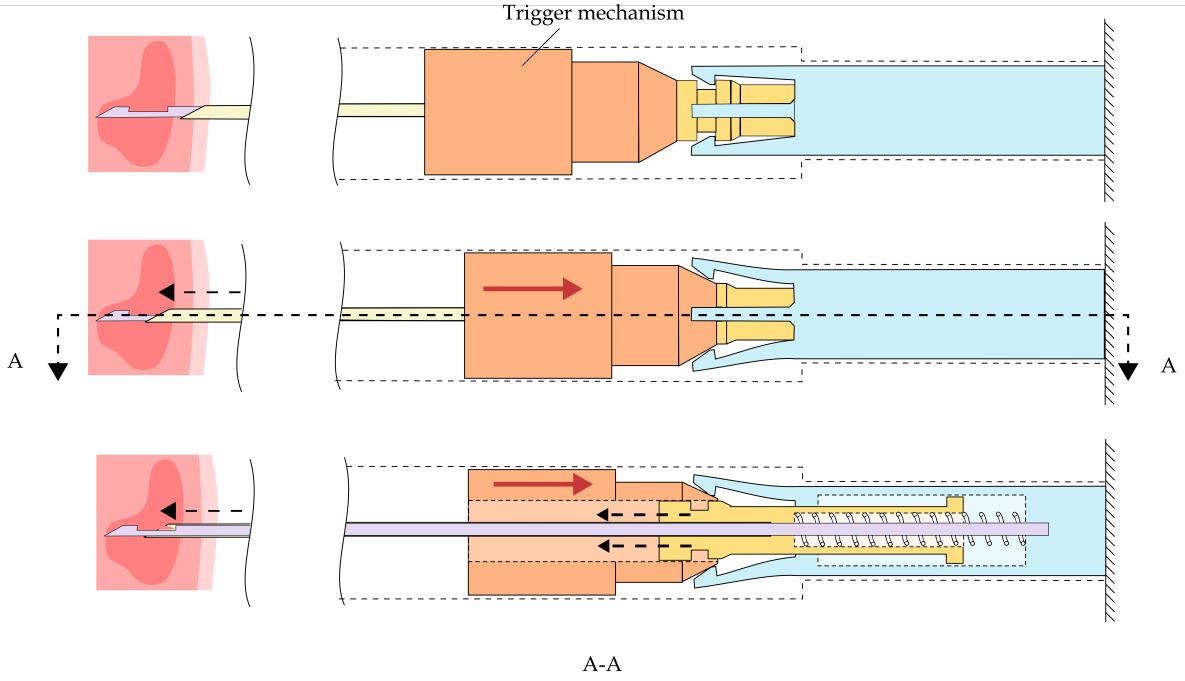


Figure 5.5: Schematic illustration of the design of the trigger. The trigger mechanism, shown in orange can slide over the inner needle tube, shown in yellow. By doing so, the trigger will lift the snap-fits of the blue outer tube out of the slot of the inner tube. This will cause the inner tube to be released and will move through the trigger enclosing a tissue sample.

5.1.2. ENCLOSE

The preloaded cartridge of the needle is now able to collect the tissue sample by firing the outer TruCut needle, which will cut the tissue sample from the lesion site. After the tissue sample has been collected, it is automatically enclosed within the two TruCut needles. After the biopsy procedure has been finished, the tissue samples must be retrieved from the instrument. To obtain the tissue from the enclosure after the biopsy procedure, the side notch which contains the tissue specimen must be uncovered. This can be achieved by loading the cartridge again, which will automatically pull back the outer needle from the side notch of the inner needle. This however causes safety hazards for the clinicians who are retrieving the biopsy samples. The cartridge can accidentally fire itself while the tissue is being retrieved. Therefore, it is more desirable to be able to collect the specimen without requiring to load the needle cartridge again.

This can be done by adding an extra part to the needle cartridge, as shown in Figure 5.6. The additional part is attached to the inner needle (both indicated in purple). This part will serve as a cap which can be attached to the outer tube with a bayonet fitting. The spring will be between this cap and the inner tube. After the procedure, the clinician will be able to only take out the inner needle from the cartridge by unlocking the bayonet fitting, and pulling out the inner needle. The inner needle will contain the tissue sample in the side notch. This additional part to the needle cartridge will both allow easy retrieval of the tissue specimen and easy assembly of the cartridge.

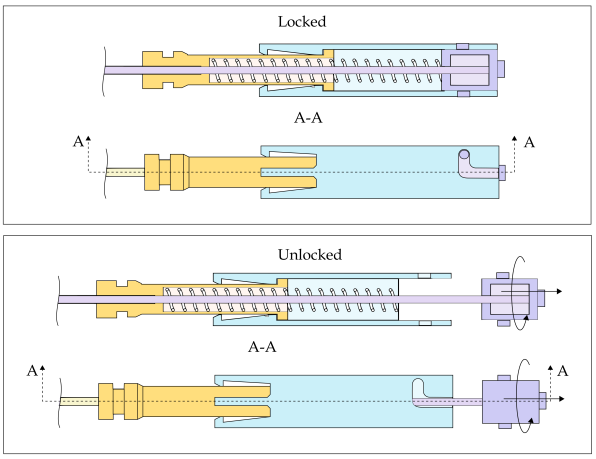


Figure 5.6: Schematic illustration of the needle cartridge. The additional cap of the cartridge, indicated in purple, will allow easy retrieval of the tissue specimen after the biopsy procedure. The retrieval can be done by unlocking the bayonet fitting and pulling out the inner needle from the cartridge.

5.1.3. TRANSPORT

The transportation of the biopsy specimens will be done by pushing and pulling the needle cartridge towards the instrument tip and back to the revolver storing chamber respectively. It is decided to transport the needle cartridges manually in both directions. This can be done by using a knob at the side

of the needle cartridge. This knob goes to the outside of the instrument via a slot at the top of the instrument. This way, the cartridge will be manually accessible, allowing back and forth transportation. The needle cartridge will slide through a duct which goes along the revolver chamber to the front of the instrument. This is also shown in Figure 5.7 (a).

When the needle cartridge has arrived at the trigger mechanism, the cartridge must be locked in place during the triggering of the loaded needles. To lock the needle package in place, the knob can be used to act as a bolt-action mechanism, also known as a bayonet fitting. This bayonet fitting will prevent the needle cartridge from moving during the triggering. A second purpose of this bayonet fitting is the positioning of the needles. The needles are required to have two separate positions.

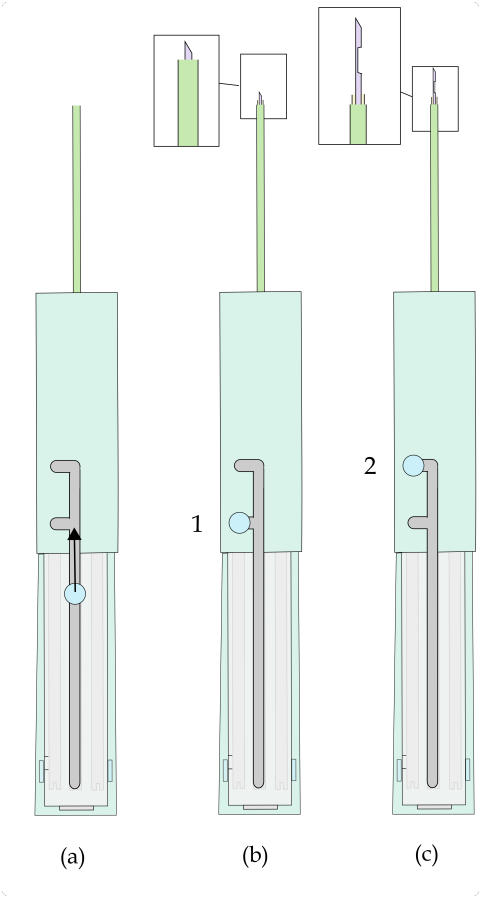


Figure 5.7: Schematic illustration of the top view of the instrument. It indicates the two positions of the bayonet fitting. (a) The needle cartridge is transported from the revolver towards the instrument tip using the handle (blue). (b) The needle package is positioned into the first bayonet position. This position allows the clinician to insert or reorient the instrument into the lesion. (c) The needle package can be transported to the second position, allowing the side notch of the inner needle to be exposed, and enabling the instrument to be triggered and to collect the tissue.

This is also shown in Figure 5.7 (b) and (c). When the needle cartridge is set into the first position, the tip of the needle can be used to insert or reorient the needle in the lesion site. The second position will push the side notch of the inner needle into the lesion. At this position the needle cartridge is able to be triggered.

5.1.4. STORE AND RELOAD

The storing of the needle cartridges will be done in a long revolver chamber. This chamber will be able to contain six needle cartridges, as shown in Figure 5.8 (a). By rotating the revolver, a new needle will be aligned with the channel towards the trigger mechanism. This way the new needle can be transported towards the instruments tip. To align each of the storing ducts in the revolver chamber with the channel towards the trigger, a ratchet mechanism is placed at the front of the revolver chamber. The ratchet consists out of a spring plunger and small indentations at the front of the revolver chamber, as shown in Figure 5.8 (b). This spring plunger will align the instrument by falling into the small dents in the revolver chamber front.

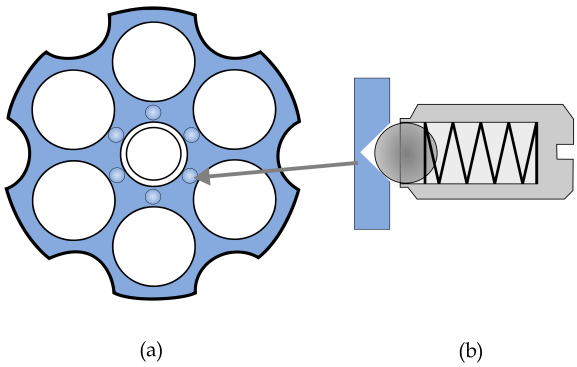


Figure 5.8: Schematic illustration of the revolver chamber and the spring plunger. The spring plunger will help align the cylinder of the revolver with the cylinder of the trigger area. (a) shows the front view of the revolver schematically, (b) shows a side view of the spring plunger and a section of the indentation in the revolver chamber.

5.1.5. INSTRUMENT LAYOUT

Next to the elaboration of the individual functions, it is necessary to design the layout of the biopsy instrument. Up until now the layout of the instrument has been illustrated as a revolver. However, the layout of the instrument can be made in a variety of ways. Figure 5.9 shows an array of instrument layout designs. As the design is inspired on the revolver, the first design of the instrument layout is based on the layout of a regular revolver. In this layout the revolver chamber comes right after the gun shaft, and behind the revolver chamber is the trigger mechanism.

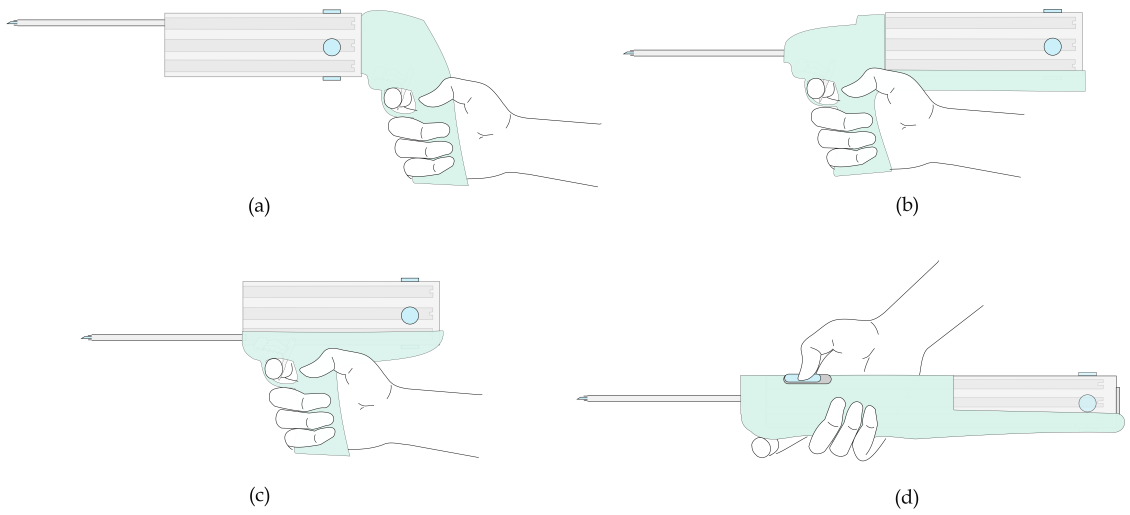


Figure 5.9: Schematic illustration of the design of the instrument layout. (a) Shows a regular revolver layout, where the revolver chamber is located in front of the trigger mechanism. (b) Shows a revolver layout with the revolver chamber behind the trigger mechanism. (c) Shows a layout where the revolver chamber is placed on top of the trigger mechanism. Finally, (d) shows a cylindrical shaped design with the trigger mechanism in front of the revolver chamber.

For a revolver this is a convenient layout as the gun is fired by triggering the back of the ammunition. In the case of the biopsy instrument the trigger is required to be in front of the needle package to shoot the outer TruCut needle. Therefore design (b) is made, where the trigger is in front of the revolver chamber. An alternative to this is design (c) where the revolver comes on top of the trigger mechanism and the handle. This design is probably not possible to implement because the trigger mechanism is required to go around the needle to trigger it. Finally, design (d) is similar to design (b) where the trigger mechanism is in front of the revolver chamber. The main difference is the way the instrument is held. Design (d) is a cylindrically shaped instrument. This shape allows a larger variety of ways to hold the device. As the biopsy instrument will be used for different locations on a body, the clinician must be able to hold the device in a variety of angles and orientations. Therefore, it is chosen to make the instrument according to this design (d). This layout will prevent awkward positions of the wrist and has the advantage that it can be held in a variety of orientations.

5.2. FINAL DESIGN

5.2.1. SPECIFICATIONS

FULL DESIGN

The elaboration of each function results in a final design, shown in Figure 5.10. The design integrates all five functions into one combined instrument. The instrument is fully manually operable, with a two handed use for reloading and transporting the needle cartridges, and a one handed use during insertion and triggering. The length of the instrument is 300 mm, with a biopsy needle length of 81 mm to 110 mm. The final design can be divided into four main parts, as shown in Figure 5.11. It consists out of: the needle cartridges which go inside the instrument (yellow), the revolver chamber (blue), the trigger (red), and the shell (green). For each of these main parts the final design and its specifications will be further described.

NEEDLE CARTRIDGE

Figure 5.12 shows the exploded view of the needle cartridge. The cartridge consists out of two TruCut needles, the inner needle, and the outer needle, respectively indicated in purple and yellow. These TruCut needles will be attached to the similar colored parts. The outer TruCut needle will be attached to the inner tube (yellow), and the inner needle will be attached to the cartridge cap (purple). The needles and their attached parts will be enclosed by an outer tube, which is indicated in blue. Between the inner tube and the cartridge cap, a spring will be placed. This spring is used to fire the outer needle during collecting of the tissue. A wave ring will be placed between the front of the inner tube and the outer tube, to reduce the impact between the walls of the tube after releasing the spring.

The outer tube will have a diameter of 10.3 mm, and the entire needle cartridge will have a length of 217 mm. The diameter of the cartridge is mainly determined by the diameter and length of the spring. The spring will have a diameter of 4.57 mm and a length of 44.45 mm. The final chosen spring constant is 0.46 N/mm.

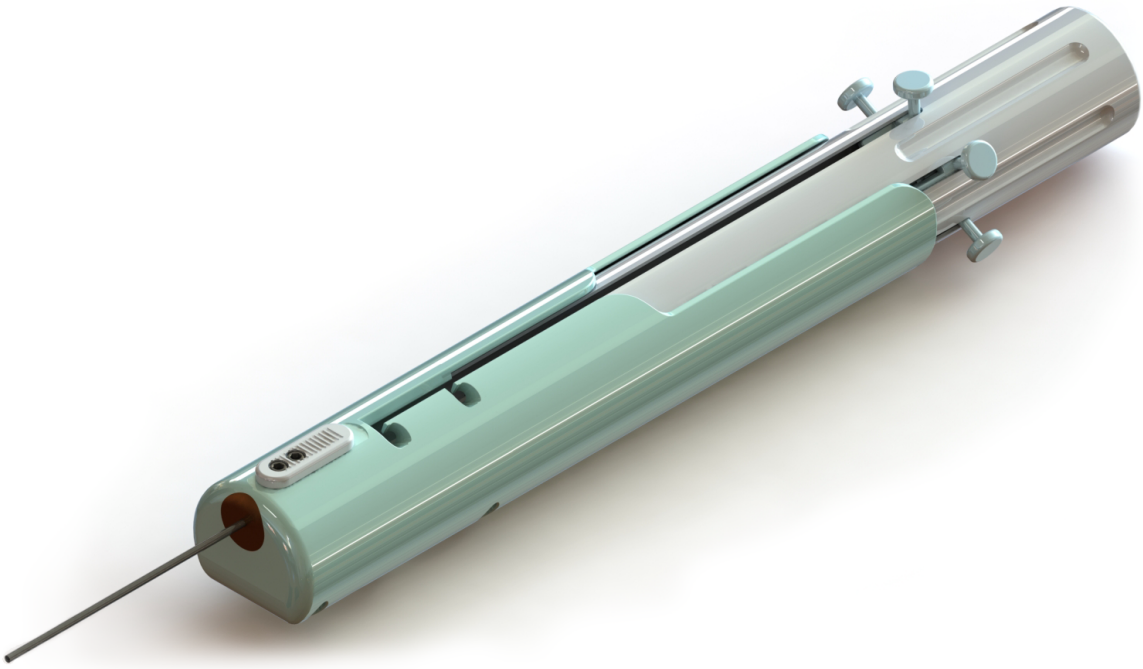


Figure 5.10: Image of the final design of the single-insertion multiple specimen biopsy instrument.

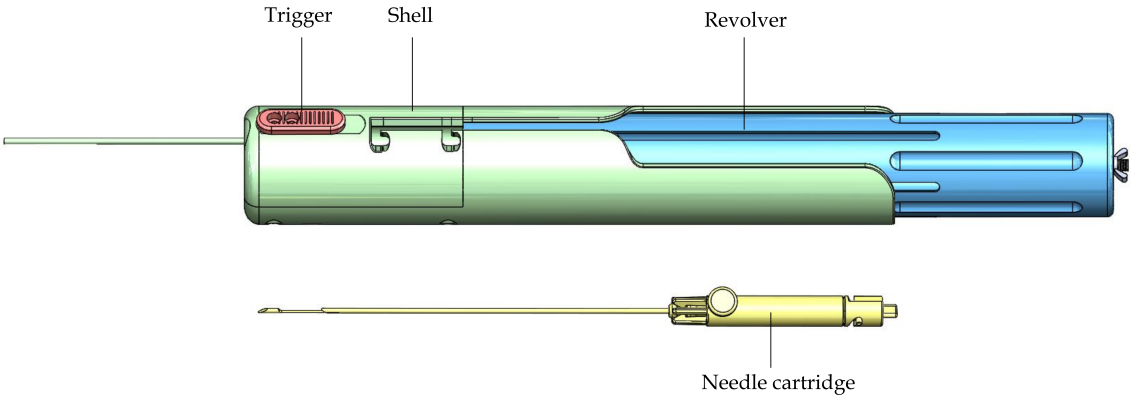


Figure 5.11: Image of the four main parts of the final design. The needle cartridge indicated in yellow, the revolver indicated in blue, the trigger indicated in red, and the shell indicated in green.

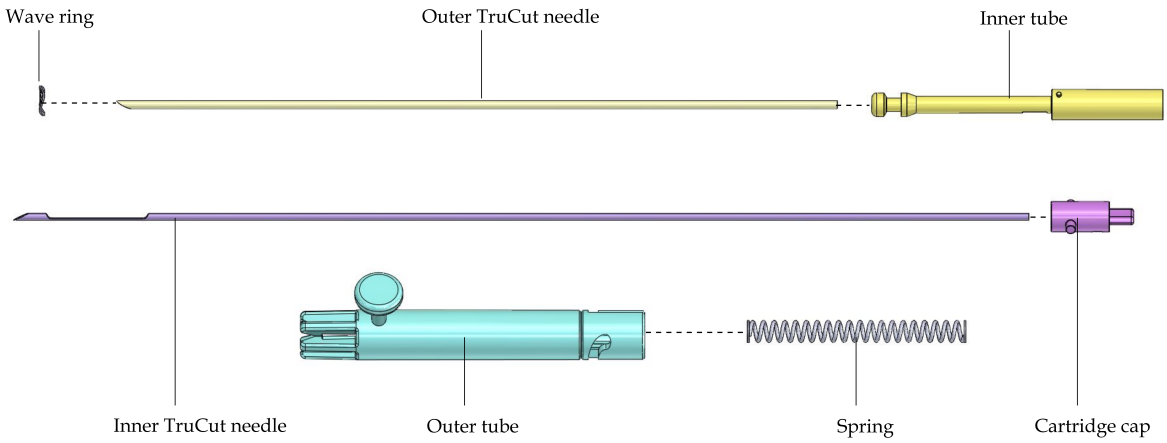


Figure 5.12: Image of the final design of the needle cartridge. The inner and outer TruCut needle are indicated in purple and yellow respectively. The parts that will be attached to the needles are indicated in similar colors. The inner needle will be attached to the cap of the needle cartridge. The outer needle will be attached to the inner tube. Finally, the outer tube is indicated in blue.

REVOLVER

The revolver is a long storing chamber in which six needle cartridges can be stored. Figure 5.13 shows an exploded view of the revolver part. The length of the revolver chamber is determined by the length of the needle cartridges. The cartridges fit entirely into the storing chamber. It therefore has a length of 220 mm and a diameter of 35 mm. At the front of the chamber are small dents which are used to align each needle chamber with the duct towards the trigger. This is done by a small spring plunger which will be connected to the shell of the instrument. Finally, the revolver is able to rotate around an axis. To make sure the rotation runs smooth, a set of sleeve bearings will be fitted into the revolver.

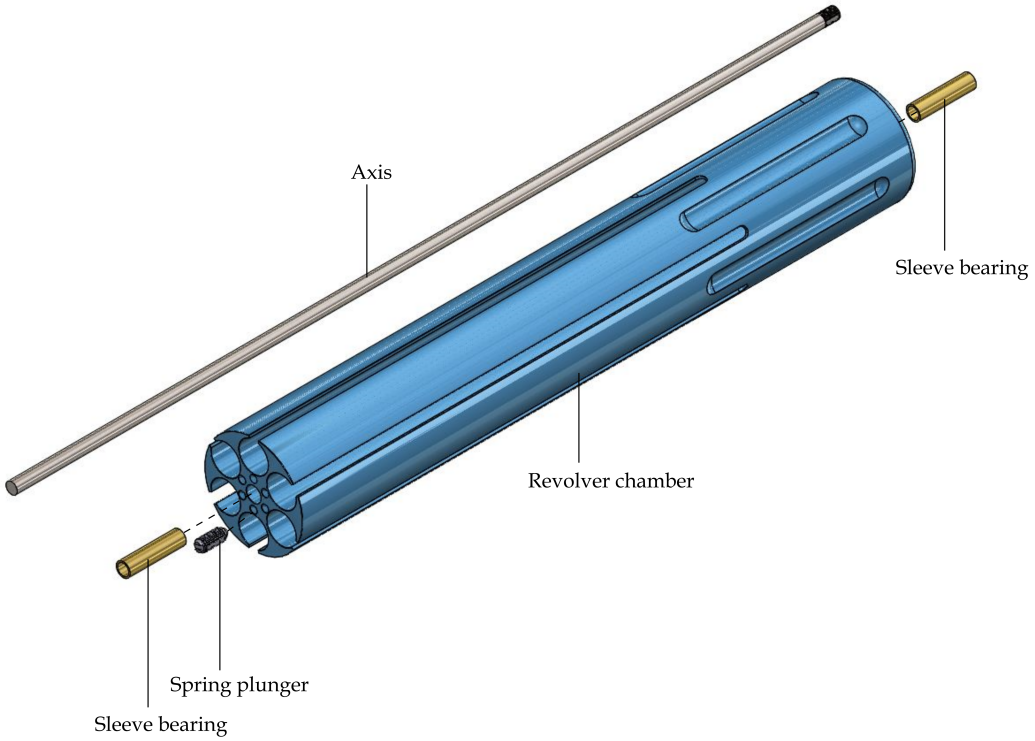


Figure 5.13: Image of the revolver chamber,the sleeve bearings, the spring plunger and the axis. The revolver chamber is indicated in blue.

TRIGGER

The trigger will be located at the tip of the instrument. Figure 5.14 shows the exploded view of the trigger part. It consists out of the trigger (orange), a knob to operate the trigger (red), a small spring, and two bolts. The trigger will be a tube which has a narrow tip with a bevel at the end. This beveled tip will lift the snap-fits of the outer tube from the slot of the inner tube, releasing the spring and firing the outer needle. The trigger will have a length of 22 mm and an outer diameter of 14 mm. On top of the trigger will be a trigger knob which can be accessed from the top of the instrument. This knob can be pulled backwards to move the trigger under the snap-fits. A compression spring is used to position the trigger back in its original place.

SHELL

The functional mechanisms will be encased by the shell, shown in Figure 5.15. This shell contains three main parts. The shell bottom, the shell top, and an attachment part with the cannula. The shell bottom will connect all the parts of the instrument. It will encase the revolver chamber, and will hold the spring plunger and the axis of the revolver chamber. The shell top has a slot for the two bolt-action positions of the needle cartridges. The top will also contain the trigger mechanism, for this a slot is made through which the trigger knob can be attached to the trigger. Located at the front of the shell top, are the cannula and its attachment part. The cannula has a length of 84 mm and is attached to an attachment part. The overall diameter of the shell is 40 mm and its length is 220 mm.

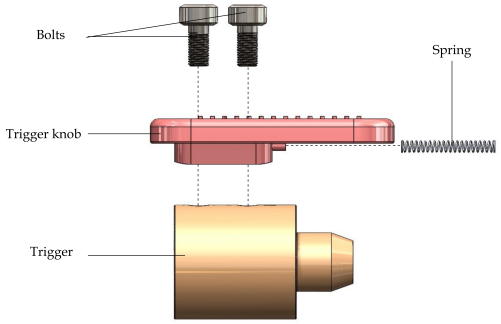


Figure 5.14: Image of the trigger part. The image shows the trigger indicated in orange, the trigger knob indicated in red, bolts, and a spring.

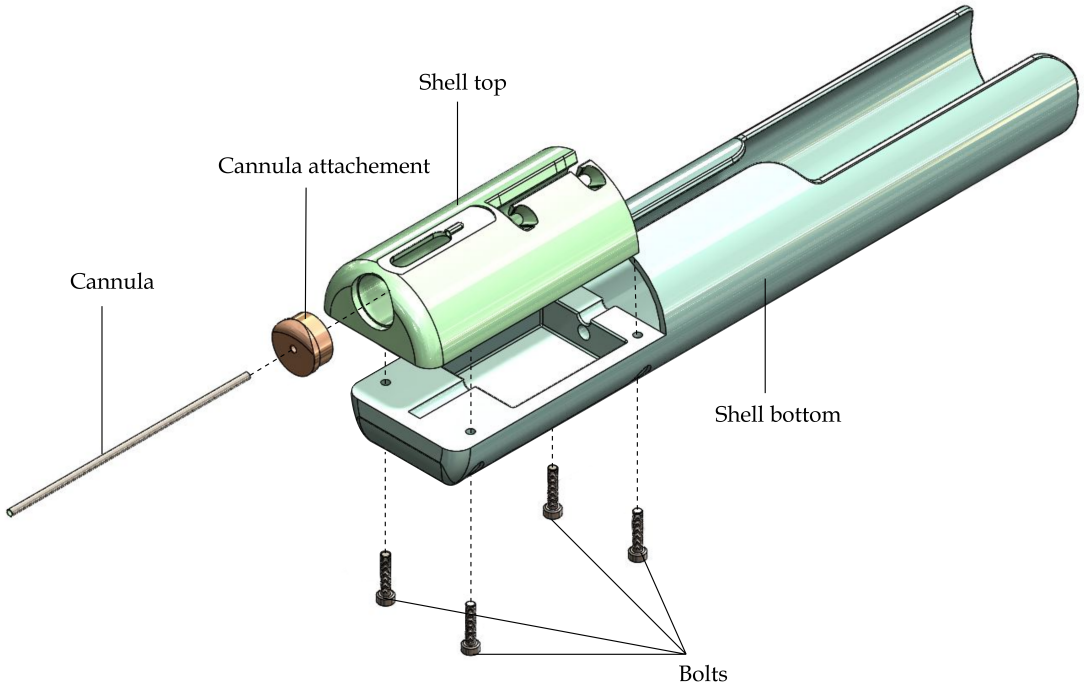


Figure 5.15: Image of the shell of the instrument. The shell contains the bottom part, a top part, a cannula attachment part and the cannula.

5.2.2. USE

CATEGORIZATION

The use of the instrument can be explained by the functional analysis as provided in Section 3.2.2. The functional analysis splits the use of the instrument into three main functions: the insertion (A), the actions of collecting multiple specimens (B), and the retraction of the instrument (C).

A: INSERTION

Figure 5.16 shows the two steps required for the insertion of the instrument. Step one is to move the first needle package to the first bayonet position. This will cause a small part of the needle tip to stick out of the cannula. After this is done, the instrument can be inserted into the lesion site.

B: ACTIONS

To retrieve a multitude of biopsy specimen a sequence of four actions are required to be carried out by the user. This is shown in Figure 5.17. The first step is to put the needle package into the second bayonet fitting. This will cause the side notch of the needle to come out of the cannula and to go into the lesion. After this, the instrument is ready to be triggered. The second step is to pull the trigger. By doing so, the outer TruCut needle will cut off the tissue specimen from the lesion. The third step is to transport the used needle back towards the revolver chamber. Finally, step four is to reload the instrument by rotating the revolver chamber. These actions can be repeated until a maximum of six biopsy specimens have been obtained.

C: RETRACTION

The final function is the retraction of the instrument. The instrument can be retracted from the body, when enough biopsy samples have been taken, up to a maximum of six samples. Figure 5.18 shows how to obtain the samples from the instrument after the procedure. First, the instrument is retracted from the body. Subsequently, the revolver chamber can be loosened from the instrument, taking out all the needles together with the chamber. Each needle can be retrieved one by one from the revolver chamber. To retrieve the sample from the needle package, the back of the package can be opened by turning the cartridge cap out of the bayonet and taking out the inner needle. After this is done, the tissue sample can be retrieved from the side notch and sent to a pathologist.

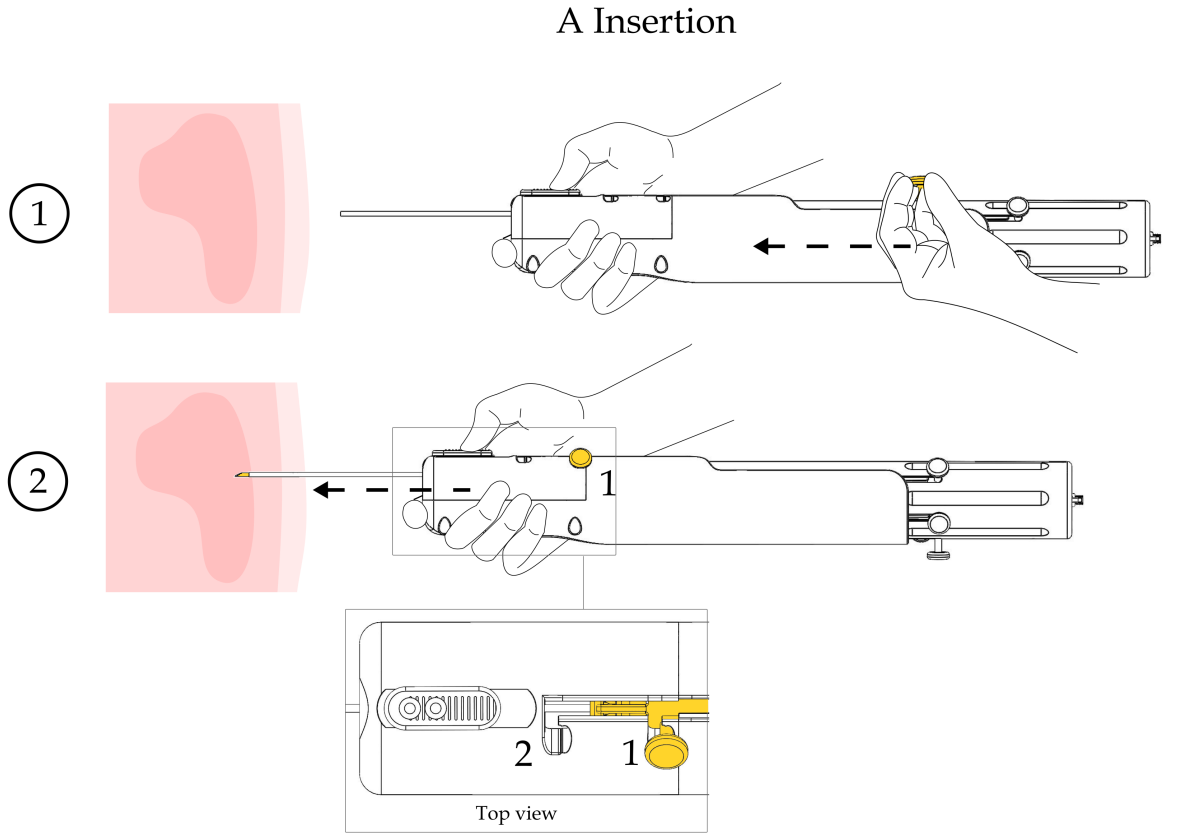


Figure 5.16: Schematic image of the use of the instrument. The image shows the steps required for the insertion of the instrument. (1) The first needle cartridge must be moved towards the tip of the instrument, (2) after positioning the needle cartridge into the first bayonet position, the instrument can be inserted.

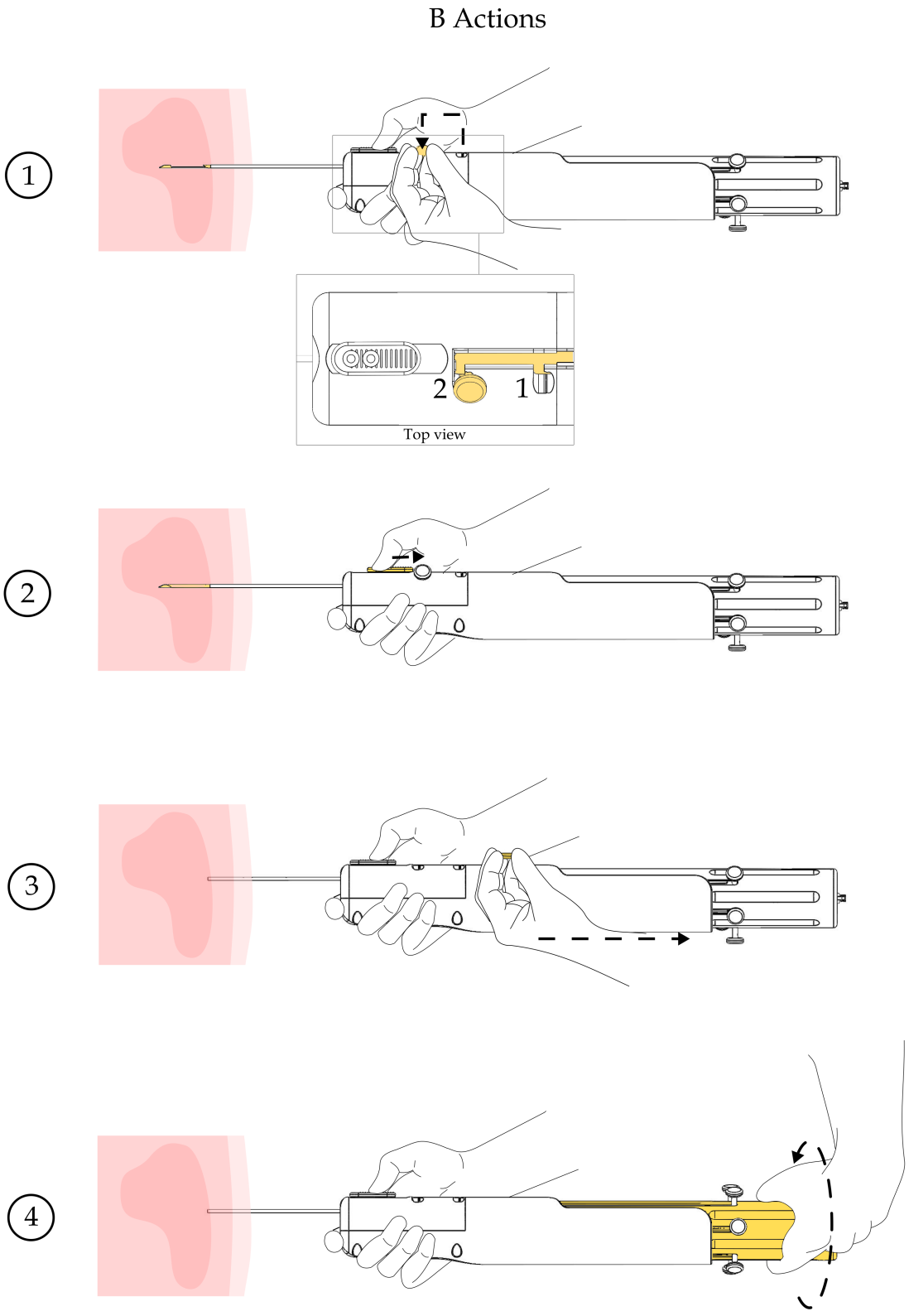


Figure 5.17: Schematic image of the use of the instrument. The image shows the steps required for the actions required to obtain multiple biopsy specimens. (1) The needle cartridge must be positioned into the second bayonet position. (2) The instrument will collect a tissue sample by pulling the trigger on top of the instrument. (3) after collecting a sample, the needle cartridge must be moved back to the revolver storage. (4) By rotating the storage the next needle can be used. These actions can be repeated until a maximal number of six biopsy specimens have been obtained.

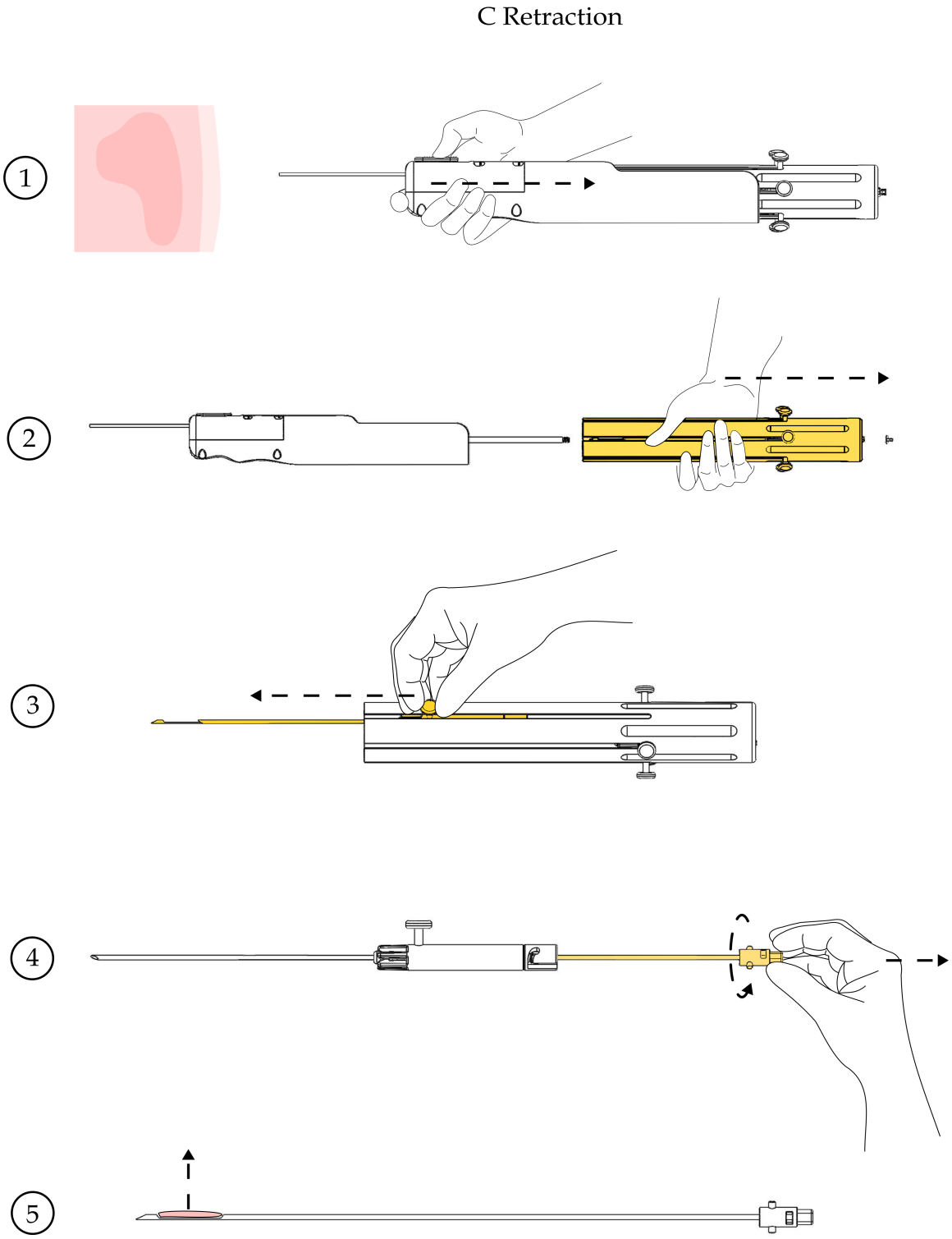


Figure 5.18: Schematic image of the use of the instrument. The image shows the steps required for the retraction of the instrument. (1) the instrument must be retracted from the body. (2) Next, the revolver chamber and its needle cartridges can be taken from the instrument. (3) Each needle cartridge can be taken out of the chamber. (4) By loosening the bayonet fitting at the back of the needle cartridge, the inner needle can be taken out of the cartridge. (5) Finally, the tissue sample can be obtained from the inner needle.

6 PROTOTYPE

6.1. PROTOTYPE FABRICATION

CATEGORIZATION

To validate the design of the single-insertion multiple specimen biopsy instrument, a prototype was built. This prototype will be used for the experiment of the proof of concept. This section will describe the fabrication process of the prototype. The section will be subdivided into the fabrication method of the four main parts of the design: the needle cartridges, the revolver, the trigger, and the shell. Please refer to Table 6.1 for a full list of parts required for the design. Technical drawings of all fabricated parts can be found in Appendix E.

NEEDLE CARTRIDGE

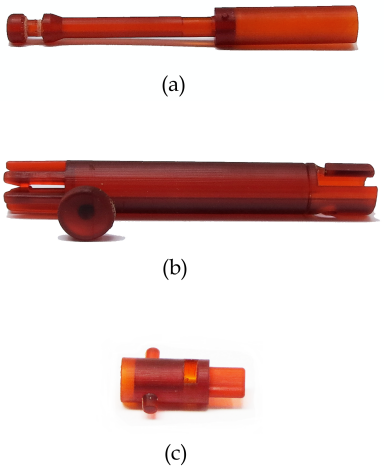
Three parts of the needle cartridge design were required to be fabricated. The other parts of the cartridge were purchased. The inner tube, the outer tube, and cartridge cap were fabricated. The fabrication of these three parts is all done using the same method. The parts were made by a digital light processing (DLP) 3D printer. By making use of 3D printing, complex shaped parts can easily be fabricated. Figure 6.1 shows the result. The parts are made of a liquid photopolymer, called R5, which has similar properties as polypropylene [58].

REVOLVER

The design of the revolver required the fabrication of three parts. Figure 6.2 shows all the fabricated parts. The revolver chamber is fabricated using a DLP 3D printer. The used material is a see-through liquid polymer E-shell 600 [59]. The axis around which the revolver will rotate is made of steel. To smoothly rotate the revolver chamber around the axis, sleeve bearings will be used. These sleeve bearings are two brass tubes inserted at both sides of the revolver. Both the bearings and axis are fabricated on a lathe.

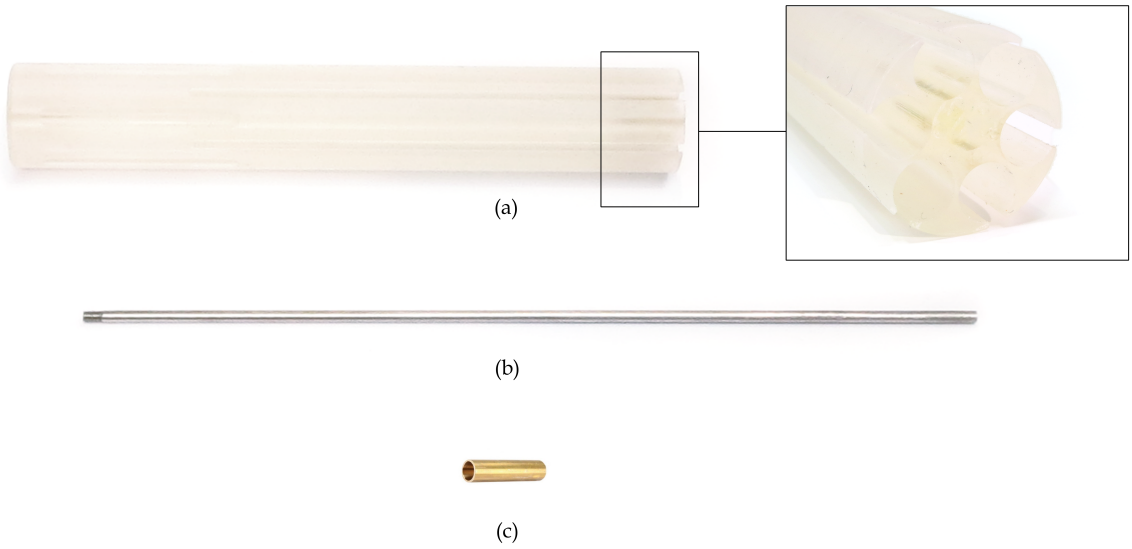
TRIGGER

The trigger consists out of a knob and the trigger itself. The knob of the trigger was fabricated using DLP 3D printing. The material used for the knob is the E-shell 600 photopolymer. The trigger was fabricated using a lathe, and is made out of bronze. Figure 6.3 shows the two parts of the trigger.



(a) (b) (c)

Figure 6.1: Photograph of the fabricated parts of the needle package. (a) Shows the inner tube of the needle package, (b) shows the outer tube of the needle package, and (c) shows the cartridge cap.

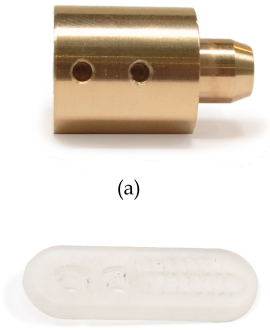


(a)

(b)

(c)

Figure 6.2: Photograph of the fabricated parts of the revolver. (a) Shows the revolver chamber, (b) shows the axis around which the revolver will rotate, and (c) shows one of the brass sleeve bearings.



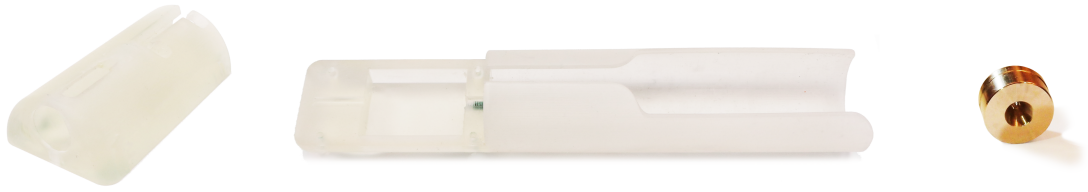
(a)

(b)

Figure 6.3: Photograph of the fabricated parts of the trigger. (a) Shows the bronze trigger, and (b) shows the trigger knob.

SHELL

For the shell, three parts were required to be fabricated. The top and bottom shell were both fabricated using a DLP 3D printer with the see-through E-shell 600 material. The last part that required fabrication is the cap which will be attached to the cannula. This cap is made out of bronze. This is because the needles of the needle cartridges are required to be guided into the cannula. For this to function correctly, the surface must be smooth. Figure 6.4 shows the three fabricated parts.



(a) (b) (c)

Figure 6.4: Photograph of the fabricated parts of the shell. (a) Shows the top part of the shell, (b) shows the bottom part of the shell, and (c) the attachment part of the cannula.

Table 6.1: List of parts of the prototype

List of parts				
Part #	Part name	Specifications	Acquired	QTY
Needle Package				
1	Inner TruCut needle	Diameter: 1.35 mm, Length: 210 mm	Purchased	6
2	Outer TruCut needle	Diameter: 1.63 mm, Length: 149 mm	Purchased	6
3	Inner tube	See Appendix E for technical drawing	DLP 3D printed	6
4	Outer tube	See Appendix E for technical drawing	DLP 3D printed	6
5	Cartridge cap	See Appendix E for technical drawing	DLP 3D printed	6
6	Spring	Diameter: 4.57 mm, Length: 44.45 mm, Spring constant: 0.46 N/mm	Purchased	6
7	Wavering	Diameter: 6.15 mm, Length: 0.76 mm	Purchased	6
Revolver				
8	Revolver chamber	See Appendix E for technical drawing	DLP 3D printed	1
9	Rotation axis	See Appendix E for technical drawing	Lathe machine	1
10	Brass tube	See Appendix E for technical drawing	Lathe machine	2
11	Washer	M4	Purchased	1
12	Winged bolt	M4	Purchased	1
Trigger				
13	Trigger knob	See Appendix E for technical drawing	DLP 3D printed	1
14	Trigger	See Appendix E for technical drawing	Lathe machine	1
15	Trigger spring	Diameter: 1.45 mm, Length: 11.18 mm, Spring constant: 0.16 N/mm	Purchased	1
16	Bolt	M2.5x5	Purchased	2
Shell				
16	Top part shell	See Appendix E for technical drawing	DLP 3D printed	1
17	Bottom part shell	See Appendix E for technical drawing	DLP 3D printed	1
18	Cannula cap	See Appendix E for technical drawing	Lathe machine	1
19	Cannula	Diameter: 2mm, Length: 84 mm, Wall thickness: 0.15 mm	Purchased	1
20	Spring plunger	M4, Length: 9 mm, Spring pressure: 4-10 N	Purchased	1
21	Bolt	M2.5x12	Purchased	4

6.2. PROTOTYPE ASSEMBLY

CATEGORIZATION

A full list of parts of the prototype is provided in Table 6.1. The assembly of these parts will be described in this section. The fully assembled prototype is shown in Figure 6.5. The prototype can be divided into two main assemblies: the needle cartridges, and the instrument.

NEEDLE CARTRIDGE

Figure 6.6 shows a photograph of the six assembled needle cartridges. Both the TruCut needles are glued to the 3D printed parts. The inner needle is glued into the cap of the cartridge. The outer needle is glued into the inner tube.

The assembly of the cartridge is done by pushing the inner tube though the outer tube, with a wave ring in between. After this, the spring can be inserted and subsequently the inner needle can be pushed through the outer needle and attached to the outer tube using the cartridge cap and the bayonet fitting.

INSTRUMENT

The instrument is assembled in steps. First, the trigger is attached to the shell top. This is done by sliding the trigger into the front of the instrument and bolting the knob through the slot in the shell top onto the trigger. Behind the trigger knob, a small spring can be placed. This spring will make sure the trigger will return to its position after triggering the TruCut needle. Subsequently, the cannula and its cap are glued into the front of the shell top. Finally, the axis is glued to the shell top. The spring plunger is attached using a helicoil into the shell bottom. Next, the bottom and top shell can be attached using bolts. To attach the revolver to the instrument, it is slid over the axis and attached at the end using a washer and a winged bolt. Figure 6.7 shows the assembly of the instrument. The revolver chamber can be loosened before and after the biopsy procedure as the needle cartridges must be stored and retrieved before and after the procedure.

Figure 6.5: Photograph of the fully assembled prototype.

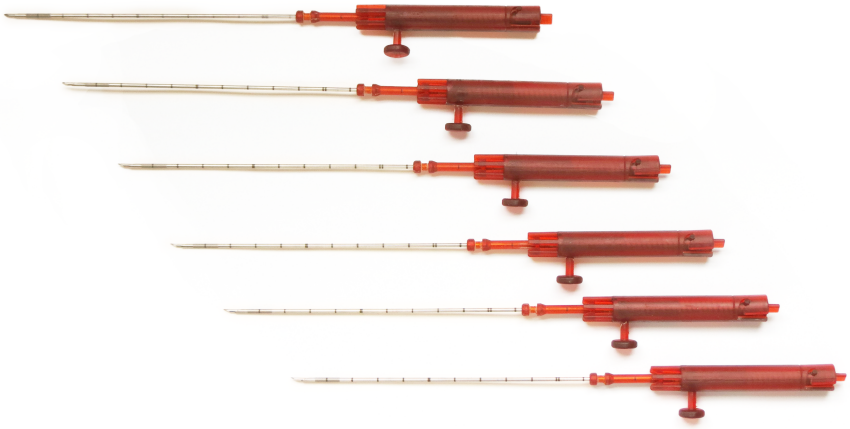


Figure 6.6: Photograph of the six fully assembled needle cartridges.

Figure 6.7: Photograph of the assembled instrument. The revolver chamber is disconnected from the rest of the instrument in the photograph.

6.3. PROTOTYPE ADAPTATION

6.3.1. PRELIMINARY TEST OF THE PROTOTYPE

A preliminary test is carried out to test the functionality of the prototype. For this test, a gelatin mixture was made to act as artificial tissue. In this initial functionality trial of the prototype, an attempt is made to obtain a multitude of samples from the artificial tissue through one insertion. The resulting biopsy samples are shown in Figure 6.8. Five samples were retrieved from the biopsy instrument through a single insertion. One of the needle cartridges contained no sample after the procedure. Two samples were retrieved from the cartridge in fragments. This marginal result is due to a malfunction of the cartridges. During the procedure four out of the six needle cartridges broke, all at the same place, as shown in Figure 6.9. The location they broke is the location where the outer needle is glued to the inner tube and where the inner tube hits the wall of the outer tube. This malfunction caused the samples to not be fully retrieved and were obtained fragmented into multiple tiny pieces after the procedure. The two needle cartridges that did not fail delivered artificial tissue samples of sufficient quality.

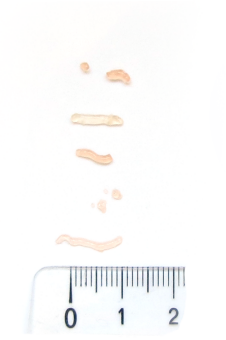


Figure 6.8: Photograph of the result of a preliminary test. The figure shows the attempt to obtain a multitude of biopsy samples through a single insertion.

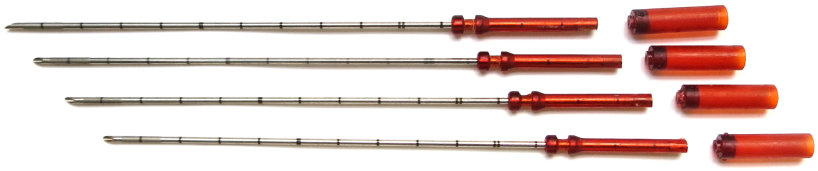


Figure 6.9: Photograph of the broken needle cartridges. They all broke at the part where the inner tube hits the wall of the outer tube after the firing of the mechanism.

A second problem occurring with the prototype is the force required to trigger the needle cartridges. This force is quite high causing difficulties with the triggering of the needle cartridges. This influences the use of the instrument, as with a high triggering force a two-handed use is required to trigger the needle cartridges. To be able to evaluate the prototype on its functionality, an adaptation of the needle cartridges is required.

6.3.2. ADAPTATION NEEDLE CARTRIDGE

In order to prevent the needle cartridges from breaking, adjustments are required to the design of the needle cartridges. These adjustments are required on three aspects of the cartridge: an adjustment to the weak spot of the inner tube, an adjustment of the spring, and an adjustment of the snap-fits of the outer tube. The adjustments applied to the design are shown in Figure 6.10.

First, the weak point in the design of the inner tube should be changed. This weak point is the place where the outer TruCut needle is glued to the inner tube. At this place a small notch is made so that the glue could easily be applied on the outer needle. The notch is adapted by decreasing the size of the notch, as shown in Figure 6.10 (a). This will make the wall of the inner tube thicker at this spot. Furthermore, the notch is relocated so that it is not as proximate to the part where the inner and outer tube collide after the cartridge has been triggered.

A second adjustment regards the chosen spring constant. A new spring is implemented in the needle cartridges. This spring has a spring constant of 0.18 N/mm. This lower spring constant will put less stress on the needle cartridge making it more reliable. Appendix C explains about the spring specifications of a variety of existing biopsy instruments. The spring specification chosen for the novel needle cartridges is proximate to the lowest spring constant as described in Appendix C.

The final adjustment made to the cartridge is the design of the snap-fits, shown in Figure 6.10 (b). The snap-fits are a critical part of the cartridge design. The snap-fits determine the force required to trigger the cartridge. The triggering force required to lift the snap-fits from the slot should be lowered. The previous cartridges required very tough snap-fits, so that the snap-fits would be able to withstand the force of the loaded spring. The lower loaded spring force allows a different snap-fit layout. Appendix D describes the influencing factors of the layout of the snap-fits on the triggering force.

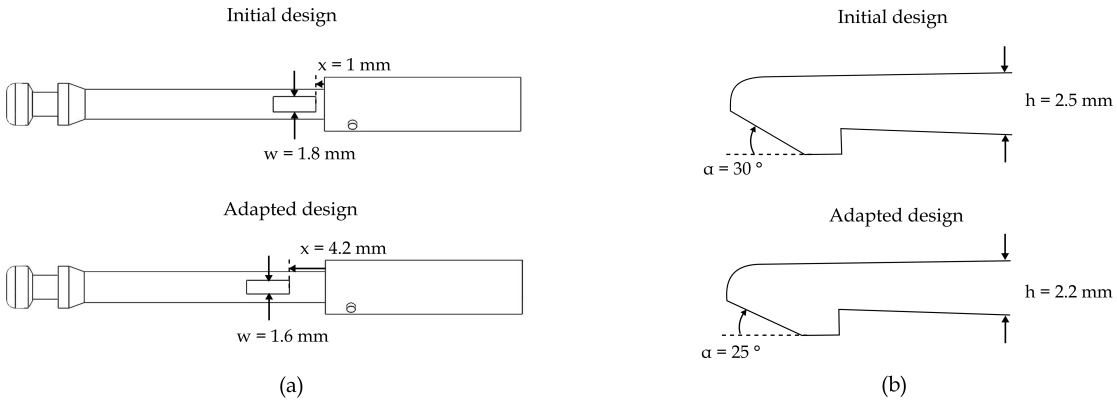


Figure 6.10: Schematic illustration of the adaptations applied to the needle cartridge. (a) Shows the adjustments applied to the inner tube. w indicates the width of the notch in the inner tube. This is made smaller. x indicates the distance of the notch from the part of the inner tube which collides with the outer tube. In the adapted design, this notch is placed further from this part. (b) Shows the adjustments made to the snap-fits of the outer tube. The angle of inclination α has been decreased, as well as the height of the snap-fit beam h.

7 EVALUATION

7.1. PROOF OF CONCEPT EXPERIMENT

7.1.1. EXPERIMENT GOAL

To evaluate the design of the novel biopsy instrument, a proof of concept experiment is performed. The design goal of the novel biopsy instrument is to be able to take multiple biopsy specimens through a single insertion. The prototype will be evaluated and validated for the following aspects:

1. The ability to take multiple biopsy samples through a single-insertion.
2. The ability to use the prototype according to the intended use.
3. The comparison between the novel instrument and an existing biopsy instrument in terms of operation speed.

7.1.2. EXPERIMENTAL METHODS

ARTIFICIAL TISSUE

The biopsy instrument will be tested on artificial tissue made out of gelatin. The gelatin is prepared using a mixture of water and gelatin powder (Gelatin powder 50 g, Van Gilse, Suiker Unie, Oud Gastel, The Netherlands). The base of the artificial tissue will be a turbid yellow color. The lesion site will be mimicked using a colored gelatin layer inside the gelatin base. The coloring will be done using blue and red pigments (Pigments, Dr Oetker, Amersfoort, The Netherlands). To prepare the artificial tissue, the gelatin powder is mixed with the right amount of water. The mixture is boiled for one minute, and subsequently poured into a glass cup.

To test which water to gelatin ratio is optimal for the TruCut biopsy needle, a small trial was performed to check the quality of the biopsy sample in relation to the gelatin mixture. For this, an existing biopsy instrument was used with the same TruCut needles as used in the novel instrument. The biopsy instrument was used to obtain six samples from varying gelatin ratios. Figure 7.1 shows the result of the trial. First a gelatin mixture was made using 2.5 wt% (25 g gelatin powder per liter water), shown in Figure 7.1 (a). The biopsy samples taken from this mixture resulted in small samples which did not maintain its structure. The second mixture used a 5 wt% ratio, shown in Figure 7.1 (b). This resulted in biopsy samples of which most of them maintained their structure after removal of the instrument. However, some of the samples were fragile and fragmented into multiple pieces. The final mixture used a 7.5 wt% ratio, shown in Figure 7.1 (c). This resulted in samples which were long, and in general maintained a good quality of biopsy samples. It was therefore chosen to use a mixture of 7.5 wt% gelatin for the artificial tissue in the experiment.

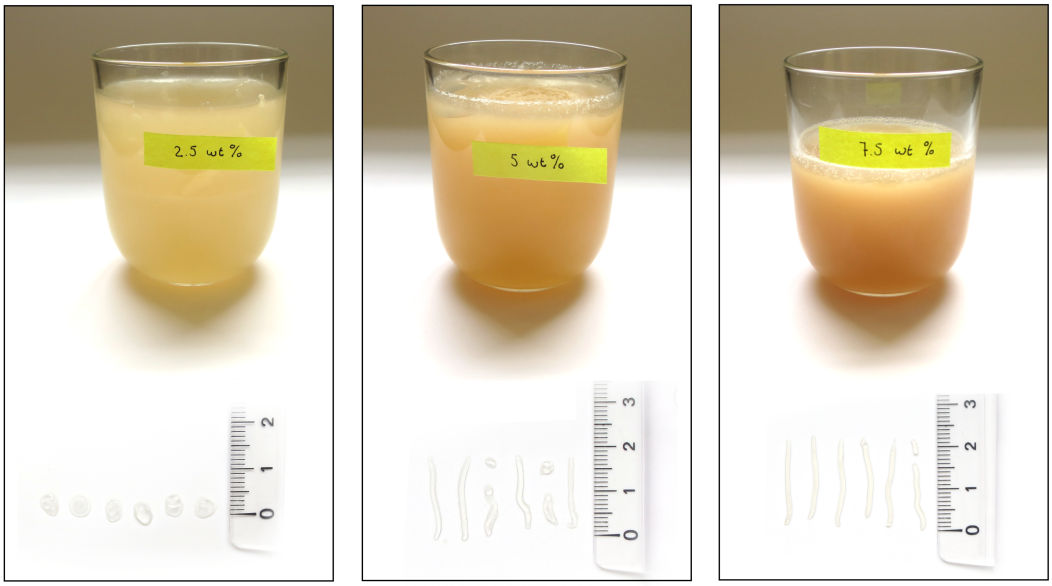


Figure 7.1: Photographs of the trial to determine the gelatin mixture for the artificial tissue. The figure shows three different gelatin mixtures, and underneath it the resulting samples taken from this mixture with a regular biopsy instrument. (a) Shows the result of a mixture of 2.5 wt%, (b) shows the result of a mixture of 5 wt%, and (c) shows the result using a mixture of 7.5 wt%.

The artificial tissue is made in three different variations. Figure 7.2 shows the three different artificial tissue models that will be used in the experiments. (a) Shows a base gelatin with a layer of red gelatin inside. (b) Is a base gelatin with a red and a blue gelatin layer inside which are separated vertically. (c) Shows a gelatin base with a layer of red and blue separated horizontally. To create artificial tissue which consists out of multiple layers, multiple steps are required. The first layer can be created by preparing a regular gelatin mixture. When the first layer is cooled down, the following layer can be added. To add the colored layers, a second and third mixture must be made with added pigments. These layers are poured onto the first base layer after it has been set. This process will result in a cup with a number of layers in different colors. The cup with the two layers separated vertically is made using a wall to separate the two layers. After they have been set, the wall can be removed from the cup. This results in three different cups containing artificial tissue for the experiments.

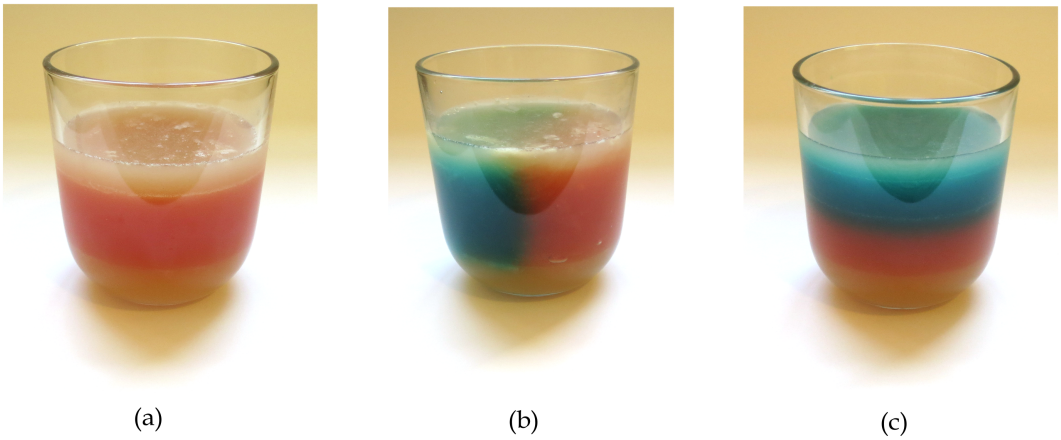


Figure 7.2: Photograph of the three varying artificial tissue models. (a) Shows artificial tissue model with a red gelatin layer within the base gelatin, (b) shows the artificial tissue model with a blue and red layer separated vertically, and (c) shows the artificial tissue model with a blue and red layer which is separated horizontally.

EXPERIMENTAL SETUP

The experimental setup for the overall experiment is shown in Figure 7.3. The setup consists out of:

1. A camera.
2. The prototype of the single-insertion multiple specimen biopsy instrument.
3. Six needle cartridges which are used in the prototype.
4. A loading device, to load the needle cartridges of the prototype.
5. Safety glasses.
6. A stopwatch.
7. Three different cups containing the artificial tissue.
8. An existing biopsy instrument (TruCore II Biopsy instrument, 18 gauge, Argon Medical Devices, Athens, USA).
9. A ruler, used to measure the obtained biopsy samples.

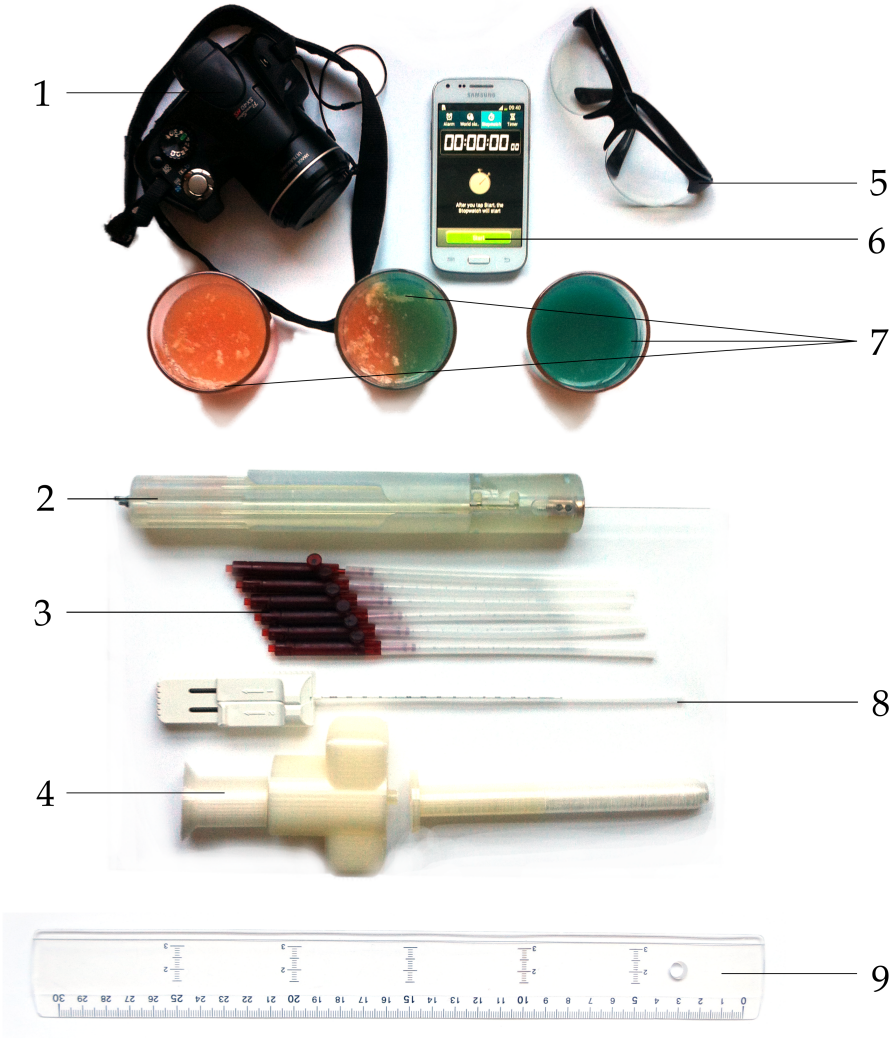


Figure 7.3: Photograph of the experimental setup.

SAFETY MEASURES

The prototype of the novel biopsy instrument has preloaded needles. Because this is a first prototype, which has not yet been fully tested for safety and reliability, it was decided to do the experiments without using external subjects to test the device. This is because for external subjects the device is unknown, and this might cause hazardous situations while handling the loaded device.

For our own safety, a loading mechanism was developed to be able to load the needle cartridges in a safe manner. During the experiment and overall handling of the prototype, safety glasses will be worn.

PROTOCOL

Experiment 1:

The first experiment will evaluate the ability of the prototype to take multiple biopsy samples through a single insertion. To evaluate this, the prototype must take at least 3 biopsy samples of sufficient quality through a single insertion. Before the start of the experiment, all the needle cartridges will be preloaded using the loading mechanism. The preloaded cartridges will be placed inside the revolver chamber. After this, the prototype will be ready for use. The instrument will be used according to the user steps as described in Section 5.2.2. For this experiment the artificial tissue with a red layer (Figure 7.2 (a)) will be used to indicate the artificial lesion site.

After the biopsy procedure is done, the samples will be taken out of the prototype according to the steps as described in Section 5.2.2. The samples will be taken from the inner needles side notch by using an other needle. The tissue samples will be arranged in an array. Next, the samples will be measured, and are considered to be of good quality if they are at least 10 mm long. This result will be recorded with the camera.

Experiment 2:

The second experiment will determine if the prototype can be used according to the intended use of the design as described in Section 3.1. This intended use describes that the design should be able to:

- Take multiple biopsy samples using different orientations.
- Take multiple samples from different lesions.
- Take multiple biopsy samples from varying depths.

The intended use of taking multiple biopsy samples using different orientations will require a similar procedure as taking multiple samples from different lesion sites. This is because if separate lesions are proximate enough to be taken using a single insertion, the instrument should be reoriented to reach the other lesion. Therefore, both these intended uses will be evaluated in a single subexperiment.

Starting the experiment, the needle cartridges must be preloaded using the loading device. After all the cartridges have been loaded, the needles will be inserted into the revolver chamber. Now the prototype will be ready for use. The first subexperiment will be done by taking biopsy samples using different orientations. This can be achieved by pulling back the instrument and reorienting it a little, after each sample has been taken. For this experiment the artificial tissue with two colors separated vertically (Figure 7.2 (b)) will be used. To determine the different orientations, a multitude of samples will be taken interspersed from the two different sides (blue and red). The second subexperiment will evaluate the intended use of taking a variety of samples from different depths. Before the second subexperiment can start, the needle cartridges have to be preloaded again using the loading device. When the prototype is ready for use, the user steps will be followed according to the method given in Section 5.2.2. For the second subexperiment, the artificial tissue with the two colored layers separated horizontally (Figure 7.2 (c)) will be used. A multitude of samples should be taken from the two different depths (blue and red layer). The results of both subexperiments will be photographed. The samples will be measured and determined to be of sufficient quality if they are at least 10 mm long.

Experiment 3:

The last experiment will compare the novel biopsy instrument to an existing TruCut biopsy instrument in terms of procedure speed. For this experiment a TruCore II biopsy instrument will be compared to the prototype. Since the use of the TruCore II is unknown to the experimenter, a short training session will be performed in advance of the experiment. The TruCore II will be used according to the steps as provided in the user manual [60]. A set of three samples will be taken for practicing the use.

The goal of the test is to obtain a set of six samples. This will be done using the TruCore II and the single-insertion multiple specimen biopsy device. The time to achieve this goal will be recorded. First, the needle cartridges of the prototype will be preloaded. After this, the prototype will be used to obtain a set of six tissue samples from the artificial tissue. After the procedure, the tissue samples will be retrieved from the prototype in accordance to the

use as described in Section 5.2.2. Each sample will be arranged in an array, measured, and recorded by the camera. The duration of this procedure will be recorded using a stopwatch. Subsequently, the TruCore II will be used according to the use as described in the user manual [60]. After each biopsy, the tissue sample will be retrieved from the instrument, and the instrument will be reused. The samples will again be arranged, measured an recorded. The duration of this procedure will be measured using the stopwatch.

7.2. RESULTS

7.2.1. EXPERIMENT 1: PROTOTYPE PERFORMANCE

The first experiment was performed in accordance to the protocol. The resulting biopsy samples are shown in Figure 7.4. Five samples were retrieved from the biopsy instrument through a single insertion. One of the needle cartridges contained no sample after the procedure. One of the retrieved samples fragmented during retrieval from the side notch. The length of the samples varied between 10 to 15 mm. All five samples were therefore of sufficient quality.

Figure 7.4: Photograph of the result of experiment 1. The figure shows the attempt to obtain a multitude of biopsy samples through a single insertion. Five samples were obtained during the experiment, with a varying length between 10 to 15 mm. One needle cartridge contained no sample.

7.2.2. EXPERIMENT 2: INTENDED USE

During the second experiment, the intended use of the design was evaluated. This was done in two subexperiments which were both carried out according to the protocol. Figure 7.5 shows the result of the first subexperiment, where five samples were obtained using different orientations of the needle. This resulted into four sufficient quality samples of the two varying colors. One needle cartridge contained a fragmented insufficient sized sample, and one contained no sample. The sample lengths varied between 8 mm to 15 mm. Figure 7.6 shows the result of the second subexperiment, where six specimens were obtained from different depths. This resulted in four differently colored samples of sufficient quality. Two retrieved samples were of insufficient size. The length of the obtained specimens varied between 5 mm to 15 mm.

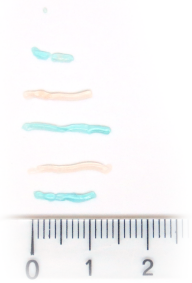


Figure 7.5: Photograph of the result of the first subexperiment of experiment 2. The figure shows the attempt to obtain a multitude of biopsy samples through a single insertion with various orientations. Five samples were obtained during the experiment, with a varying length between 8 to 15 mm. One needle cartridge contained no sample.

Figure 7.6: Photograph of the result of the second subexperiment of experiment 2. The figure shows the attempt to obtain a multitude of biopsy samples through a single insertion from various depths. Six samples were obtained during the experiment, with a varying length between 5 to 15 mm.

7.2.3. EXPERIMENT 3: INSTRUMENT COMPARISON

The third experiment is a comparison between the procedure duration of the prototype and an existing biopsy instrument named the TruCore II. The experiment was performed according to the protocol. Figure 7.7 shows the samples obtained by the prototype during this experiment. During the procedure, the prototype obtained six samples, of which three were of sufficient quality. One sample was fragmented, and two samples were of insufficient size. The overall procedure took 5 minutes and 7 seconds. The result of the procedure time measurement of the prototype can be compared with the performance of an existing biopsy instrument. For the TruCore II instrument, experiment 3 is carried out according to protocol. The array of samples taken with the TruCore II biopsy instru-

ment is shown in Figure 7.8. Four out of six samples taken were of sufficient quality. Two of the samples were fragmented. Using the TruCore II it took 3 minutes and 50 seconds to obtain six biopsy samples.

Figure 7.7: Photograph of the result of experiment 3. The figure shows the attempt to obtain a multitude of biopsy samples using the prototype. Six samples were obtained during the experiment, with a varying length between 3 to 11 mm.

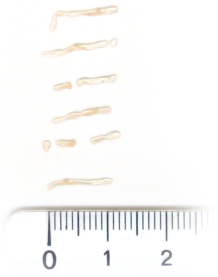


Figure 7.8: Photograph of the result of experiment 3. The figure shows the attempt to obtain a multitude of biopsy samples using an existing biopsy instrument (TruCore II). Six samples were obtained during the experiment, with a varying length between 2 to 15 mm.

8 Discussion

8.1. Research Outline

Core-needle biopsy techniques provide a minimally invasive way of obtaining a tissue specimen from a lesion. To be able to carry out a proper diagnosis, the tissue specimen should sufficiently represent the lesion. For this reason, it is often required to obtain several samples from a certain lesion site. This research outlined a design project of a novel core-needle biopsy instrument. The aim of the design was to provide a solution to obtaining a multitude of biopsy samples, without requiring to puncture the lesion site multiple times. This would decrease the invasivity of the biopsy procedure, as well as the procedure duration. During this research, a design of the novel biopsy instrument was developed and prototyped. This instrument was designed to be able to take multiple biopsy samples through a single insertion. The prototype was evaluated based on its performance. Furthermore, potential purposes of the design in terms of functionality, and a comparison of the prototype with an existing core-needle instrument in terms of operating duration were evaluated. The design and evaluation of the single-insertion multiple specimen biopsy instrument came with a number of limitations. This chapter will discuss these limitations, and provide recommendations for future research.

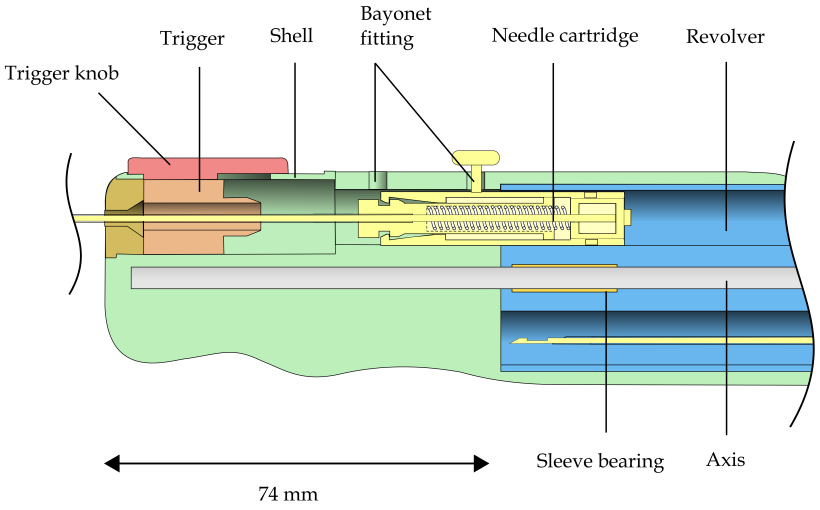
8.2. Design Limitations and Recommendations

8.2.1. Instrument Size

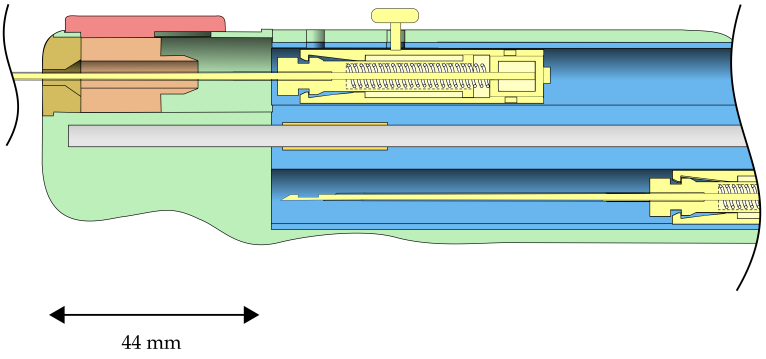
The current design of the novel instrument has an unusual length for a handheld instrument. The length of the instrument, excluding the needle, is 300 mm. This instrument length is mainly determined by the length of the needle, which must be able to fit entirely inside the revolver chamber. Adding to the length of the device, is the front part of the shell. This part consists out of two bayonet fittings, used for positioning the needle cartridge, and a trigger mechanism. Together, this results in an uncommonly long instrument. This length might cause inconvenience during the handling of the instrument. Therefore, reducing the length of the instrument would be a benefit in terms of use. Also, reducing the length is aesthetically desirable. A smaller instrument will appear less intimidating.

For the current design, the instrument length could be minimized by adjustments to the bayonet fitting and the trigger mechanism. This is shown in Figure 8.1. Figure 8.1 (a) shows a section of the side of the current design of the instrument. The bayonet fitting and trigger add a length of 74 mm to the front of the revolver chamber. This length can be reduced by implementing the two bayonet fittings in the revolver chamber, as shown in Figure 8.1 (b). This way, the shell will only require to contain the trigger. This would decrease the instrument length by approximately 30 mm. The length of the instrument could be further reduced by designing a very narrow trigger mechanism, as shown in Figure 8.1 (c). Making the trigger shorter, would additionally reduce the size about 15 mm.

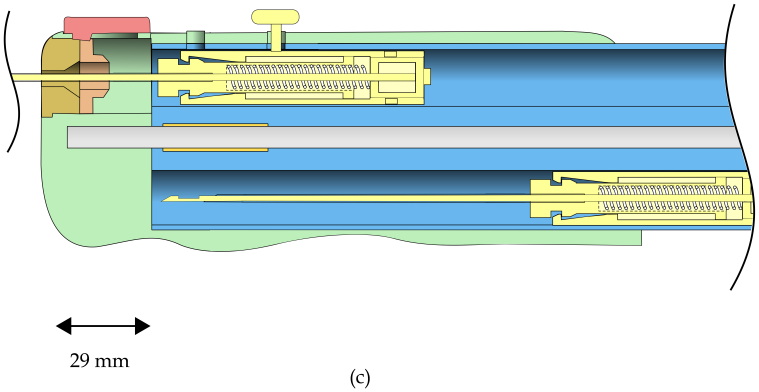
The diameter of the instrument is determined by the revolver chamber. The needle cartridges must fit in a tangential manner within the diameter of the chamber. In general, the instrument diameter suffices to the requirements, but note that the diameter can be adjusted in accordance to adjustments to the needle cartridges. When a spring is chosen with a larger or smaller diameter, the diameter of the cartridge can be adjusted and therefore the entire diameter of the instrument.



(a)



(b)



(c)

Figure 8.1: Schematic illustration of the length reduction of the instrument. The image shows a section of the side view of the instrument. (a) Shows the current design of the instrument, the bayonet fitting and the trigger add a length of 74 mm to the front of the instrument. (b) Shows a length reduction by integrating the bayonet fitting in the revolver chamber. This will result in a length of the front of approximately 44 mm. (c) The length can be further educed by reducing the length of the trigger, this will result in a front part of approximately 29 mm.

8.2.2. SPRING CONSTANT

A second limitation to the current design is the choice of the spring constant. The spring inside the needle cartridges determines the layout of the entire needle cartridge. The length and the diameter of the spring determine the size of the cartridge. Also, the spring constant determines the design and layout of the snap-fits. A thorough search was carried out to find suitable information about the springs used in existing biopsy instruments. This search delivered only one suitable paper. This paper, made by Wendt *et al.*, compared the cutting velocities with the biopsy quality [57]. The information in this paper provided information from which the spring constant could be estimated for a variety of conventional core-needle biopsy instruments. This is elaborated in Appendix C.

In the research by Wendt *et al.*, the cutting velocities measured in the five different biopsy instruments varied between 5 m/s to 25 m/s through tissue [57]. This is a large mutual difference. Wendt *et al.* made a comparison of the cutting velocities with the biopsy sample quality. This quality is determined by the relative weight of each sample. Wendt *et al.* concluded that the optimal cutting velocity of a biopsy instrument should be 12 m/s through tissue. However, when looking at the results, the biopsy specimen quality varied between types of tissue. This means that a certain instrument performed best in for example liver tissue, while another instrument with a different cutting velocity would receive the best biopsy sample from kidney tissue. This could mean that different type of tissues would have a different optimal cutting velocity. Next to this, the instrument with the lowest cutting velocity did result in the lowest biopsy sample quality. However, a higher cutting velocity did not necessarily mean that the tissue specimen quality was also higher. This could mean that the cutting velocity is not the only influencing factor of the biopsy quality. This is can probably also be influenced by the length of the side notch, the shape of the needle, and the sharpness of the outer needle.

Further research is required to know what the influence of a variety of factors is on the biopsy sample quality. This would result in the knowledge about the optimal cutting velocity in relation to other influencing factors of the biopsy quality. A recommendation should be made for the spring constant required for the biopsy instrument.

8.2.3. SNAP-FIT DESIGN

The needle cartridge requires a set of snap-fits to be made at the front of the outer tube. For the needle cartridge, an important aspect of the snap-fit layout is that it can hold the loaded spring force. This spring force will determine the cutting velocity, which in turn influences the sample quality, as discussed in Section 8.2.2. Next to this, the size and shape of these snap-fits also determine the so called mating force. This force determines the force required to mate, and also to release the snap-fits.

For the design, an optimal configuration of the snap-fit layout had to be chosen, which both can hold the loaded spring-force and requires an acceptable trigger force. From the initial experiment as described in Section 6.3.1, the needle cartridges could easily hold the loaded spring force of the spring with a spring constant of 0.46 N/mm. However, the required triggering force was too large. The high triggering forces caused difficulties in the use of the instrument. To trigger the mechanism, a two-handed use was required. Therefore, adjustments to the snap-fit design were required. These adjustments are elaborated in Appendix D. The final design of the snap-fits resulted in a set of snap-fits which were able to be triggered by a one-handed use. However, for safety reasons it was chosen to use a spring with a spring constant of 0.18 N/mm. This indicates that the design of the snap-fit layout is not yet optimal. This is due to unknown material properties of the used material for the needle cartridge. Also, the optimal spring constant of the spring inside the needle cartridge is unknown. Furthermore, the exact desired triggering force is unknown. For a future redesign, one must find an optimal compromise between the chosen spring constant ideal for cutting, and an ideal triggering force.

8.2.4. MATERIAL

The prototype material was largely made out of a liquid photopolymer used for a DLP 3D printer. The parts of the shell, the revolver, and the needle cartridges were 3D printed because this allowed complex designs to be easily manufactured. Even though using this material has many advantages, it also comes with its limitations.

The needle cartridges are made of a photopolymer named R5 [58]. The material properties of R5 are largely unknown. This is because this 3D printing material is relatively new, but also because the manner of 3D printing influences the material properties. As stated in Section 8.2.3, these unknown properties of the material caused difficulties determining the size and layout of the snap-fits. This is why a couple of trials were required before the snap-fits were reliable enough to be loaded by the spring. The first attempts often resulted in broken snap-fits. Not only did the unknown material properties cause malfunctions, many malfunctions of the snap-fits also occurred due to changes of the material over time. The R5 material is initially flexible, but over

time the material becomes more rigid. This is due to the reaction of the material to surrounding light after production. This often caused the snap-fits to suddenly fail.

A second limitation to the chosen material of the prototype was the transportation of the needle cartridges. A high friction force was subjected between the material of the needle cartridges and the material of the shell. This caused the needle cartridge to not always slide as smoothly through its duct as desired. This influenced the usability of the prototype.

Further research can be done to find out ideal material for the instrument, which both provides reliable needle cartridges and easy transportable needle cartridges.

8.2.5. USE

The use of the instrument is described in Section 5.2.2. The prototype could be used in accordance to the steps as described in this section. During the evaluation of the prototype, a few limitations to the prototype and therefore the user experience were found.

First, the reloading of the instrument is done by rotating the revolver chamber and aligning the next chamber with the duct towards the trigger mechanism. To properly align each chamber with the trigger duct, a ratchet mechanism was designed. However, this ratchet did not properly align the revolver chamber with the trigger duct. This caused difficulties during reloading. An adjustment of the ratchet mechanism is desired. The design should be adjusted in such a way that it will be able to properly align each storage duct.

A second limitation to the use of the instrument was the transportation of the needle cartridges. After use, each cartridge must be transported back to the revolver chamber. The user must fully transport each cartridge needle into the chamber, or else the needle tip of the cartridge will hit the shell wall during reloading. If the clinician is unaware of this, the needles might be damaged.

A final limitation to the use of the instrument was the traceability of the needle cartridges. With the current design, it is possible for the clinician to transport an already used needle cartridge to the front of the instrument. Because the needle cartridge has already been unloaded, the needle cartridge can not be triggered anymore, preventing the clinician from being able to collect another tissue sample with the cartridge. However, it will add up to the procedure duration. To prevent this from happening and to improve the traceability of the needle cartridges an adjustment is required. The cartridges could for example be numbered so that the clinicians may know which ones are used and which cartridge contains which number of tissues.

Further adjustments and research must be done on the user experience of the instrument. This research should include the functionality of the design, but also adjustments in terms of instrument layout and ergonomics. Next to this, the user experience should also be separately evaluated by experienced clinicians.

8.3. EVALUATION LIMITATIONS AND RECOMMENDATIONS

8.3.1. EXPERIMENT 1: PROTOTYPE PERFORMANCE

The performance of the design in terms of the functionality was evaluated using a prototype. The prototype was used to perform a set of three experiments, described in Chapter 7. The first experiment assessed the prototype on the ability to obtain a multitude of biopsy specimens through a single insertion. This first experiment resulted in a set of 5 sufficiently sized samples. Two factors which could influence this first experiment will be discussed below.

The samples of the experiments were obtained from an artificial tissue. This artificial tissue was made to be able to perform the procedure with the prototype. The artificial tissue consisted out of gelatin with multiple colored layers. This gelatin was developed to be able to easily obtain tissue samples using the TruCut needles as implemented in the prototype. This however, will not be the case in an actual biopsy procedure. In order to know the ability of the prototype to take biopsy samples from a lesion site, a similar follow-up evaluation should be done with the prototype. Instead of artificial tissue, the prototype should be evaluated using real tissue in this follow-up experiment.

An other factor which might influence the results of the experiment is the experimenter. Due to safety measures, no external subjects were used during the experimenting of the prototype. This might result in a different outcome of the experiment. An experienced radiologist, for example will know how to optimally take biopsy samples. A follow-up evaluation could be done by experienced clinicians.

8.3.2. EXPERIMENT 2: INTENDED USE

The second experiment was performed to assess the prototype in terms of the intended use as described in Section 3.1. This intended use is evaluated to determine the possibilities in terms of use of the prototype. During a visitation with a radiologist and oncologist, the clinicians gave suggestions of

possible uses of the single-insertion multiple specimen biopsy instrument. This evaluation is therefore meant to be explorative.

The experiment is performed on two different artificial tissues. The first artificial tissue was a gelatin base with two vertically separated colored layers, and the second artificial tissue was a gelatin base with two horizontally separated colored layers. Both artificial tissues were used to perform the evaluation of the intended use. The size of the artificial lesion sites made of gelatin may however not be representative of an actual lesion site. It might be possible that similar use of the instrument must be done on very small lesion sites. This might influence the functionality and the use of the instrument. To explore further possibilities in terms of use an functionality of the instrument, an experienced clinician should evaluate the instruments performance and purpose.

8.3.3. EXPERIMENT 3: INSTRUMENT COMPARISON

The final experiment was a comparison between an existing biopsy instrument (TruCore II) and the prototype. This experiment assessed the duration of obtaining a set of six artificial tissue samples using both instruments. This final experiment came with a variety of limitations.

The first limitation is the number of executed trials of the experiment. The procedure of the experiment was only performed once for each instrument. This is due to a safety factor. Both the prototype and the existing biopsy instrument are not made for cyclic use. This is why the experiment could not be performed a large number of times. This experiment therefore results in a mere indication of the procedure time to take multiple samples with both instruments.

A second limitation of this experiment is the experimenter. Just as in the previous experiments, this experiment was not performed using external subjects due to safety. This might cause the results to be biased by the experimenter.

Finally, the experiment is limited by the artificial tissue. Both instruments are evaluated on the procedure duration of obtaining six samples from the artificial tissue. This artificial tissue however, consists out of a very large artificial lesion site. This caused for both instruments, that no effort was required to find the lesion in the artificial tissue. An actual procedure does not only involve the retrieval of multiple biopsy specimens, but it also involves a search and an accurate insertion into the lesion site. Implementing this additional step in the procedure, might largely influence the duration of the retrieval of multiple specimens.

Further research on duration comparison between an existing biopsy instrument and the prototype should involve the ability to perform the experiment a large number of times. It also should involve external subjects to perform the experiment, preferably by clinicians. Finally, a comparison in terms of accuracy of the instruments should be performed.

8.4. FUTURE RESEARCH

8.4.1. DESIGN

Future improvements of the design of the single insertion multiple specimen biopsy instrument can be applied on many levels. Future research can be done on the geometry of the instrument. An exploration on how to reduce the length of the instrument can be carried out. This will result in a redesign of the instrument, which will improve the usability.

Another future research can look into ways to make this particular system semi-, or even fully-automatic. This would enable rapid collecting of biopsy specimens. Having the advantage that the overall procedure time will decrease drastically.

Furthermore, the instrument has to be made in such a way that can be used in a medical environment. The material of the instrument should be biocompatible and also it should be able to be sterilized. Next to this, the use of the instrument in a clinical setting should be researched. This will involve determining if the needle cartridges will be preloaded by the manufacturer or by the clinicians in advance of the biopsy procedure. Also, it should be decided on how to recycle the instrument. This involves determining if only the needle cartridges are disposable, or if the entire instrument will be disposable.

Finally, a future research can focus on the ergonomics of the instrument. How will the shape and layout be optimal for the use of the clinician. For this, background research on the way the clinician will use the instrument must be carried out.

8.4.2. EVALUATION

Future research on the design of the novel core-needle biopsy instrument must include a thorough evaluation of the design. The design was mainly tested in terms of performance and functionality. For further evaluation of the design, the prototype or novel versions of the instrument must be tested on real tissue. The real tissue will cause the system to behave differently as it is more tough, and consists of a different structure than the artificial tissue made out of gelatin.

Next to this, the instrument should be evaluated on the ability to accurately obtain multiple biopsy specimens from a small lesion site. During exist-

ing biopsy procedures, the lesion site is found using radio graphic imaging. When the lesion is found, the needle is guided into the lesion. This procedure should be carried out with the prototype to see if it is able to accurately obtain tissue samples in this manner.

Finally, an evaluation should be done on the safety and reliability of the instrument. The instrument should be very reliable, as the preloaded cartridges should not accidentally fire themselves during the use of the instrument.

9 CONCLUSION

9.1. SUMMARY OF MAIN FINDINGS

9.1.1. AIM OF THE RESEARCH

The aim of this research was to provide a novel design of a single-insertion multiple specimen biopsy instrument. As described in Chapter 1, conventional core-needle biopsy instruments are required to puncture the lesion site a couple of times to obtain a multitude of tissue samples. This is done to ensure an accurate diagnosis. This research focused on the design of a novel instrument which avoids unnecessary damage to the patient by preventing the necessity of multiple insertions. Before the start of the design process, a small search was performed on the state of the art, described in Chapter 2. A general search on conventional biopsy instruments which are able to take a multitude of samples through a single insertion was done. In this search, no results were found. Next to this, a consult with a radiologist, oncologist, and pathologist did not result in known instruments available on the market. Finally, a patent database search was performed. This search resulted in several devices with the aim of taking multiple biopsies through a single insertion. The patented designs however, all came with limitations regarding the retrieval of multiple biopsy samples. These limitations added two additional criteria to the main design goal. The design must both preserve the tissue structure and prevent cross contamination of the several tissue specimens.

9.1.2. DESIGN REQUIREMENTS

The design requirements, as described in Chapter 3, provide a set of geometric and functional conditions the design must fulfill. These requirements are used to assess the design on its completion. Table 9.1 provides a list of the geometric design requirements, and a list of the acceptance criteria as given in Chapter 3. The table also includes the result of the final design for each requirement, and whether the requirement has been achieved yes or no. Table 9.2 provides a list of functional requirements and the results.

The geometric requirements are all met by the design of the novel instrument. The design is adaptable to fit a variety of TruCut needle geometries. The instrument length can be altered in accordance to the desired needle length. Also, the instrument can be adapted to varying diameters of the TruCut needles. Furthermore, the design also fulfills all the functional requirements. Important aspects of the functional requirements are the tissue integrity and the prevention of cross contamination between tissue samples. The design uses the TruCut mechanism to both collect and enclose the sample. This causes the sample to be fully captured inside the two TruCut needles. This both protects the tissue structure and prevents cross contamination between tissue samples.

9.1.3. EVALUATION

EXPERIMENT 1: PROTOTYPE PERFORMANCE

The performance of the design is evaluated in a first experiment. This experiment assessed the prototype on the ability to obtain a multitude of biopsy specimens through a single insertion. In this experiment, an attempt was made to obtain six biopsy samples of a sufficient quality. The biopsy specimen is stated to be of a sufficient quality if it is larger than 10 mm. The experiment resulted into five sufficient sized artificial tissue specimens. From this initial experiment can be concluded that the instrument is indeed able to take a multitude of samples through one insertion of the needle.

EXPERIMENT 2: INTENDED USE

The second experiment comprised an assessment of the prototype in terms of the intended use as described in Section 3.1. The first part of this intended use was to evaluate whether the biopsy instrument is able to obtain several biopsy samples through a single-insertion in different orientations, or possibly different lesions which are proximate to each other. This was done using multi-colored artificial tissue. An attempt was made to obtain a set of six tissue samples. This resulted into four sound quality samples. From this result can be stated that the

first part of the intended use can be performed by the prototype. However, the reorienting the needle over a large distance, resulted into displacement of the artificial tissue within the cup. To prevent damaging the surrounding tissue unnecessarily, the reorientation of the needle should only be done over very small distances. A second part of the intended use described the ability of the instrument to obtain a multitude of biopsy samples in varying depths in the tissue. This was evaluated with an artificial tissue which consisted out of multiple colored layers. During the experiment an attempt was made to obtain six biopsy samples in two varying depths. This resulted into four sufficient quality tissue samples. This indicates that the prototype is able to obtain several samples from varying depths.

EXPERIMENT 3: INSTRUMENT COMPARISON

The final experiment was a comparison between the prototype and an existing TruCore II biopsy instrument. Both instruments were compared in terms of operation time to take six biopsy samples. The prototype took 5 minutes and 7 seconds to obtain a set of three sufficient sized samples. The existing biopsy instrument took 3 minutes and 50 seconds to obtain a set of four sufficient quality samples. This means that obtaining a multitude of samples is faster using a TruCore II biopsy instrument than using the prototype. However, the experiment tested both prototypes for taking a sample from a very large artificial lesion site. This means that there was no limitation in terms of accuracy of the obtaining of tissue. The existing biopsy instrument required no search for the lesion site with each insertion, whereas the prototype would in theory gain time by not requiring finding the lesion site multiple times. To evaluate this, would require a different type of experiment. Which did not fit within the scope of this project.

Table 9.1: List of geometric requirements

#	Geometric Requirements	Acceptance criteria	Design result	Achieved y/n
1.1	Needle shaft length	Range of 60-200 mm	110 mm (the design is adaptable to varying needle lengths)	Yes
1.2	Needle tip and shaft diameter	Maximally 2.1 mm	2 mm (the design is adaptable to varying needle diameters)	Yes
1.3	Needle shaft shape	Cylindrically shaped	Cylindrically shaped	Yes
2.1	Biopsy length	Minimally 10 mm	The instrument is able to take biopsies with a length of 20 mm.	Yes
2.2	Biopsy diameter	Minimally 0.4 mm	The instrument is able to take biopsies with a diameter of 1 mm.	Yes
3.1	Instrument grip length	Minimally 75 mm	130 mm	Yes
3.2	Instrument grip diameter	Maximally 75 mm	40 mm	Yes

Table 9.2: List of functional requirements

#	Functional Requirements	Acceptance criteria	Description	Achieved y/n
A	Insert and reach	Needle tip	The needle has a needle tip	Yes
B	Collect			
1.1	Biopsy retrieval number	Minimally 3 biopsy samples	The instrument is able to obtain 6 biopsy samples.	Yes
	Enclose			
2.1	Integrity	No loss of structural architecture of tissue samples	The tissue sample is enclosed within the two TruCut needles. No more loss of structural integrity is applied than with existing TruCut instruments.	Yes
2.2	Sanitation	No direct contact between tissue samples	The tissue samples are enclosed within their own set of TruCut needles. Varying tissue samples will not come into contact with each other.	Yes
	Transport			
3.1	Integrity	No loss of structural architecture of tissue samples during transport	The tissue samples are enclosed within a set of TruCut needles during transportation. The integrity of the tissue remains intact.	Yes
3.2	Traceability	Each specimen should be traceable in the retrieval sequence of the biopsy samples during transportation	The tissue samples remain traceable during transportation. Each needle cartridge is transported and stored one by one	Yes
	Store			
4.1	Traceability	Each specimen should be traceable in the retrieval sequence of the biopsy samples during storage	The needle cartridges and their samples are traceable in the storage. However, the current prototype does not provide a clear traceable numbering of storage chambers and needle cartridges.	Yes
	Reload			
5.1	Intuitive reloading	The user must be aware of when the instrument is reloaded.	The user must transport the loaded needles by hand through the instrument. This way the user will know when the next needle cartridge is ready for triggering. If a used cartridge is accidentally transported towards the trigger, the cartridge will not be able to take a sample as it has already been unloaded.	Yes
C	Accessibility	Easy removal of biopsy	The tissue sample is able to be removed from the instrument in a similar way to existing biopsy devices, or by taking out the entire inner needle.	Yes

9.2. POTENTIAL PURPOSES

Core-needle biopsy instruments provide the advantage that a tissue sample can be obtained in a minimally invasive manner. The tissue sample which provides histological information, can be obtained without requiring an incision to be made. To increase the accuracy of the core-needle biopsy, the novel design is able to take a multitude of samples through a single insertion of the needle. This has the advantage that the instrument will not require to puncture the lesions site multiple times. Furthermore, the novel design has some potential future purposes. The single-insertion multiple specimen biopsy instrument has the potential that it could eventually rapidly take away tissue. This would be possible if the instrument can be used in a semi- or even fully automatic manner. This would result in very short biopsy procedures. Furthermore, a potential purpose of the design is the ability to entirely remove a lesion. If enough tissue specimens are obtained by the instrument, the entire lesion could be removed through a single insertion. This would make the performance of an excisional biopsy procedure unnecessary. The core-biopsy would provide the advantages of the excisional biopsy (described in Section 1.1.2), without requiring to make an incision. This would allow clinicians to remove the lesion as a treatment strategy, and use this tissue for diagnosis, all through a single insertion.

ACKNOWLEDGMENTS

In this section I would like to thank everyone who has supported me to deliver this project. First of all, I would like to express my very great appreciation to the ones closets to me. I would like to thank my parents, who have supported me in many ways throughout my studies, and of course Michiel who has always been around to help me with everything.

I would like to send special thanks to my supervisor Aimée for helping me throughout both my literature study and my graduation project, by committing time and effort to go through my work and deliver useful feedback. Furthermore, I would like to thank Paul for his expert insights and advice on this design project. My special thanks are extended to David who helped me with the realization of the prototype, and Bob who helped me in the last few weeks of my graduation project with his insights and advice of the last chapters and the presentation.

Furthermore, I would like to thank the people of PAL Dordrecht, with a special thanks to Cees Damsma, for giving me a personal tour through their pathological laboratory. I would also like to thank the oncologist and radiologist Roderick Schmitz and Dries van Engelen for helping me with my questions on the subject of biopsy and providing me with their expert knowledge and suggestions.

Finally, I would like to thank all the people who helped me with this project in any way. Thanks to everyone who have checked and corrected my chapters. A special thanks to everyone who helped me with the presentation. It is greatly appreciated!

BIBLIOGRAPHY

[1] M. Lindsay, *One hundred great guns* (Walker and Company, a division of Publications Development Corporation, 720 Fifth Avenue New York, N. Y. 10019, 1967).

[2] R. Talac and R. F. McLain, *Biopsy principles and techniques for spinal tumors,* Seminars in Spine Surgery **21**, 70 (2009).

[3] H. I. Vargas, R. V. Agbunag, and I. Khalkhali, *State of the art of minimally invasive breast biopsy: Principles and practice,* Breast Cancer **7**, 370 (2000).

[4] L. J. Layfield, *Fine needle aspiration of the breast: review of the technique and a comparison with excisional biopsy,* Current Diagnostic Pathology **2**, 138 (1995).

[5] A. Pandit and W. Aston, *Biopsy techniques and principles of tumour surgery,* Surgery **29**, 89 (2011).

[6] M. C. Prasant, S. Anuroop, D. P. Ashutosh, and M. A. Fareedi, *Focus on basic principles of biopsy: A review,* Merit Research Journal of Medicine and Medical Sciences **2**, 001 (2014).

[7] R. Else, *Biopsy - principles and specimen management,* In Practice Techniques **8**, 112 (1986).

[8] S. J. Withrow, *Biopsy principles,* Veterinary Quarterly **20**, S14 (1998).

[9] [CareFusion], *Soft tissue biopsy needles,* Brochure CareFusion Corporation .

[10] [The National Breast Cancer Foundation], *Biopsy,* World Wide Web electronic publication. www.nationalbreastcancer.org/breast-cancer-biopsy (04-06-2018).

[11] [Argon Medical Devices], *Biopince full core biopsy system,* BioPince Brochure Argon Medical Devices .

[12] K. Schässburger, S. Paepke, A. Saracco, E. Azavedo, C. Ekström, and H. Wiksell, *High velocity pulse biopsy device enables controllable and precise needle insertion and high yield tissue acquisition,* Physica Medica **46**, 25 (2018).

[13] M. Edwards and S. Maitland, *Kidney biopsy,* World Wide Web electronic publication. http://mediwikis.com/wiki/index.php/Trucut_needle_biopsy (04-19-2018).

[14] R. Schmitz and D. van Engelen, *Groene hart ziekenhuis, depart. oncology and radiology,* Personal interview (2018).

[15] C. Damsma, *et al.*, PAL Dordrecht, *Pathology: Specimen handling and diagnosis.* Personal interview and tour (2018).

[16] A. Mandal, *Biopsy analysis,* World Wide Web electronic publication. www.news-medical.net/health/Biopsy-Analysis.aspx (04-09-2018).

[17] N. K. Andeen and M. Tretiakova, *Kidney tumor - adult malignancies,* World Wide Web electronic publication. www.pathologyoutlines.com/topic/kidneytumormalignantclearcelleosinophilic.html (04-19-2018).

[18] J. Taylor, O. Thompson, T. J. Coonahan, and G. A. Gray, *Single-insertion, multiple sample biopsy device with integrated markers,* (2012), patent no. US8267868 B2.

[19] M. S. Banik and D. E. Robinson, *Multi-motion cutter multiple biopsy sampling device,* (1995), patent no. US5471992.

[20] M. S. Banik, J. E. Young, S. E. Swaffar, M. B. Mosholder, K. E. Hughes, J. B. Yates, N. J. Herdman, J. M. Harris, and A. A. Alten, *Moveable sample tube multiple biopsy sampling device,* (1999), patent no. US5871453.

[21] D. E. Robinson and M. S. Banik, *Multiple biopsy sampling coring device,* (1996), patent no. US5573008.

[22] M. S. H. Chu and Y. Chin, *Instrument for collecting multiple biopsy specimens,* (1998), patent no. US5810744.

[23] B. M. S. and D. E. Robinson, *Multi-motion side-cutting biopsy sampling device,* (1997), patent no. 5601585.

[24] T. J. Coonahan, S. O. Thompson, and J. Taylor, *Single-insertion multiple sampling biopsy device usable with various transport systems and integrated markers,* (2012), patent no. US8282574 B2.

[25] L. S. Miller, *Multiple biopsy device,* (2003), patent no. US6530891 B2.

[26] R. Peliks, *Tissue removal device and method of use,* (2016), patent no. WO2016/196536 A1.

[27] G. W. Bryan and P. A. Matula, *Biopsy apparatus,* (2002), patent no. US6488636 B2.

[28] B. H. Diamond, D. E. Robinson, A. J. Dassa, and C. Warich, *Multiple biopsy sampling device,* (2000), patent no. US6142957.

[29] A. J. Dassa and B. H. Diamond, *Multiple biopsy sampling forceps,* (1998), patent no. 5840044.

[30] T. Gundberg, O. Kjeldsen, and H. Harboe, *Endoscopic device for multiple sample biopsy,* (2015), patent no. WO2015/063071 A1.

[31] T. V. Taylor, *Multiple-specimen, endoscopic biopsy forceps,* (2002), patent no. US6419640.

[32] N. L. Nakao, *Needle biopsy forceps with integral sample ejector,* (2010), patent no. US7775989 B2.

[33] J. A. Hibner, *Biopsy device with sample storage,* (2010), patent no. US7740596 B2.

[34] J. A. Hibner, A. T. Beckman, L. Reichel, C. W. Cicenas, and L. C. Stonis, *Biopsy device with replacable probe and incorporating vibration insertion assist and static vacuum source sample stacking retrieval,* (2011), patent no. US7867173 B2.

[35] J. A. Hibner, W. D. Haberstich, K. E. Hogue, S. T. W. V., and M. D'arcangelo, *Biopsy sample storage,* (2012), patent no. US8118755 B2.

[36] J. A. Hibner, *Tissue sample serial capturing biopsy device,* (2007), patent no. US7753857 B2.

[37] J. A. Hibner, A. T. Beckman, L. Reichel, C. W. Cicenas, and L. C. Stonis, *Biopsy device with replaceable probe and incorporating vibration insertion assist and static vacuum source sample stacking retrieval,* (2011), patent no. US7867173 B2.

[38] M. R. Treat, *Multiple bit, multiple specimen endoscopic biopsy forceps,* (2003), patent no. US6632182 B1.

[39] D. S. Zimmon, *Apparatus for serial collection, storage and processing of biopsy specimens,* (2000), patent no. 6071248.

[40] F. H. Burbank, T. J. Fogarty, W. E. Manska, M. A. Ritchart, T. J. Ryan, and Z. E. A., *Apparatus for automated biopsy and collection of soft tissue,* (1999), patent no. 5928164.

[41] D. Farascioni, *Biopsy apparatus and method,* (2000), patent no. 6019733.

[42] S. O. Thompson, T. J. Coonahan, and J. Taylor, *Single-insertion, multiple sampling biopsy device with linear drive,* (2012), patent no. US8262582 B2.

[43] D. Turkel and J. A. Kortenbach, *Colposcopic biopsy punch with removable multiple sample basket,* (1994), patent no. 5643307.

[44] J. J. Damarati, *Multiple biopsy device,* (2005), patent no. US6858014 B2.

[45] A. K. Glaser, N. P. Reder, Y. Chen, E. F. McCarty, C. Yin, L. Wei, Y. Wang, L. D. True, and J. T. C. Liu, *Light-sheet microscopy for slide-free non-destructive pathology of large clinical specimens,* Nature Biomedical Engineering **1** (2017), 10.1038/s41551-017-0084.

[46] C. K. Liam, *Pleural biopsy with the tru-cut needle,* Med J Malaysia **51**, 332 (1996).

[47] G. P. Coral, A. D. P. Antunes, A. P. A. Serafini, F. B. Araujo, and A. A. Mattos, *Liver biopsy: Importance of specimen size in the diagnosis and staging of chronic viral hepatitis,* Rev Inst Med Trop Sao Paulo **58** (2016), 10.1590/S1678-9946201658010.

[48] [RCPA], *Kidney biopsy,* World Wide Web electronic publication. http://www.rcpa.edu.au/Library/Practising-Pathology/Macroscopic-Cut-Up/Specimen/Genitourinary/Kidney/Kidney-biopsy (05-16-2018).

[49] C. Öbek, T. Doğanca, S. Erdal, S. Erdoğan, and H. Durak, *Core length in prostate biopsy: Size matters,* The Journal of Urology **187**, 2051 (2012).

[50] M. L. Nicholson, T. J. Wheatley, T. M. Doughman, S. A. White, J. D. T. Morgan, P. S. Veitch, and P. N. Furness, *A prospective randomized trial of three different sizes of core-cutting needle for renal transplant biopsy,* Kidney International **58**, 390 (2000).

[51] [Department of defense human factors engineering technical advisory group], *Human engineering design data digest,* Design Guide (2000).

[52] [Skallagrim], *How a firearm works - animation (1911 semi-auto handgun),* [Video file]. Retrieved from https://www.youtube.com/watch?v=rJMXXuGhINE (2013, Sep 13).

[53] Q. S.Hoober, *et al., Why aren't revolvers considered to be semi-automatic?* World Wide Web electronic publication. https://www.quora.com/Why-arent-revolvers-considered-to-be-semi-automatic (10-19-2018).

[54] [TheSeoulTrain], *How a revolver works,* [Video file]. Retrieved from https://www.youtube.com/watch?v=TXliIJ_66FQ (2010, Oct 8).

[55] [NobleEmpire], *How does m249 saw machine gun work?* [Video file]. Retrieved from https://www.youtube.com/watch?v=FJad-g95S78 (2018, Apr 15).

[56] [Picswe], *Biopsy needle,* [Figure], World Wide Web electronic publication.https://www.picswe.com/pics/biopsy-needle-96.html (10-22-2018).

[57] O. Wendt, C. Siewert, T. Lüth, R. Felix, and U. Boenick, *Schnittgeschwindigkeiten und biopsieerfolg unterschiedlicher stanzbiopsieinstrumente,* Radiologe **41**, 484 (2001).

[58] [EnvisionTEC], *R5,* World Wide Web electronic publication. https://envisiontec.com/wp-content/uploads/2016/09/MK-MTS-R5R11-V01-FN-EN.pdf (03-11-2018).

[59] [EnvisionTEC], *E-shell 600,* World Wide Web electronic publication. https://envisiontec.com/wp-content/uploads/2016/09/2018-E-Shell-600.pdf (03-11-2018).

[60] [Argon medical devices], *Tru-core ii and tru-core ii uro automatic biopsy instrument,* Product description and user manual (2017).

[61] F. Jelínek, *Steering and Harvesting Technology for Minimally Invasive Biopsy* (TU Delft Institutional Repository, 2015).

[62] [Bayer Material Science], *Snap-fit joints for plastics, a design guide,* Design guide (21-11-2018).

A APPENDIX: PATENT DATABASE SEARCH QUERY

A.1. INTRODUCTION

This appendix contains an elaboration of the search query used for the patent database search. Two patent databases are searched: Free Patents Online (FPO), and Espacenet. The query strings used for the search in each database consists out of a series of keywords and boolean operators such as AND and OR. The terms consists out of a number of five different expressions which together define the goal of the search. For each expression a number of synonyms are added to broaden the search. The AND operator combines each search term, and the OR operator adds variations to the search query which will expand the search scope. Furthermore, the search can be made more specific by searching for terms within patent titles or patent abstracts. For the FPO database this could be done by adding the operators TTL/ (title) and ABST/ (abstract) in front of the string of terms. In the Espacenet database this could be done by adding a separate search string in the title or abstract search bar. The results of the database search in this thesis were retrieved on November 16th 2018.

A.2. FREE PATENTS ONLINE SEARCH QUERY

The FPO database was searched using the query string:

> *TTL/(Biopsy) AND ABST/((Instrument* OR Device* OR Tool* OR System* AND Specimen OR Sample OR Tissue AND Collect* OR Stor* OR Obtain) AND (Multi* OR Dual* OR Triple* OR Variety OR Numer* OR Series OR Serial))*

This search was performed on US patents only, and a date range of 20 years was applied to this search. This resulted in a total number of 92 patents.

A.3. ESPACENET SEARCH QUERY

The Espacenet database was searched, using the search query:

> *Title: (Biopsy)*
> *Abstract: (Instrument* OR Device* OR System*) AND (Specimen OR Sample OR Tissue) AND (Collect* OR Stor*) AND (Multi* OR Serial)*

This search was performed on worldwide patented designs. Espacenet only allows a set of ten keywords in its query string, excluding the operator terms. Therefore, less synonyms to certain expressions were used in this search. Also, for the search on Espacenet a date range was not added to the search, as the Espacenet database is less extensive. This resulted in a total number of 47 patents.

B Appendix: Conceptual Designs

Elaboration and Selection

B.1. Introduction

This appendix contains an elaboration of the conceptual designs and a thorough description of the selection procedure. Five categories of conceptual designs are made based on the functions the novel biopsy instrument will need to execute. The instrument has to collect the tissue samples, enclose them, transport the containers with the tissue samples inside, store them inside the instrument, and finally reload the instrument.

B.2. Collect

To collect a biopsy specimen, the tissue has to be cut away. Existing devices such as the TruCut and the BioPince are able to do this. However, to broaden the scope of the design, a small brainstorm was performed on the retrieval of the specimen. The specimen can either be retrieved from the top or the side of the needle. Figure B.1 shows a variety of ideas for each category.

Collect: Top

1. **Twist:** This concept shows a simple hollow needle which retrieves the tissue through a puncture. The tissue can be loosened by wriggling and twisting the needle.
2. **Barbs:** This concept uses a needle which obtains the tissue through a puncture. The end of the tissue can be loosened by pulling the needle from the body, ripping the tissue loose. The barbs inside the needle will hold the sample in the needle.
3. **Tweezers in:** Uses a regular needle to obtain the tissue through a puncture. The tissue can be loosened from the body by tearing it loose, using tweezers inside the needle shaft.
4. **Vacuum:** The tissue can be obtained by applying a strong vacuum. Subsequently, the tissue can be loosened by pulling the needle from the body, tearing loose the tissue sample.
5. **Tweezers out:** This conceptual idea consists of tweezers on the outside of the needle. The tweezers can cut off the tissue at the front of the needle.
6. **BioPince out:** This concept is the regular BioPince mechanism. The tissue is obtained by the puncture of the hollow needle. After this, the tissue is cut loose with the pincer at the front.
7. **BioPince in:** An alternative to the regular BioPince mechanism is to use a pincer which cuts off the tissue at the front from inside the needle shaft.
8. **Sphere:** This concept consists out of a needle with a small sphere in the tip. The sphere is hollow and has a circular opening with sharp edges. This sphere can be used to "nibble" off a bit of tissue. The cavity inside the sphere holds the tissue. By subsequently turning the sphere, the tissue is cut loose with the sharp edges.
9. **Beak:** This concept is based on the design as made by F. Jelinek [61]. The inner beak-like compartment cuts away a small piece of tissue by pushing it through a conical shaped opening. this way the toothed segments bend and "bite" away the tissue.

COLLECT: SIDE

1. **TruCut out:** The TruCut out concept is the same mechanism as the existing TruCut design. An inner needle with a side notch captures the tissue, subsequently an outer needle cuts the tissue sample from the body.

2. **TruCut in:** This concept uses the same idea of the TruCut out concept. This time the tissue sample is cut from the inside of the needle.

3. **Twist cut:** This concept uses the twisting of an outer needle to cut the tissue. By twisting the outer needle around the side notch, the blade will cut the tissue from the body.

4. **Double side notch:** The tissue can be loosened from the body by using two needles with a side notch. The outer needle can be rotated around the inner needle to cut the tissue sample.

5. **Pull:** For this concept a single hollow needle is required. The tissue sample is taken by pulling the needle out of the body, a sharp edge on the needle side notch cuts the tissue loose while pulling it out.

6. **Tip cut:** This concepts uses an outer needle to cut the tissue, similar to the TruCut mechanism. Instead of cutting from the bottom to the top, like a regular TruCut needle, this mechanism will cut the tissue from the top to the bottom with a blade located at the tip of the needle.

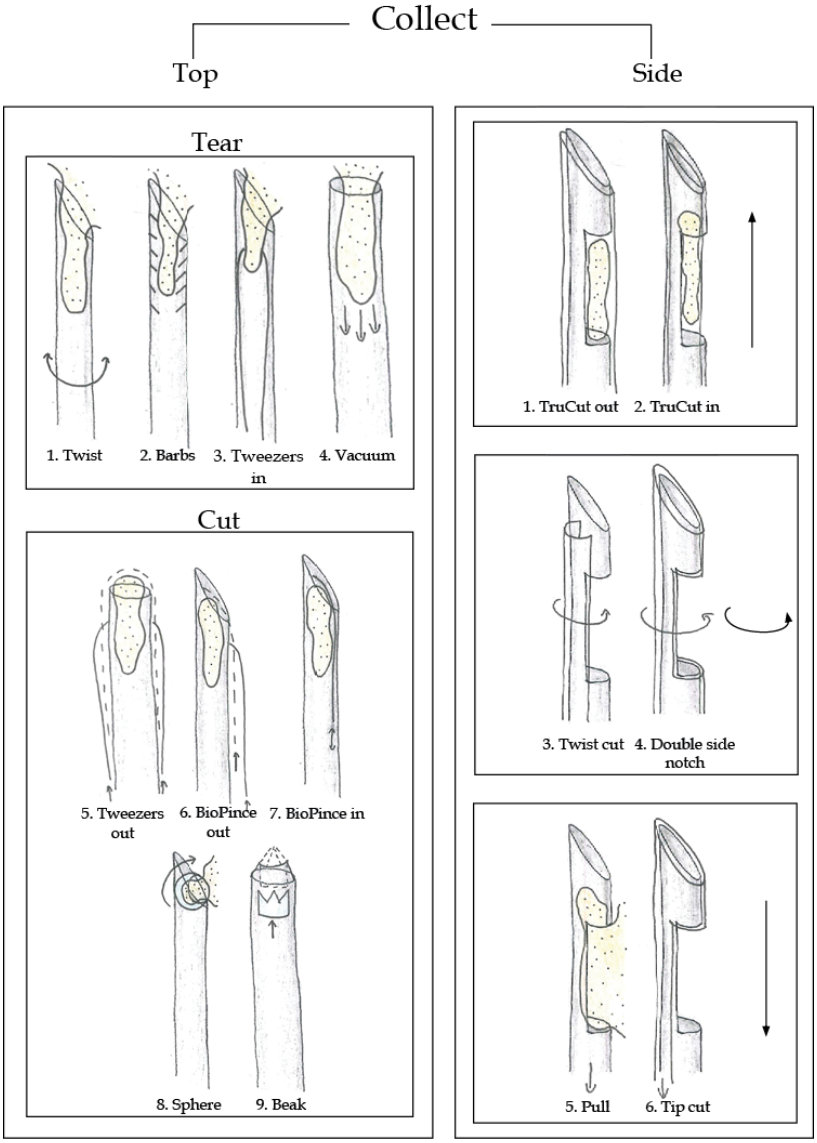


Figure B.1: Schematic overview of brainstorm session for collecting mechanisms.

SELECTION

Important aspects to consider for the collecting function of the instrument are the invasivity and the complexity of the mechanism. The most important criterion is the invasivity. The goal of the instrument is to be minimally invasive. This means that the instrument should do as less harm to the patient as possible. Therefore, the instrument should only obtain the required amount of tissue and not damage surrounding tissue.

A second important aspect is the complexity of the design. Because the needle requires to be made out of small parts it is important to consider the complexity of the mechanism. Complex mechanisms might not be able to fit inside a small needle shaft, or make the mechanism fragile or hard to produce.

Tables B.1, B.2, and B.3, show a tables with the selection described for each concept. The final selection for the collecting of the biopsy specimen is the existing TruCut out design (Figure B.1 side 1). The existing mechanism has proven itself in practice and is a reliable and simple system to continue designing with.

Table B.1: Selection procedure collecting concepts.

Top			
Concept	Invasivity	Complexity	Description
1. Twist	High	Low	The twist concept has a low complexity, for it only consists out of a hollow needle. The invasivity however becomes high as the needle requires to loosen the tissue from the body by twisting and turning the needle, this might damage surrounding tissue unnecessarily.
2. Barbs	High	High	The invasivity of the concept is high because the loosening of the tissue requires tearing the tissue. This causes an uncertain amount of tissue to be taken from the body. Therefore, this concept might cause unnecessary damage to the surrounding tissue. Also, this concept has a high complexity as small barbs are required to be made inside the needle shaft.
3. Tweezers in	High	Medium	The invasivity of this concept is high as the tissue is torn loose from the body. This does not control the amount of tissue that is being taken. Possibly causing more damage to the body than required. This concept has a medium complexity. This is because the tweezers require to go around the tissue sample inside the needle, on a very small scale this is hard to achieve.
4. Vacuum	High	Low	The complexity of this design is low. This concept is similar to fine-needle aspiration, but instead uses a larger needle to obtain tissue structure. Again, the invasivity is high due to an uncontrolled amount of tissue that is being taken, as the tissue requires to be torn from the body.
5. Tweezers out	Low	Medium	This concept has a low invasivity. As the right amount of tissue can be cut from the body. This concept has a medium complexity, as the tissue has to be cut in front of the needle with two tweezers. These have to be guided along the needle, just like the BioPince mechanism.
6. BioPince out	Low	Medium	The BioPince out concept has a low invasivity as this mechanism is able to cut a predetermined volume of tissue. The design has a medium complexity. Compared to collecting mechanisms which use a side notch to obtain tissue, the BioPince concept is more complex. This is because an additional needle is required for the insertion of the BioPince.

Table B.2: Selection procedure collecting concepts.

Concept	Invasivity	Complexity	Description
7. BioPince in	Low	High	The invasivity of this design is low as the right amount of tissue can be cut away from the body. This concept has a high complexity. The inner pincer needs to go around the tissue sample to cut off the specimen. This requires good guidance of the pincer, or else it might push the tissue out of the needle.
8. Sphere	Low	High	The invasivity of this concept is low, as a small amount of tissue can be cut away. However, this concept has a high complexity as the sphere has to be very small. Also, the sphere must be rotated to cut the tissue. To achieve this on a small scale will be very complex, if not impossible.
9. Beak	low	High	The invasivity of this concept is low as a small amount of tissue is cut away from the body. This concept has a high complexity. The beak has to be very small. Also, to be able to cut the tissue sample, the teeth of the beak have to be deformed during the biopsy procedure.
Side			
Concept	Invasivity	Complexity	Description
1. TruCut out	Low	Low	The TruCut out is the same as the existing TruCut mechanism. It has a low complexity, as it only consists out of an inner needle and an outer needle. The invasivity is low as it only damages the puncture site and the tissue where the sample is taken from.
2. TruCut in	Low	Medium	The invasivity is low as the required amount of tissue is taken without damaging surrounding tissue. The complexity of this design is medium. The mechanism is very similar to the existing TruCut mechanism. However, because the cutting mechanism is inside the needle, this leaves potentially less space for the transport mechanism.
3. Twist cut	Low	Medium	The invasivity of this concept is low as it cuts away the required amount of tissue. This concept has a medium complexity. This is because the outer needle must be rotated around the inner needle. During the collecting of the tissue, it has to be made sure that the outer needle is not (partly) in front of the side notch, preventing the tissue to go into the notch.
4. Double side notch	Low	High	The invasivity is low as this mechanism cuts away the required amount of tissue. This concept is complex as the outer needle requires a side notch as well as the inner needle. Again, one has to make sure that the side notch of the outer needle does not (partly) cover the inner side notch, keeping the tissue from going into the side notch.

Table B.3: Selection procedure collecting concepts.

Concept	Invasivity	Complexity	Description
5. Pull	High	Low	The complexity of this mechanism is low as it requires a single needle. The invasivity however, is high as an undetermined amount of tissue will be taken from the body.
6. Tip cut	Low	High	The complexity of this design is high. Cutting from the top of the needle has no advantage over cutting the tissue from the bottom of the needle. Also, this design requires a small cutting area at the tip of the needle, making it fragile. The invasivity is low as it cuts away the required amount of tissue.

B.3. ENCLOSE

The enclosing of the tissue specimen is important as it may prevent structural damage and cross-contamination during transportation of the sample. Several concepts were created for the enclosing of the tissue. It was decided that the container should be cylindrically shaped as this shape fits best into the needle shaft. Figure B.2 shows the concepts created for enclosing. The concepts can be categorized in either partially enclosing or fully enclosing containers.

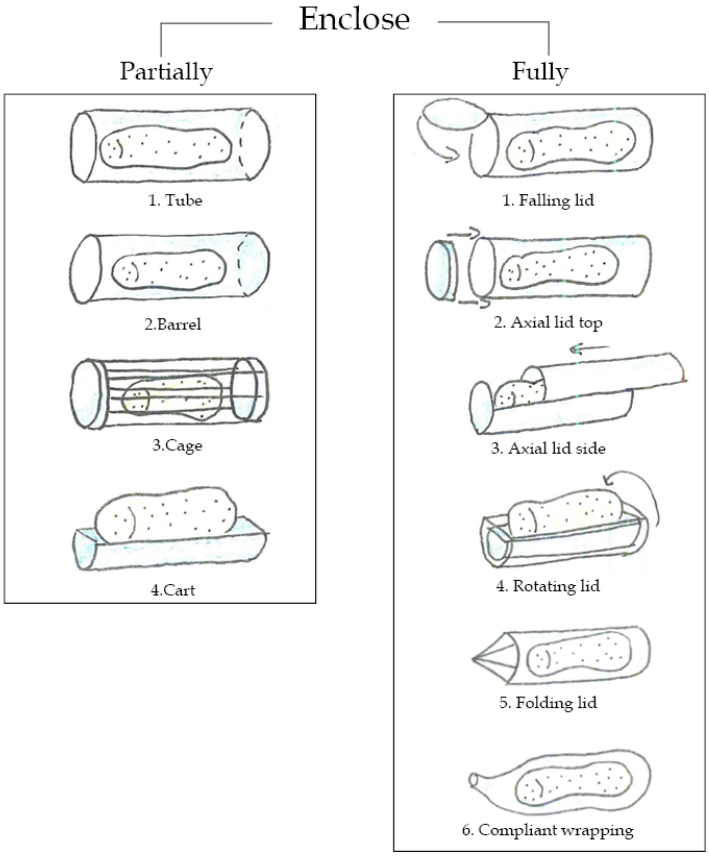


Figure B.2: Schematic overview of brainstorm session for enclosing mechanisms.

ENCLOSE: PARTIAL

1. **Tube:** This concept is a simple hollow tube. To capture the tissue, the tube can slide over the tissue to enclose it.
2. **Barrel:** The barrel concept is practically the same as the tube concept. The barrel however has one end closed.
3. **Cage:** This concept is a cage around the tissue, only partially enclosing it.
4. **Cart:** The cart concept, uses a hollow half cylinder in which the tissue can be put.

ENCLOSE: FULL

1. **Falling lid:** This concept is a barrel like tube with one end permanently closed. A lid which is already attached to the barrel falls after the tissue has been captured. This fully encloses the tissue sample.
2. **Axial lid top:** This concept again has a barrel with one end closed. To fully enclose the sample, a lid can be attached axially on the top of the barrel.
3. **Axial lid side:** Here a cart like container captures the tissue sample, and a lid on the side slides over the sample to fully enclose it.
4. **Rotating lid:** The rotating lid concept uses a double cart-like container. By rotating the bottom cart, the biopsy specimen can be fully enclosed.
5. **Folding lid:** By folding the end of the container the tissue sample can be fully enclosed after capturing it.
6. **Compliant wrapping:** This concept is a fully compliant container, just like a balloon. By wrapping it around the tissue sample, the specimen will be fully enclosed.

SELECTION

For the enclosing concepts important aspects to consider are the complexity of the design and the exposure of the tissue sample. The design should not be too complex as it might not be possible to be implemented on a small scale. This is the most important design criterion for this function. The second most important criterion is the exposure of the sample. To prevent structural damage and cross-contamination during the transportation of the sample, the tissue should not be exposed too much. Tables B.4 and B.5 show an elaboration of the selection for each enclosing concept.

For the final selection can be concluded that the best way to enclose a biopsy specimen is to use a partially enclosed system. Fully enclosing the specimen is unnecessary and adds complexity, as the tissue sample is protected well enough with partial enclosure. The selected concept is the barrel concept (Figure B.2 partially 2). This design can be easily used to capture the specimen sample. Also, the barrel concept is the best concept as it leaves the tissue the least exposed of all the partially enclose concepts.

Table B.4: Selection procedure enclosing concepts.

Partially			
Concept	Complexity	Exposure	Description
1. Tube	Low	Medium	The complexity of this concept is low, as it consists out of a single hollow tube. The exposure is medium as the tissue remains exposed at two sides.
2. Barrel	Low	Low	This concept has a low complexity as it consists out of a hollow tube with the back end closed. The exposure of the tissue is low as only one side of the tissue is exposed.
3. Cage	High	High	This concept has a high complexity. This is because the tissue is surrounded by a small cage. This is hard to fabricate, and it unnecessarily exposes the tissue at the sides.
4. Cart	Low	High	The complexity of this design is low. It consists out of a hollow compartment cut into half. The exposure of the tissue is pretty high as half of the tissue is exposed.

Table B.5: Selection procedure enclosing concepts.

Fully			
Concept	Complexity	Exposure	Description
1. Falling lid	High	Low	The complexity of this concept is high as a lid should be designed which encloses the tissue by falling down. This will be hard to build on a small scale. The tissue is not exposed as it is fully enclosed.
2. Axial lid top	Medium	Low	The complexity of this design is medium. It is complex as it requires to store the lids in the tip of the needle. The tissue is not exposed as it is fully enclosed.
3. Axial lid side	Medium	Low	This concept has a medium complexity. The lid can easily close the compartment by sliding over the tissue. However, it becomes more complex to keep the lid stored inside the needle, and align it with the rest of the container. The tissue is not exposed as it is fully enclosed.
4. Rotating lid	High	Low	This concept is complex as the lid should be rotated over the tissue sample. This requires an additional mechanism in the needle. The tissue is not exposed as it is fully enclosed.
5. Folding lid	High	Low	The complexity of this mechanism is high as the lid of the needle must be folded after tissue retrieval. This is hard to achieve on a small scale. The tissue is not exposed as it is fully enclosed.
6. Compliant wrapping	High	Low	The complexity of this design is high. Wrapping a tissue sample in compliant capsule requires some sort of vacuum to wrap the sample. On this small scale, this is too complex. The tissue is not exposed as it is fully enclosed.

B.4. TRANSPORT

The transportation of the tissue specimen is essential to make way for a new biopsy specimen. The categorization of the transportation methods is done based on the force applied to the tissue container. This can either be a pushing force, a shear force, or a pulling force. Figure B.3 shows an overview of the concepts.

TRANSPORT: PUSH

1. **Fluid pressure:** The container with the tissue sample can be transported by pushing using fluid pressure.
2. **Pushing segments:** This concept transports the tissue samples by pushing the specimens using segments. The outer needle grabs one segments after obtaining the tissue and pushes the tissue further into the needle shaft.
3. **Shooting:** The container can be transported by shooting it back to the instrument handle. This can be done by loading a spring and releasing it when the tissue has been obtained.

TRANSPORT: SHEAR

1. **Shear friction force:** By creating a shear friction force the container can be transported through the needle shaft. By making sure the friction force acting on the container and the outer needle is larger than the friction force between the container and the inner needle, the container will be transported through the needle shaft using a shear force.
2. **Conveyor belt:** By making a conveyor belt inside the inner needle the tissue sample can be transported. The friction between the belt and the container will move the container to the instrument's handle.
3. **Peristaltic motion:** By making use of a peristaltic motion of the outer needle the tissue sample can be transported.

TRANSPORT: PULL

1. **Vacuum:** This concept uses a vacuum applied on the container to pull it back in the needle shaft.
2. **Pulling rod:** By attaching a rod to the container, it can be pulled back through the needle shaft.
3. **Tweezers:** The tweezers concept uses two pincers to grab the container at the back. The tweezers subsequently pull the container through the needle shaft.

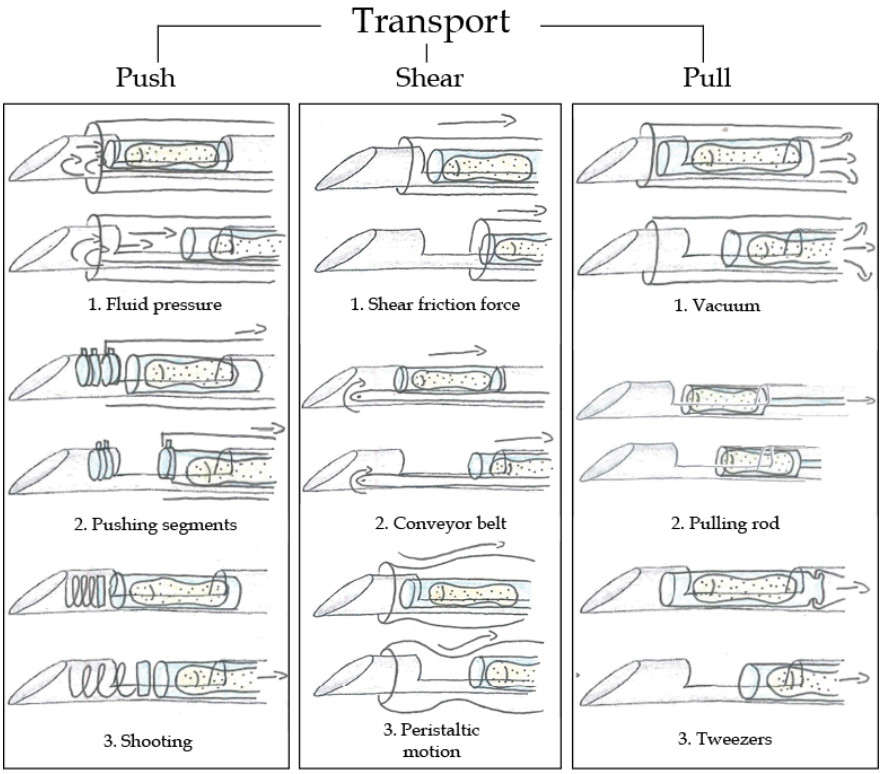


Figure B.3: Schematic overview of brainstorm session for transport mechanisms.

SELECTION

The selection criterion for the transport mechanism is the complexity of the design. In the needle shaft not much space is available for the transportation mechanism. Making it too complex might make it fragile or even impossible to implement. The elaboration of the selection of each concept is shown in Table B.6. Based on the complexity of the mechanism the selected concept is the pulling rod concept (Figure B.3 pull 2).

Table B.6: Selection procedure transportation concepts.

Push		
Concept	Complexity	Description
1. Fluid pressure	High	This design is complex as the fluid must be brought to the front of the needle to push back the container. This requires an extra tube inside the needle to be made to get the fluid in front.
2. Pushing segments	Medium	This concept is medium complex. It is implementable on a small scale, however the segments must be stored inside the tip of the needle. This will make the needle unnecessarily long at the tip.
3. Shooting	High	This design has a high complexity. In order for this concept to work, the spring must be able to shoot back the sample through the entire shaft. Every time a new specimen has to be collected, the spring requires to be reloaded. This make the system unnecessarily complex.

Shear		
Concept	Complexity	Description
1. Shear friction force	Medium	This concept has a medium complexity. The concept is fairly simple as it just consists out of the basic TruCut mechanism with two needles. The complexity in this concept is the fact that the outer needle must transport the container with a shear force, this means the friction properties between the inner and the outer needle should be different. Also, the side notch must be longer than the regular side notch of the needle to be able to store multiple samples.
2. Conveyor belt	High	This concept is too complex. It would require to be made out of very small parts. This concept is ineligible.
3. Peristaltic motion	High	This concept is too complex as well. To make a peristaltic motion a flexible outer needle should be designed.

Pull		
Concept	Complexity	Description
1. Vacuum	Medium	This concept has a medium complexity. No additional parts are needed inside the needle shaft. However, the needle must be able to be sealed properly to prevent leakage.
2. Pulling rod	Low	This concept is easy to implement. The rod can be attached to the container with for example a magnet.
3. Tweezers	Medium	This concept has a medium complexity. This concept is similar to the pulling rod concept. The tweezers however, are required to grab onto the container. This can be quite complex inside a narrow needle shaft.

B.5. STORE

After the biopsy samples have been taken, they must be stored. The storing of the samples can either be done inside the needle shaft or inside the instrument's handle. Figure B.4 shows and overview of the concepts made for storing. The samples can be stored axially, radially, or tangentially in both the shaft and the handle. In the handle it is also possible to store the containers in parallel direction. These storing mechanisms are inspired on existing storing mechanisms in guns, as discussed in Section 4.2.

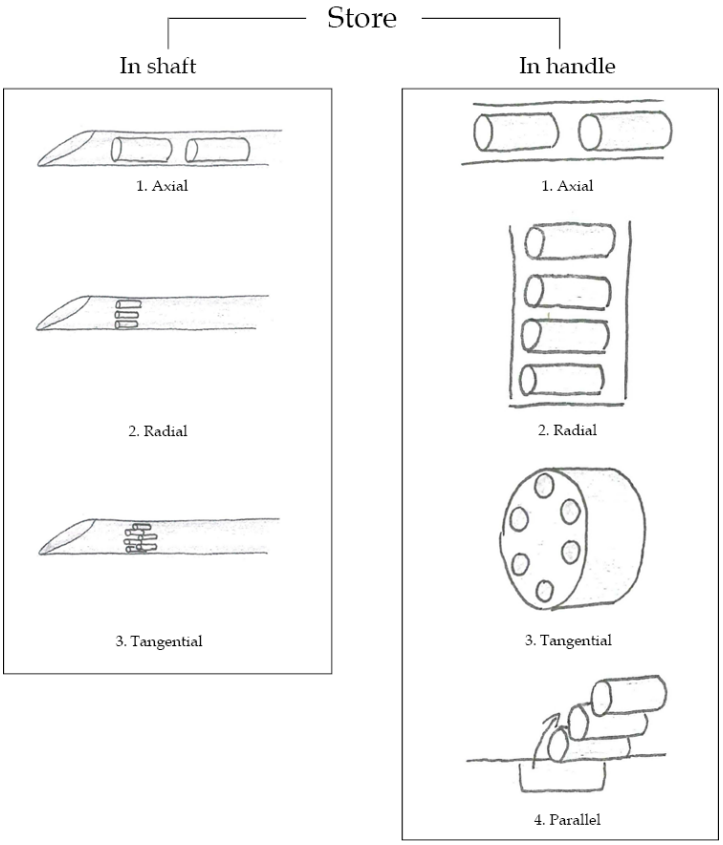


Figure B.4: Schematic overview of brainstorm session for storing mechanisms.

STORE: IN SHAFT

1. **Axial:** The axial storing in the needle shaft results in a horizontal stacking of the containers.
2. **Radial:** The radial storing in the needle shaft results in a vertical stacking of the samples.
3. **Tangential:** Tangential storing in the needle results in a revolver-chamber-like storing in the shaft.

STORE: IN HANDLE

1. **Axial:** The axial storing in the instrument handle results in a horizontal stacking of the containers. This principle is found in a Winchester 1873.
2. **Radial:** The radial storing in the instrument handle results in a vertical stacking of the containers. This principle is also found in a semi-automatic handgun.
3. **Tangential:** The tangential storing of the containers is also found in a revolver.
4. **Parallel:** The parallel storage in the instrument handle could be by creating a parallel line of specimen, as can be found in a machine gun.

SELECTION

Important selection criteria for the storing concept is that the storing should not be too complex to implement, and it should be space efficient. Tables B.7 and B.8 show the individual selection of each concept. The best storage mechanism is in a tangential manner in the instrument's handle. This is because most space is available in the handle.

Table B.7: Selection procedure storing concepts.

In shaft			
Concept	Complexity	Space efficiency	Description
1. Axial	Medium	Low	Axial storing in the needle shaft is medium complex. The containers can simply be pushed backwards in the needle shaft one after another. The system is complex due to the reloading of each container. The empty containers should be available in the front of the needle. In this part not much space is available making it a complex mechanism. The concept has a low space efficiency as the empty containers would be required to be stored inside the needle tip.
2. Radial	High	High	This concept is too complex as the biopsy samples would require to be very small for this to work. Due to the fact that the biopsy samples would require to be very small, this is a space efficient concept. However, it won't comply to the requirements of the design.
3. Tangential	High	High	This concept is too complex as the biopsy samples would require to be very small for this to work. Due to the fact that the biopsy samples would require to be very small, this is a space efficient concept. However it won't comply to the requirements of the design.

In handle			
Concept	Complexity	Space efficiency	Description
1. Axial	Medium	Low	Axial storage in the handle is a concept that has a medium complexity. This is mainly because of the reloading of the instrument. To reload the new samples, they will either have to be inserted one by one in front of the old samples, or the new containers have to be contained in the front of the needle. The space efficiency is low. The storing in an axial direction will cause the instrument to become long as all the samples are stored behind each other.
2. Radial	Medium	High	The storage in radial direction is very space efficient. However, the system is medium complex. The mechanism is prone to jamming. When pushing the empty container into the shaft, the container must be precisely aligned with the needle shaft. Therefore, if the reloading is not done properly, the mechanism might jam.

Table B.8: Selection procedure storing concepts.

Concept	Complexity	Space efficiency	Description
3. Tangential	Low	High	Tangential storage inside the instrument's handle has a low complexity. The mechanism consists out of a single barrel which can be rotated to reload the instrument. The design also has a high space efficiency, as this storing mechanism will not require an additional reloading mechanism.
4. Parallel	High	High	For this concept the biopsy containers must be put into a strip where they are attached parallel to each other. The mechanism inside the instrument handle should be able to grab the strip and loosen the containers one by one and put them back into the strip. This concept is unnecessarily complex. The space efficiency is high, as the instrument handle requires no storage space, as the strip of containers goes outside of the handle.

B.6. RELOAD

The reloading function of the instrument will make sure that a used container will be replaced with a new container. In essence the reloading is a combination of transporting the container to the storage, retrieving an empty container from the storage and transporting this empty container back to the tip. This reloading of the empty container could be done using a separate storage, and a separate mean of transportation. This would mean that the storage of the unused containers would be a different storage than the storage part of the filled containers. This would allow the system to reload an empty container right after the previous container has been transported. Another design choice can be made based on whether the reloading should be automatic or non-automatic. Section 4.2 has shown that the loading of a gun can be done in either a non-automatic, a semi- automatic, or a fully automatic manner.

For this function no elaborate conceptual designs were made. However a choice was made between making a separate reloading mechanism or not, and the level in which it would be automatic or not.

SELECTION

For this function, a selection was made based on the complexity criterion. For the biopsy instrument, before a new container can be reloaded, the used container must be back in the revolver storage. It will be complex to achieve this in a semi-automatic way, and a full-automatic way. This is because to be able to make the reloading automatic, an external energy source would be required. It is therefore decided to keep the reloading of the instrument non-automatic.

Another aspect of the reloading function is the manner of storage of the unused containers. The reloading of the instrument could be done with a method varying from the current transportation and storing method. However this would require double storage systems and complex reloading mechanisms. To keep the system simple and easy in use it was decided to use the same storage for new and used needles. The reloading will be done by manually rotating the revolver barrel.

B.7. CONCLUSION

To conclude this design phase, a final overview of the selected conceptual designs will be given. The final selection of the concepts for each category are

- **Collect:**
  - TruCut mechanism
- **Enclose:**
  - Barrel container
- **Transport:**
  - Pulling rod
- **Store:**
  - Tangential direction
- **Reload:**
  - Non-automatic

C Appendix: Spring Specification

C.1. Introduction

This appendix contains an elaboration of the determination of the spring specification. The specifications of the spring used in current biopsy instruments vary between instruments. No clear information is found about the specifications of the spring in commonly used TruCut devices. A single research is found in which the cutting velocity of TruCut devices is compared to the sample quality. This cutting velocity is determined by the spring constant of the spring used in the instrument. Also, an available spring of an existing TruCut instrument is measured to determine the specifications. Based on this information, a decision will be made of the spring specifications used for the design of the single-insertion multiple specimen biopsy instrument. The main specification which will be determined will be the spring constant.

C.2. Determination of Spring Constant

The study that contained information about the TruCut cutting specifications, is done by Wendt *et al.* [57]. The research compares the cutting velocities of five different TruCut instruments and their sample quality. The quality of the sample is determined by the relative weight of the sample, which is a quotient of the measured weight of a specimen and the reservoir volume of the needle. The sample quality is considered to be better than other samples if the relative weight is higher. With the information found in this research an estimation could be made of the spring constants used in existing TruCut instruments.

The research provided an overview of cutting velocities measured over a distance of 22 mm. The results of this are shown in Figure C.1. The graphs show the cutting velocities by cutting through a variation of tissue. In each graph a red line indicates the maximum cutting velocity through kidney tissue. The blue line indicates the maximum velocity of the needle reached through the air. The information of these graphs can be used to estimate the spring constant for each biopsy instrument.

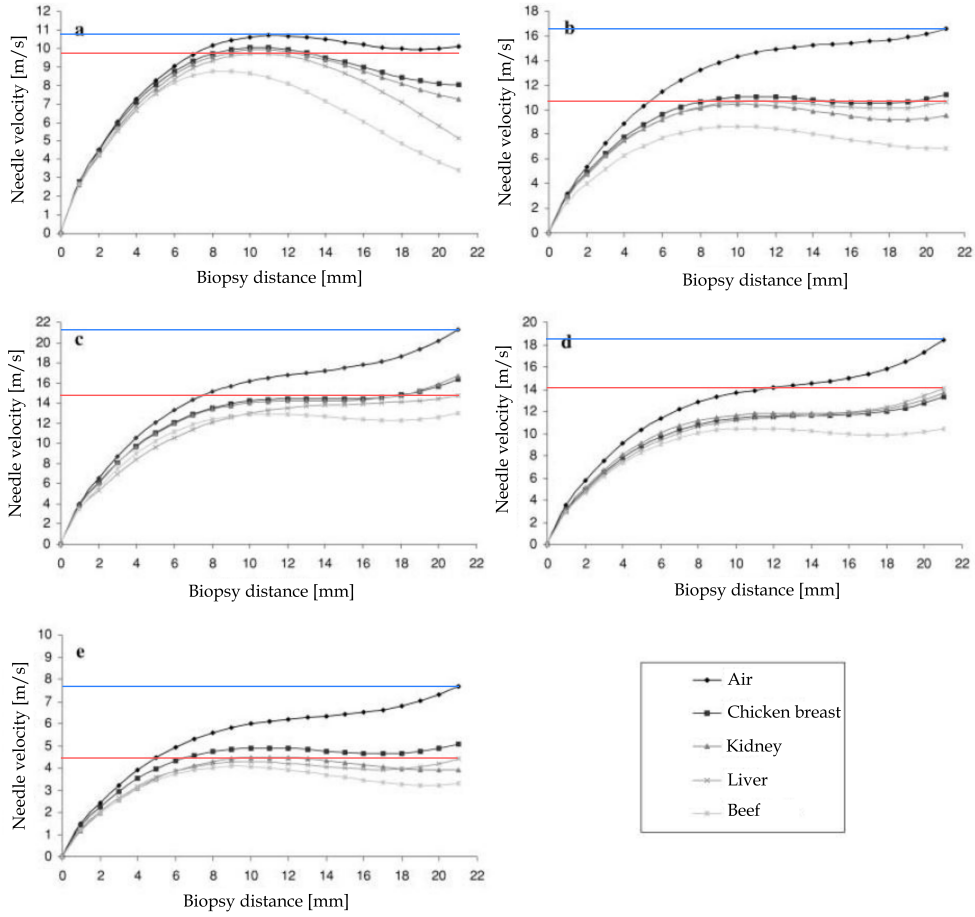


Figure C.1: Graphs showing the needle velocity in relation to the biopsy distance. The biopsy distance indicates the distance traveled by the needle. The cutting velocities are measured using five different mediums. In each graph the red line indicates the maximum cutting velocity through kidney tissue, and the blue line indicates the maximum cutting velocity through air. The graphs show a variety of brands of TruCut biopsy instruments: (a) SOMATEX, (b) COOK, (c) DAUM, (d) E-Z-EM, and (e) BIP. (Figure obtained from Wendt [57])

The velocities in the graph indicate the velocity reached by the outer TruCut needle. This outer needle is loaded by compressing a spring. Releasing this spring will shoot the outer needle over the inner needle, causing the outer needle to cut a tissue sample. For the estimation of the spring specification, the cutting velocities through air as given in Figure C.1 will be used. By using the cutting velocity through air, the friction on the system is assumed to be negligible.

Figure C.2 shows a schematic representation of the spring system of the needle. In the figure, the mass m represents the mass of the outer needle, k is the spring constant in N/mm, and v is the velocity in m/s. When the mass is at x=0 the spring is in its equilibrium position. In Figure C.2 (a) the spring is compressed 22 mm. In Figure C.2 (b) the spring is released and the mass reaches its maximum velocity at x=0.

The law of conservation of energy states that the potential energy will equal the kinetic energy when neglecting the energy loss through friction:

$$\frac{1}{2}kx^2 = \frac{1}{2}mv^2 \tag{C.1}$$

Where k is the spring constant in N/mm, x is the travel distance in mm, m is the mass in g, and v is the velocity in m/s. This can be rewritten as:

$$k = \frac{mv^2}{x^2} \tag{C.2}$$

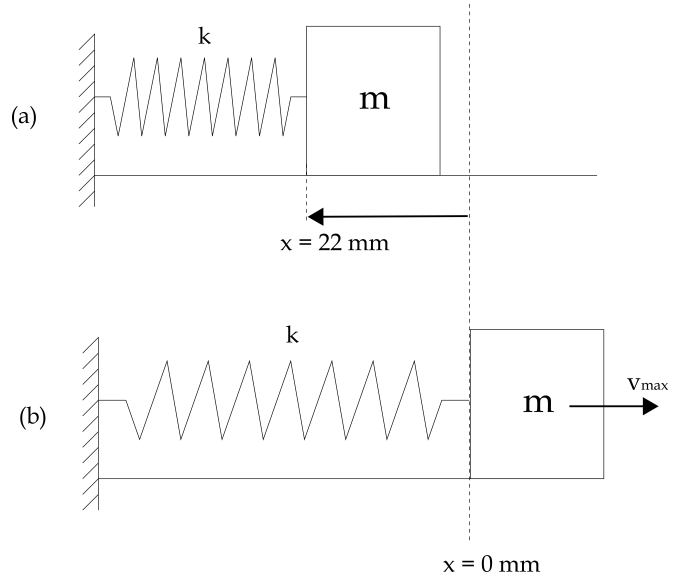


Figure C.2: Schematic representation of the spring system of the needle. (a) Is the spring compressed over a distance of 22 mm. (b) After the release of the compressed spring the mass will reach a maximum velocity v at $x = 0$. In the figure, m indicates the part of the TruCut needle that is being fired, and k indicates the spring constant.

The distance traveled by the outer needle x is estimated to be 22 mm, as this is the distance traveled by the needle in the research.

The mass of the part of the instrument that is being fired has to be estimated. The total fired mass is the mass of the outer needle together with the mass of the part of the instrument which is attached to the outer TruCut needle:

$$m = m_{needle} + m_{attachment} \tag{C.3}$$

The mass of the needle can be determined by:

$$m_{needle} = \rho * V_{needle} \tag{C.4}$$

Where ρ is the density of the material of the needle, and V is the volume of the material of the needle in mm^3. It is assumed that the needle is made out of stainless steel. The density of stainless steel is $\rho = 0.008 g/mm^3$. Since the outer needle is a hollow cylinder, the volume of the needle is given by:

$$V_{needle} = (\pi r_{out}^2 - \pi r_{in}^2) * L_{needle} \tag{C.5}$$

Where r_{out} the outer radius in mm, r_{in} is the inner radius in mm, and L the length of the needle in mm. It is assumed that the geometry of the outer needle of the design will be similar to the geometry of an existing outer TruCut needle. The geometry of the outer needle of the existing TruCut instrument is given by: $r_{out} = 0.75$, $r_{in} = 0.6$, and $L = 175mm$. Filling this in Equation C.5, gives: $V_{needle} = 111.3mm^3$. This results in:

$$m_{needle} = 0.008 * 111.3 = 0.89 gram$$

The same goes for the mass of the attachment part of the outer needle. The weight of the attachment part of the existing biopsy instrument can be determined by:

$$m_{attachment} = \rho * V_{attachment} \tag{C.6}$$

Where the ρ of the attachment part is the density of plastic, which is $\rho = 0.00138 kg/mm^3$. $V_{attachment}$ is the volume of the attachment part. This part is hard to determine, as this might differ per instrument. For now, it is assumed that it is a block of plastic with a volume of $V_{attachment} = L * b * h = 35 * 10 * 1 = 350 mm^3$. This results in:

$$m_{attachment} = 0.48\ gram$$

The estimated weight of the attachment part is about 0.5 grams. Therefore, the total mass results in approximately 1.4 gram.

For each of the five TruCut biopsy instruments the spring constant can now be determined using Equation C.2. The result is shown in Table C.1.

Table C.1: Estimation of spring specifications of variation of TruCut biopsy instruments.

Instrument brand	Maximum needle velocity through air	Spring constant
(a) SOMATEX	11 m/s	0.35 N/mm
(b) COOK	16.5 m/s	0.79 N/mm
(c) DAUM	21.5 m/s	1.33 N/mm
(d) E-Z-EM	18.5 m/s	0.99 N/mm
(e) BIP	7.5 m/s	0.16 N/mm

A measurement done on an existing biopsy instrument (unknown brand) resulted in a spring with a spring constant of 1.13 N/mm. This appears to be a similar spring constant as the DAUM or the E-Z-EM spring constants.

Knowing a variety of spring constants, a decision can be made about the spring constant to use for the design of the novel biopsy instrument. The research done by Wendt *et al.* provided a comparison between the sample quality and the cutting velocity. Figure C.3 shows a graph which plotted the relative weight of the biopsy samples against the cutting velocity of the five different instruments. Figure C.3 (a) shows the relative weight of samples taken from the kidney, and Figure C.3 (b) shows the relative weight of the samples taken from the liver. The SOMATEX biopsy instrument takes the best kidney sample, and the DAUM instrument obtains the best liver samples.

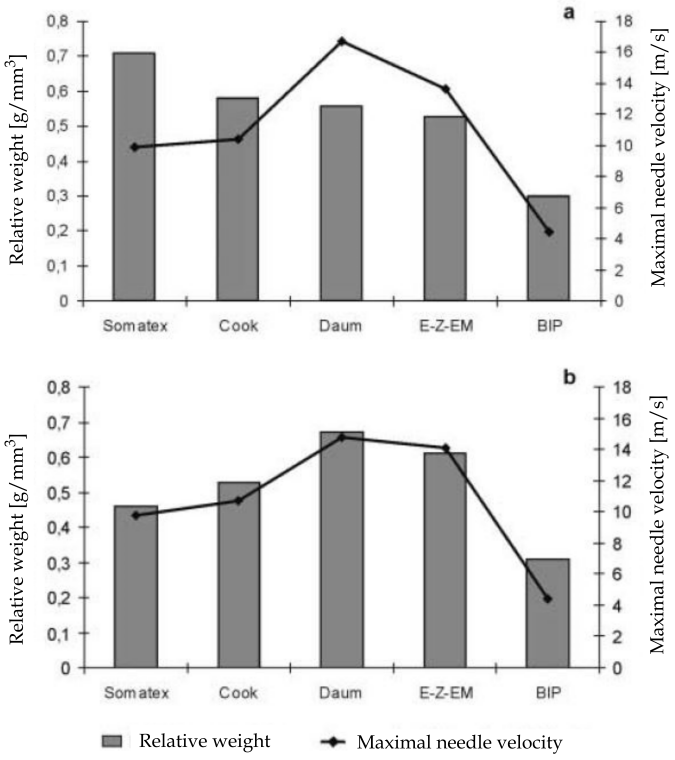


Figure C.3: Graphs showing the relative weight of biopsy samples and maximum cutting velocity of a variety of biopsy instruments. (a) Shows the results of samples taken in kidney tissue, and (b) shows the results of samples taken in liver tissue. (Figure obtained from Wendt [57])

The difference between these instruments cutting velocity is quite large. The higher cutting velocities do not necessarily obtain the best sample qualities. Therefore, it is decided to choose a spring specification comparable to the spring used in the SOMATEX instrument (a spring constant around 0.35 N/mm). For a first prototype it is safer to use a spring with a lower spring constant, because it will put less stress on the collecting mechanism. This will make the first prototype more reliable and less prone to malfunction. The design will be made in such a way that lighter or heavier springs might be implemented in a later stage.

D Appendix: Snap-fit Analysis

D.1. Introduction

This appendix contains an analysis of the snap-fit specifications of the needle cartridge. The outer tube of the needle cartridge contains a set of six snap-fits surrounding the front of the tube, as shown in figure D.1. The layout of these snap-fits determines the manageable amount of load applied by the compressed spring, for this purpose the snap-fits should become as strong as possible. However, the layout will also influence the so called "mating force". This force is the force needed to push the snap-fit into the slot, as well as the force required to release the snap-fit. In this appendix, an analysis is performed on the mating force of the snap-fit. For the design, it is desired to have a low mating-force, as the triggering of the needle cartridge should be easy for the user.

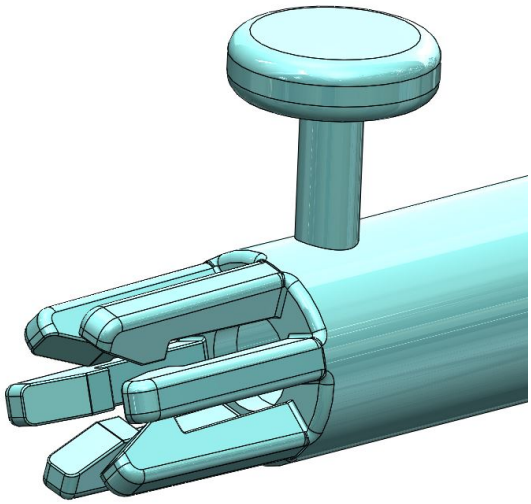


Figure D.1: Figure of the design of the outer tube of the needle cartridge. The figure shows the six snap-fits surrounding the front part of the outer tube.

D.2. Snap-fit Analysis

The layout of the snap-fit is shown in Figure D.2. In the figure, L indicates the length of the snap-fit beam, h the height of the beam, b the width of the beam, y the deflection distance, and α the angle of inclination. Finally, P indicates the deflection force.

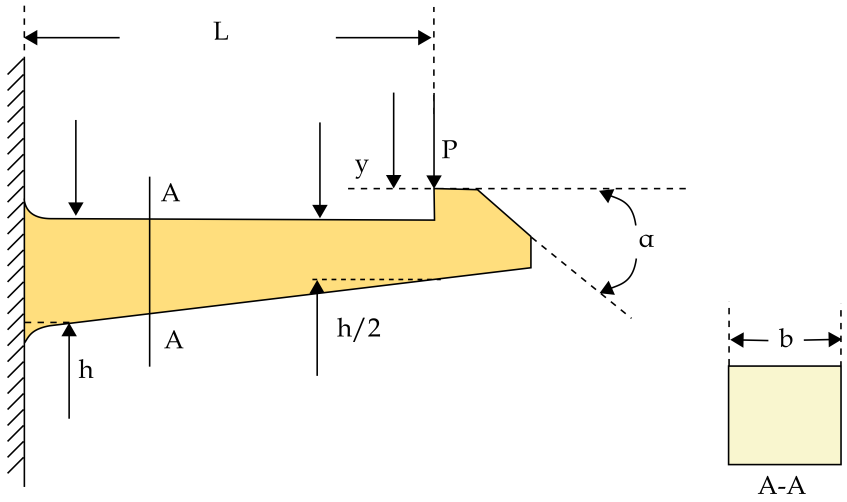


Figure D.2: Schematic illustration of the snap-fit layout. The layout is determined by the length, height and width of the snap-fit beam, L, h, and b, and also by the deflection distance y, deflection force P, and the angle of inclination α. (Figure obtained from Bayer material science [62])

Each of these specifications determine the eventual mating force W. The mating force W can be determined along a series of steps. These steps were obtained from a design guide for snap-fits joints by Bayer material science [62]. The first step is to determine the height h of the snap-fit beam. This height can be found using:

$$h = \frac{1.09\epsilon L^2}{y} \tag{D.1}$$

Where L is the length of the snap-fit beam in mm, y is the deflection distance in mm, and ϵ is the strain on the snap-fit. For the layout of the snap-fit design the length of the snap-fit beam is unknown, and will be determined iteratively. The deflection distance y is determined to be 1 mm, as the slot of the inner needle tube allows a maximum depth of 1 mm. The strain ϵ is depended on the permissible strain ϵ_{pm}. It is estimated to be:

$$\epsilon_{pm} = 4\% \tag{D.2}$$

$$\epsilon = 0.5\epsilon_{pm} = 2\% \tag{D.3}$$

This estimation is based on the permissible strain as provided in the snap-fit design guide [62]. In this guide a permissible strain of 4% is given for a polycarbonate material. Unfortunately the permissible strain of the R5 material used for the prototype is unknown.

The next step is to determine the deflection force P. This is determined by:

$$P = \frac{bh^2}{6} * \frac{E_s\epsilon}{L} \tag{D.4}$$

With b as the width of the snap-fit beam in mm, h the beam height in mm, E_s the elasticity modulus of the material in MPa or N/mm^2, ϵ the strain of the material, and L the length of the snap-fit beam in mm. The width of the snap-fit is determined by the maximum width which fits on the outer tube. For six snap-fits surrounding the outer tube, the maximum width of each beam is 2 mm. The snap-fit will be made out of a photopolymer R5 [58], as described in Chapter 6. The known R5 material properties are provided in a list provided by the supplier [58]. The modulus of elasticity of R5 is $E_s = 1190MPA$.

The final step is to determine the mating force W. This mating force is given by:

$$W = P * \frac{\mu + tan\alpha}{1 - \mu tan\alpha} \tag{D.5}$$

Where P is the deflection force in N, μ is the friction coefficient of the material, and α is the angle of inclination. The friction coefficient μ is estimated to be equal to the friction coefficient of polypropylene. This estimation is done, because the R5 data sheet states that the material is similar to polypropylene [58]. The friction coefficient of polypropylene is $\mu = 0.25$. The angle of inclination of the snap-fit is an unknown variable.

D.3. SNAP-FIT DESIGN ITERATIONS

With the provided information given above, the snap-fit layout for this design is mainly determined by two unknown variables: the length of the beam of the snap-fit L, and the angle of inclination α. Both variables will influence the mating force. The mating force can be decreased by increasing the length of the snap-fit beam. It can also be decreased by decreasing the angle of inclination α, as shown in Figure D.3.

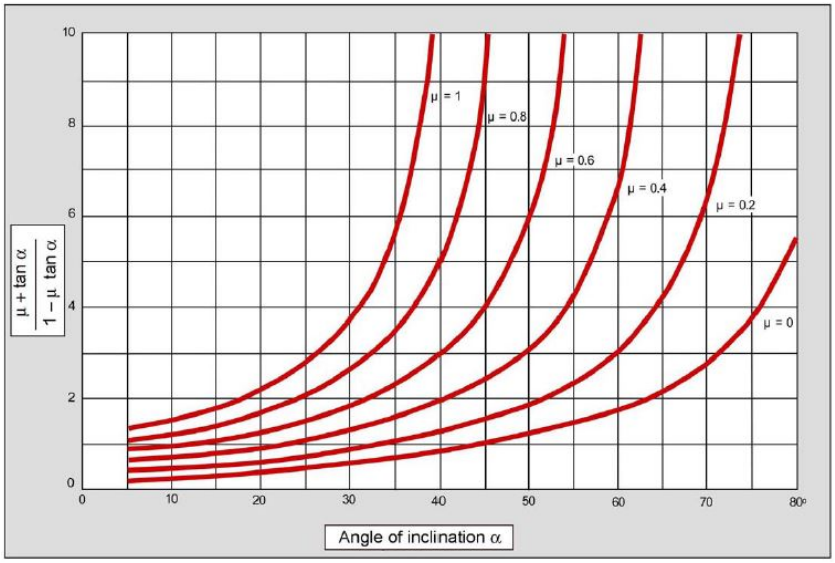


Figure D.3: Graph showing the angle of inclination α and the determination of $\frac{\mu+tan\alpha}{1-\mu tan\alpha}$. The decrease of the angle of inclination α will decrease the mating force. (Figure obtained from Bayer material science [62])

A suitable snap-fit layout has to be found which is both able to withstand the loaded spring force, and with which trigger force is manageable. Figure D.4 shows schematic illustrations of the iterations of the snap-fit design.

The first iteration, shown in Figure D.4 (a), was done by estimating the suitable length of the snap-fit to be 10 mm. Filling this into Equation D.1 provided an h of 2.18 mm. Using this height in Equation D.4, the resulting deflection force P is 3.77 N. By making use of the graph shown in Figure D.3, it was determined that an inclination angle of 30° would be suitable for this design. This could be filled in in Equation D.5, which resulted in an mating force W of 3.65 N. After this initial estimation, a trial was done to see if the snap-fits with this chosen layout was suitable to hold the desired loading force. This first snap-fit layout resulted into a needle cartridge which was not able to withstand the loaded spring force. The snap-fits slowly broke one by one.

For a second iteration, shown in Figure D.4 (b), it was decided to neglect Equation D.1, because the strain influences the determination of the beam height a lot using this equation, and it is unknown whether the estimation of the permissible strain is proximate to the real permissible strain of the material. Instead of using this first equation, the beam height h is set as a variable as well. In this second iteration the beam length L is set to 8.50 mm, the angle of inclination α remained 30°, and the height h is set to 2.50 mm. This height was the maximum which could fit on the front of the outer needle tube. Filling this into Equation D.4 and D.5, resulted in a deflection force P of 5.83 N, and a mating force W of 5.70 N. This iteration resulted in a needle cartridge which could withstand the loaded spring force, without malfunctioning. However, the mating force resulted into a too high triggering force. To trigger the mechanism the user is required to use two hands, which is undesirable for the usability of the instrument.

A final iteration was done on the design of the snap-fits, as shown in Figure D.4 (c). For this final layout the beam length L remained 8.50 mm, the angle of inclination was set to $\alpha = 25°$, and the height of the beam h was slightly adjusted to be 2.02 mm. This resulted in a deflection force P of 4.52 N, and a mating force W of 3.66 N. This snap-fit layout appeared to be able to withstand the loaded spring force, however for safety reasons, it was still chosen to use a spring with a lower spring constant for the final evaluation. The required trigger force of the snap-fits is sufficient for a one-handed use.

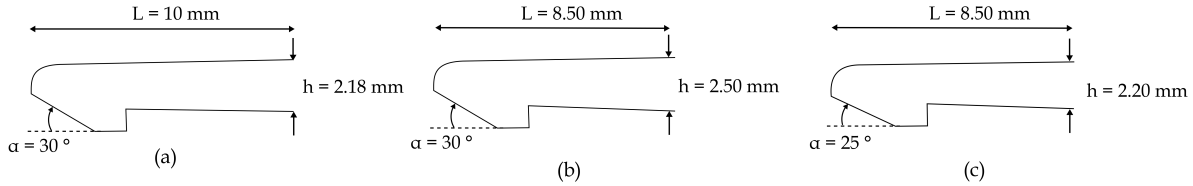
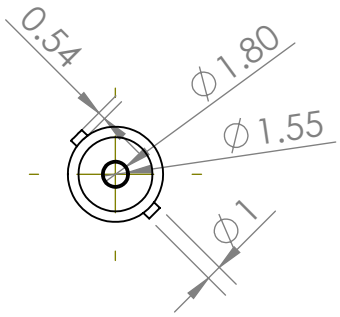


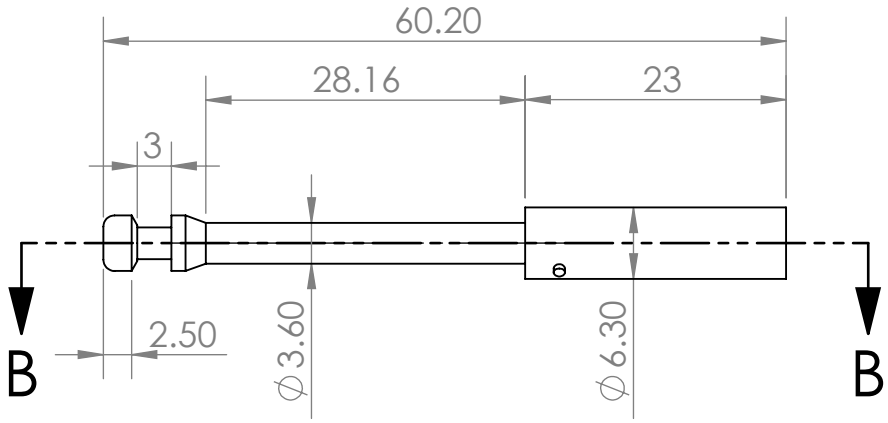
Figure D.4: Schematic illustration of iterations of the snap-fit layout. (a) Shows the initial chosen snap-fit layout, (b) shows the second iteration of the snap-fit layout, and (c) shows the final used snap-fit design for the needle cartridges.

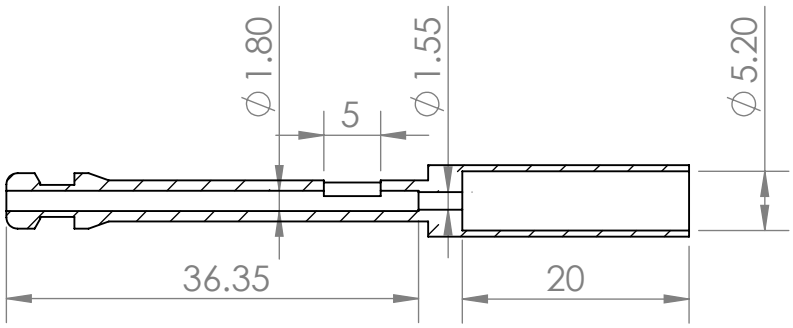
E Appendix: Technical Design Drawings

Table E.1: List of fabricated parts

List of parts			
Part #	Part name	Acquired	QTY
Needle Package			
1	Inner tube	DLP 3D printed	6
2	Outer tube	DLP 3D printed	6
3	Cartridge cap	DLP 3D printed	6
Revolver			
4	Revolver chamber	DLP 3D printed	1
5	Rotation axis	Lathe machine	1
6	Sleeve bearing	Lathe machine	2
Trigger			
7	Trigger knob	DLP 3D printed	1
8	Trigger	Lathe machine	1
Shell			
9	Top part shell	DLP 3D printed	1
10	Bottom part shell	DLP 3D printed	1
11	Cannula cap	Lathe machine	1



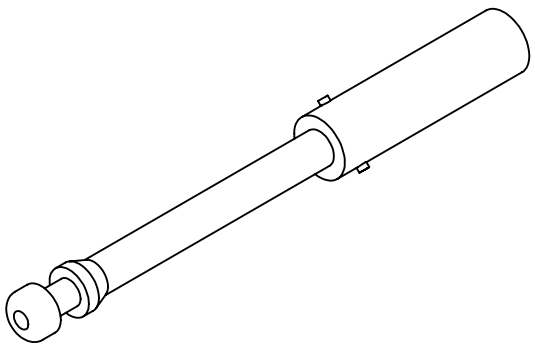




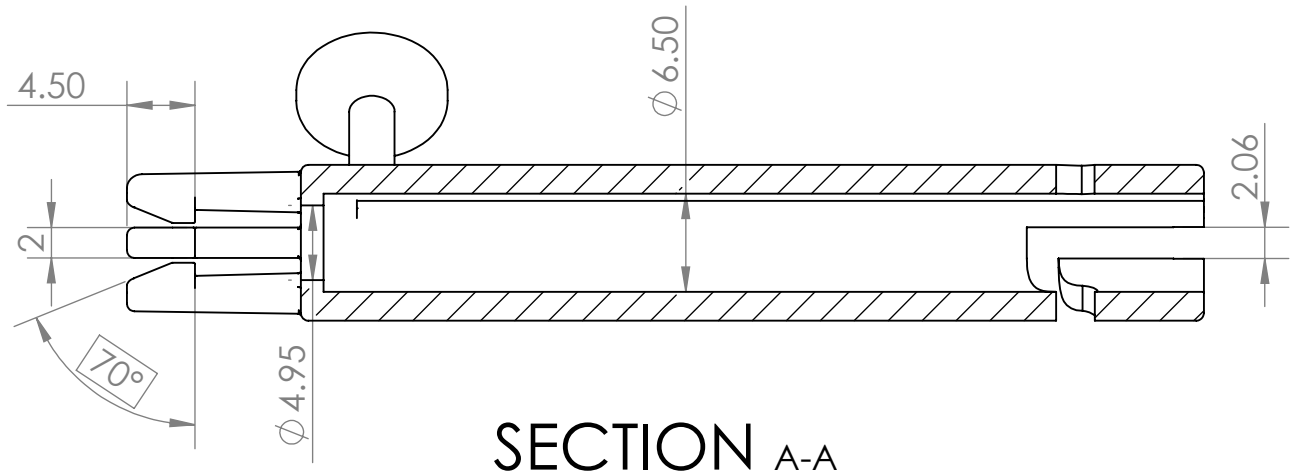
SECTION B-B

SCALE 3 : 2

Isometric view:

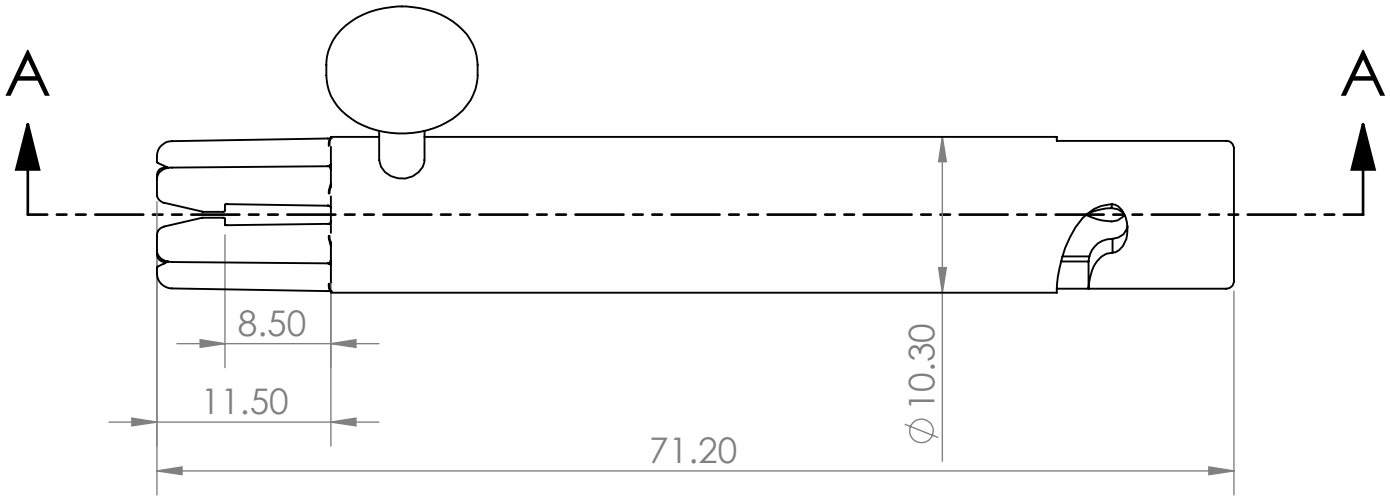


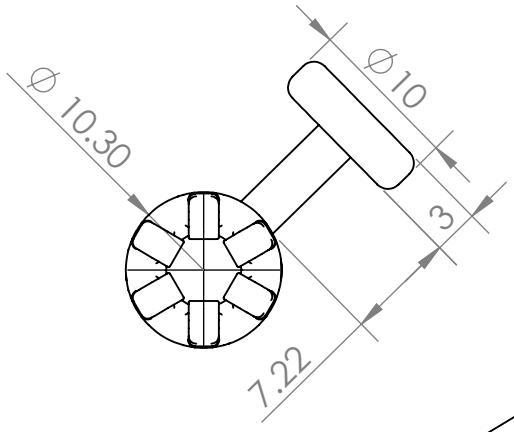
TU Delft	DATE: 19-11-2018	MATERIAL: R5 Photopolymer	Units: mm
NAME Josette Kuipéri		Inner tube	A4
			Scale: 3:2



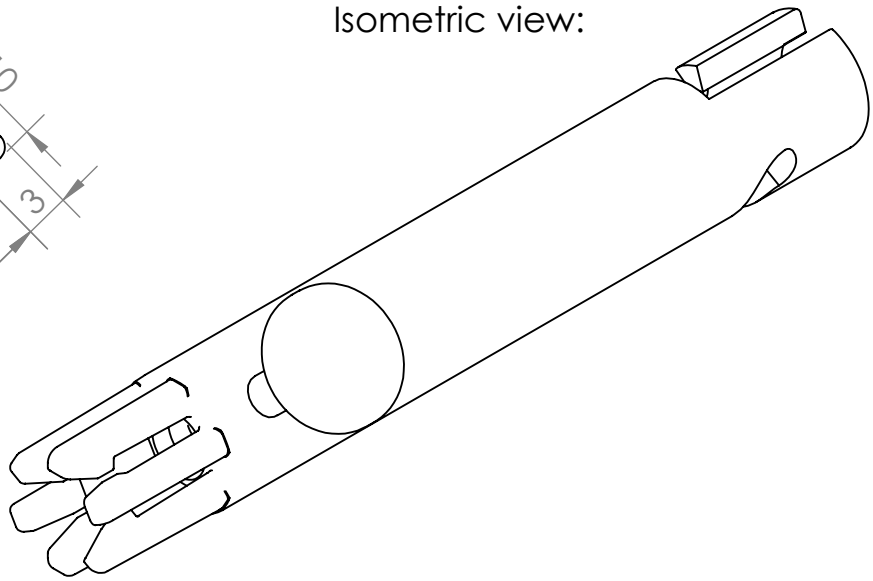
SECTION A-A

SCALE 2 : 1

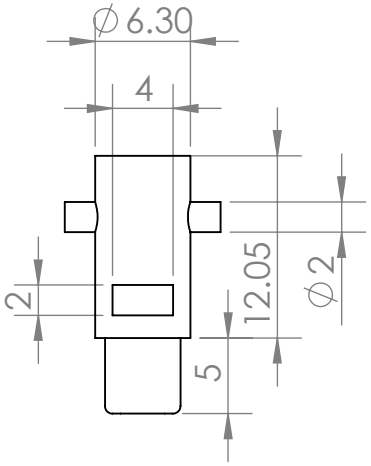


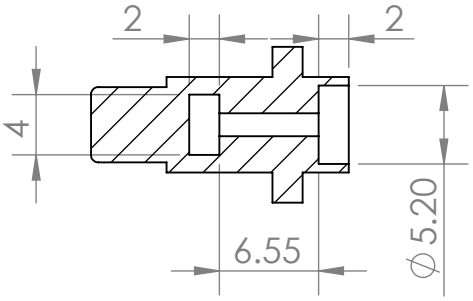


Isometric view:

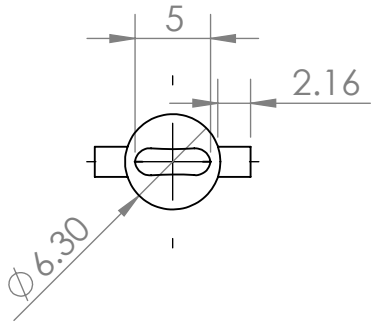


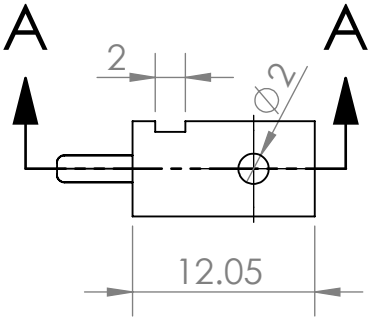
TU Delft	DATE: 19-11-2018	MATERIAL: R5 photopolymer	Units: mm
NAME Josette Kuipéri	Outer tube	A4	Scale: 2:1



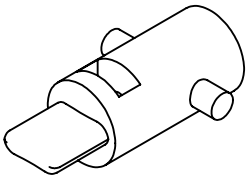


SECTION A-A

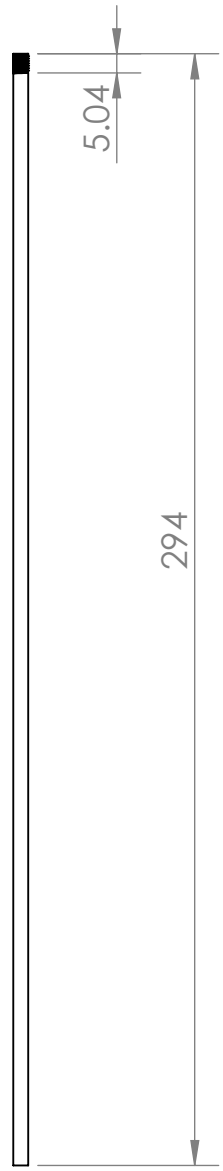




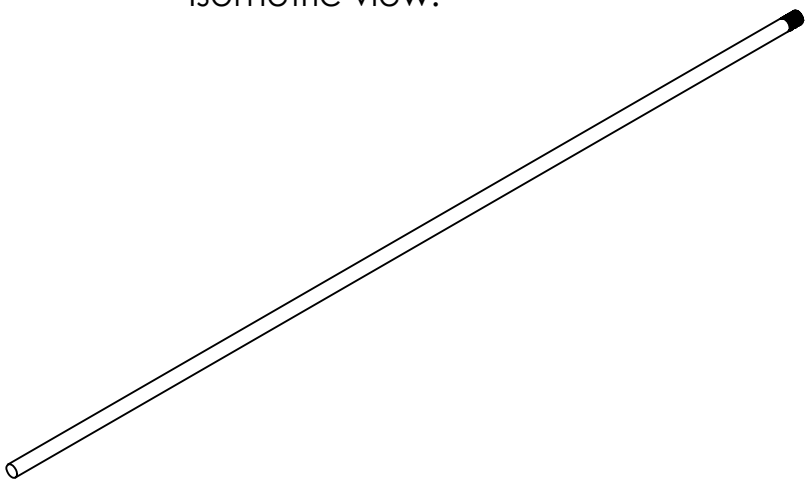
Isometric view:



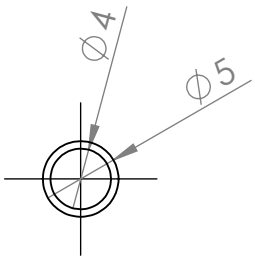
TU Delft	DATE: 19-11-2018	MATERIAL: R5 photopolymer	Units: mm
NAME Josette Kuipéri	Cartridge cap	A4	Scale: 2:1

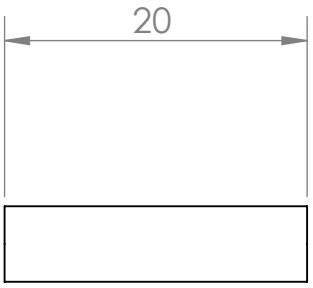


Isometric view:

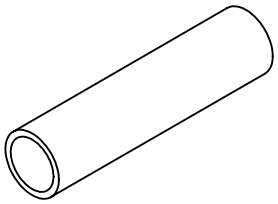


TU Delft	DATE: 19-11-2018	MATERIAL: Steel	Units: mm
NAME Josette Kuipéri	Axis		A4
			Scale: 1:2

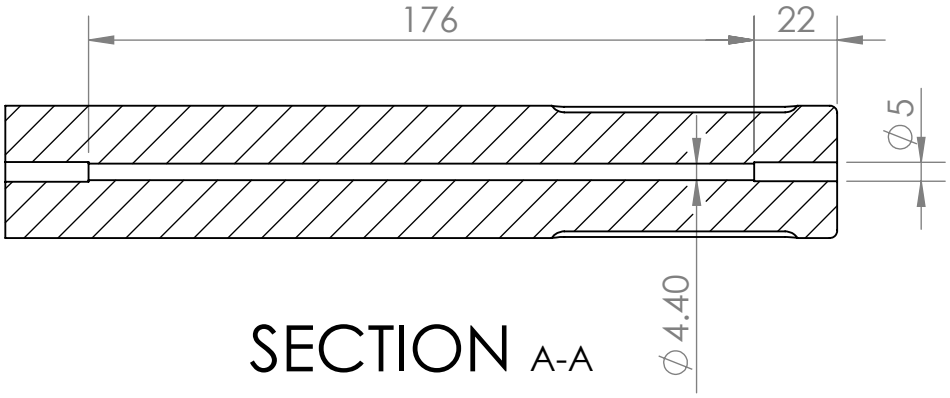




Isometric view:

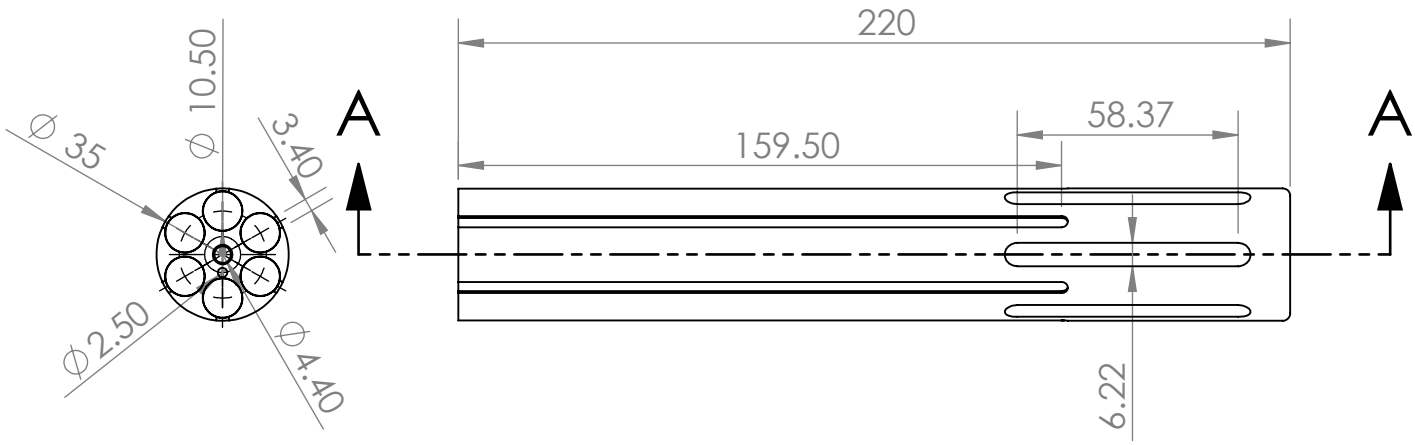


TU Delft	DATE: 19-11-2018	MATERIAL: Brass	Units: mm
NAME Josette Kuipéri		Sleeve bearing	A4
			Scale: 2:1

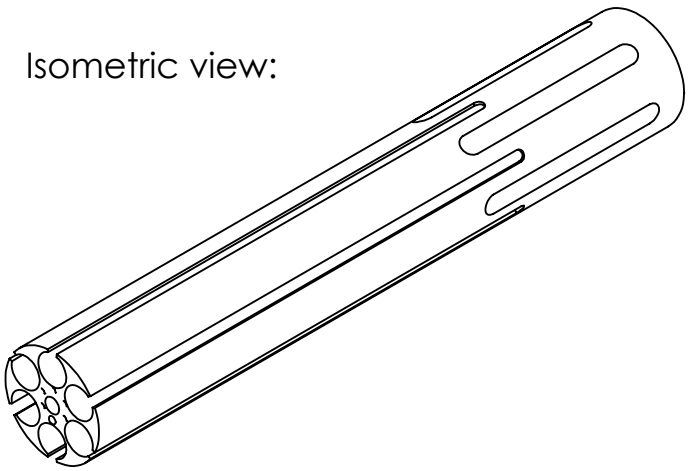


SECTION A-A

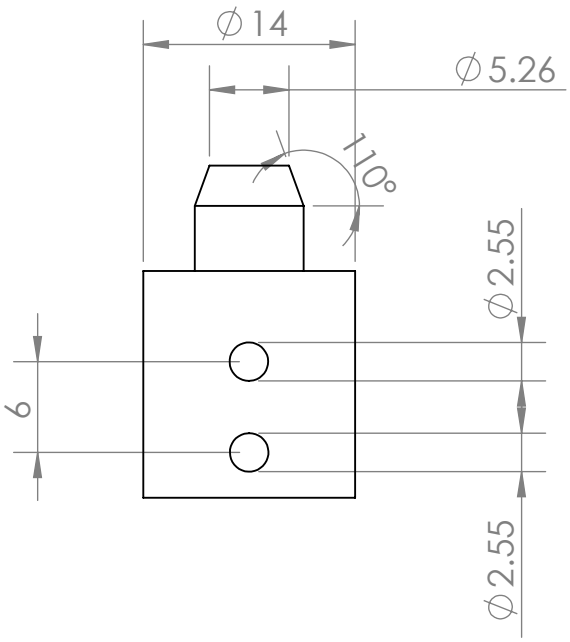
SCALE 1 : 2

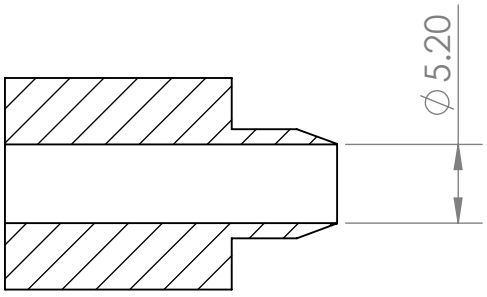


Isometric view:

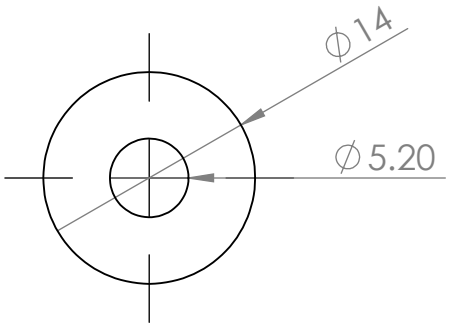


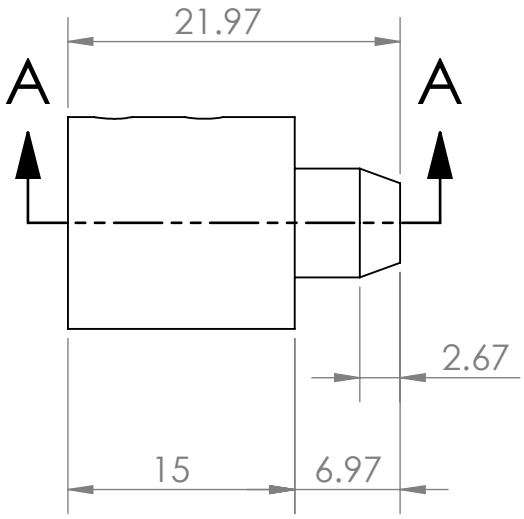
TU Delft	DATE: 19-11-2018	MATERIAL: E-shell 600 photopolymer	Units: mm
NAME Josette Kuipéri		Revolver	A4
			Scale: 1:2



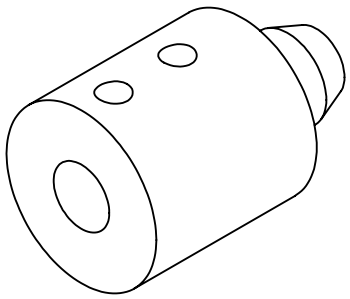


SECTION A-A



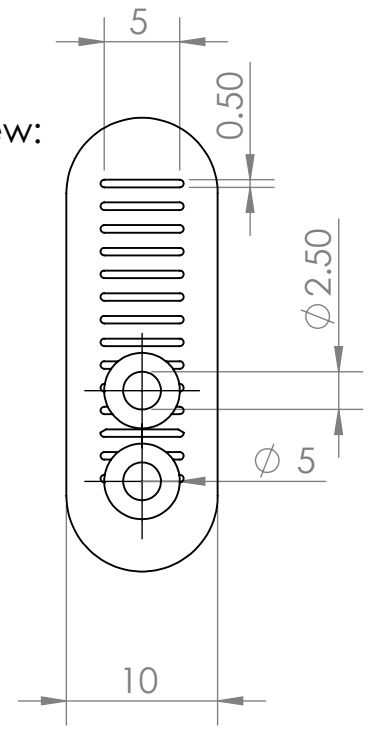


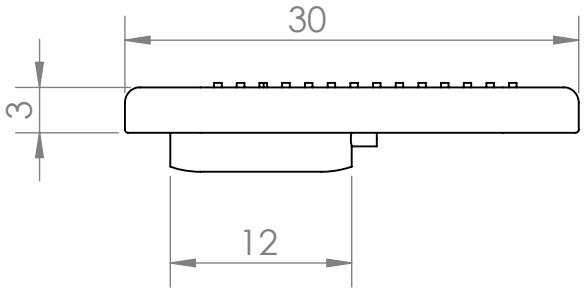
Isometric view:



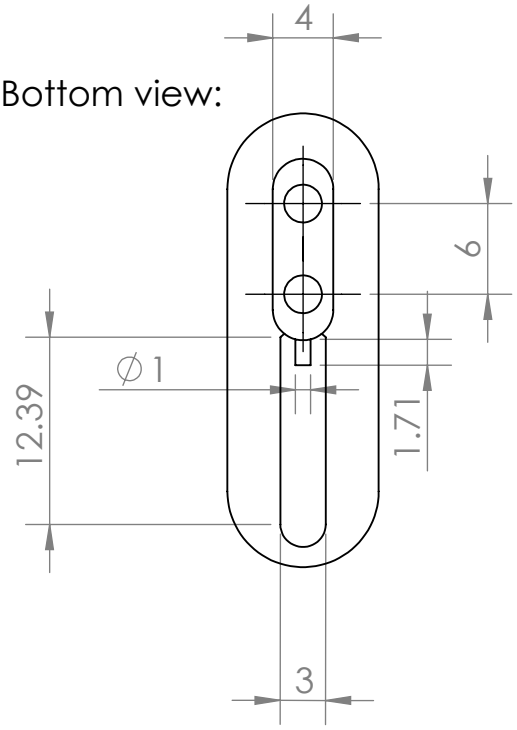
TU Delft	DATE: 19-11-2018	MATERIAL: Bronze	Units: mm
NAME Josette Kuipéri		Trigger	A4
			Scale: 2:1

Top view:

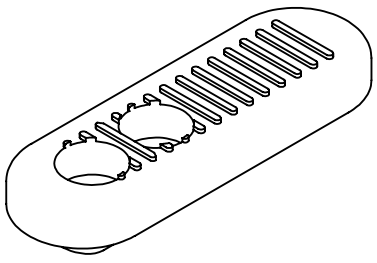




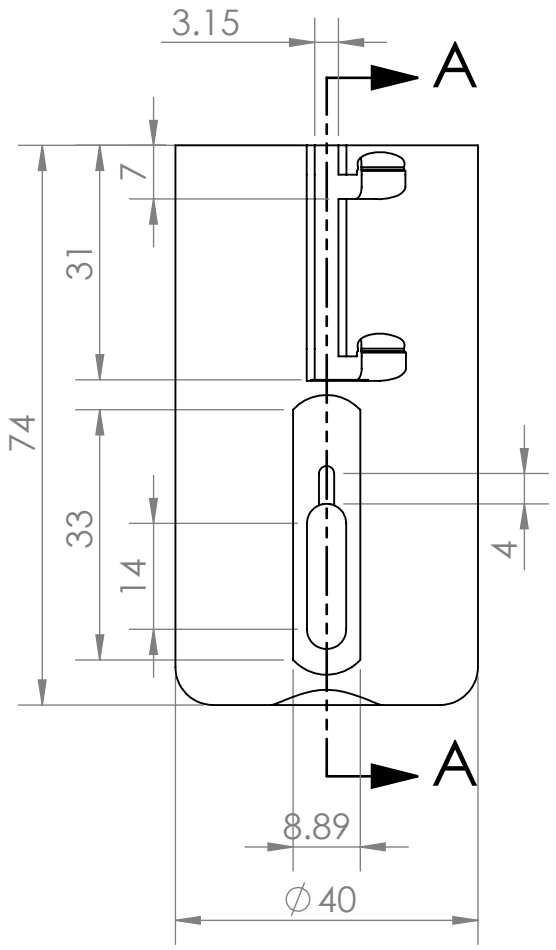
Bottom view:

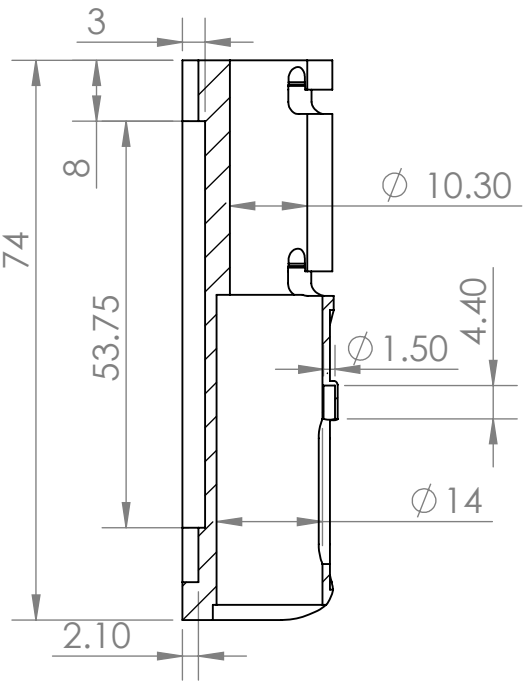


Isometric view:

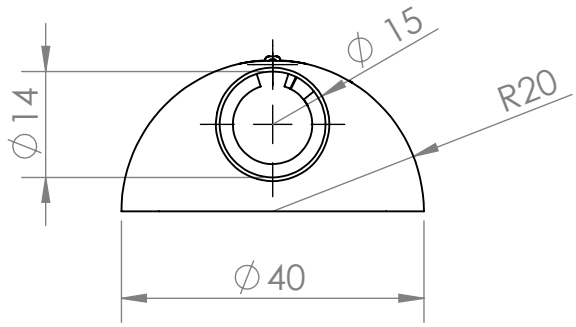


TU Delft	DATE: 19-11-2018	MATERIAL: E-shell 600 photopolymer	Units: mm
NAME Josette Kuipéri		Trigger knob	A4
			Scale: 2:1

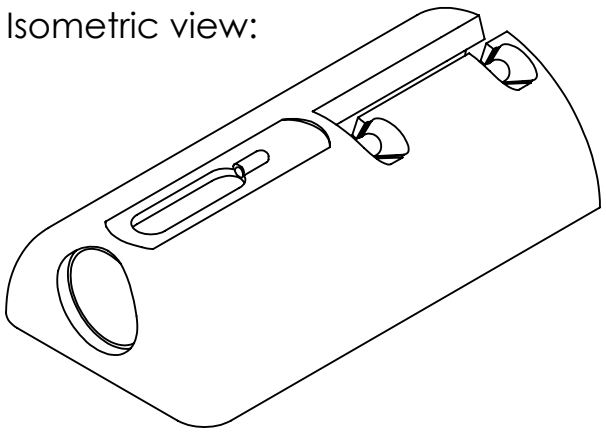




SECTION A-A

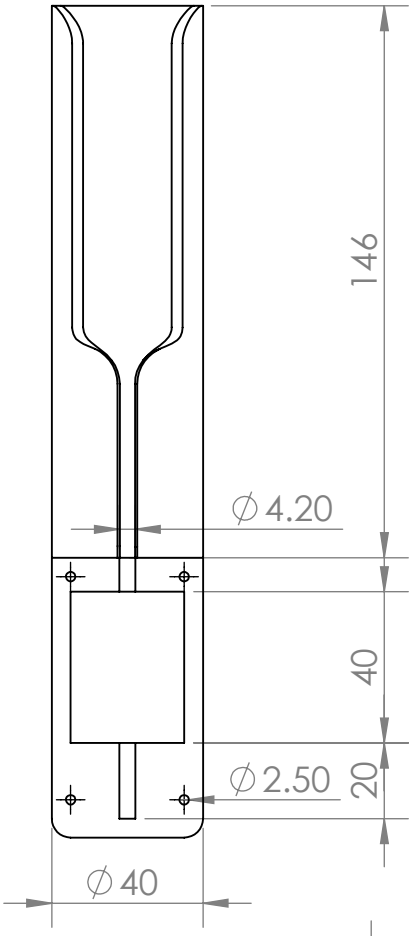


Isometric view:

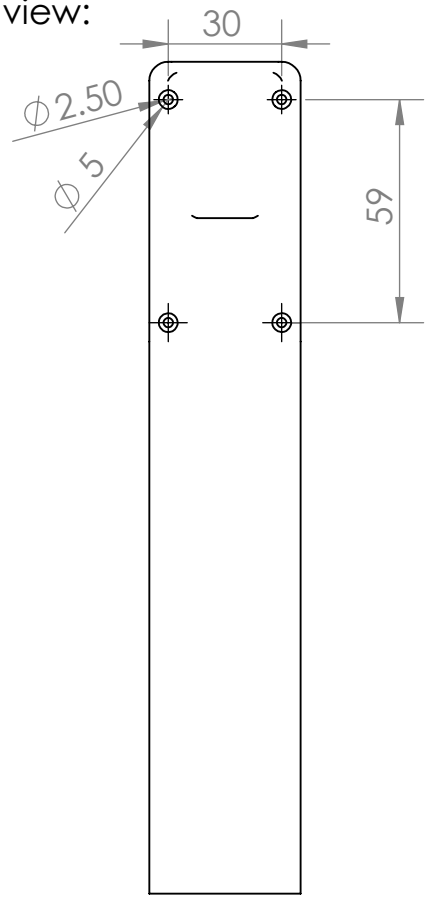


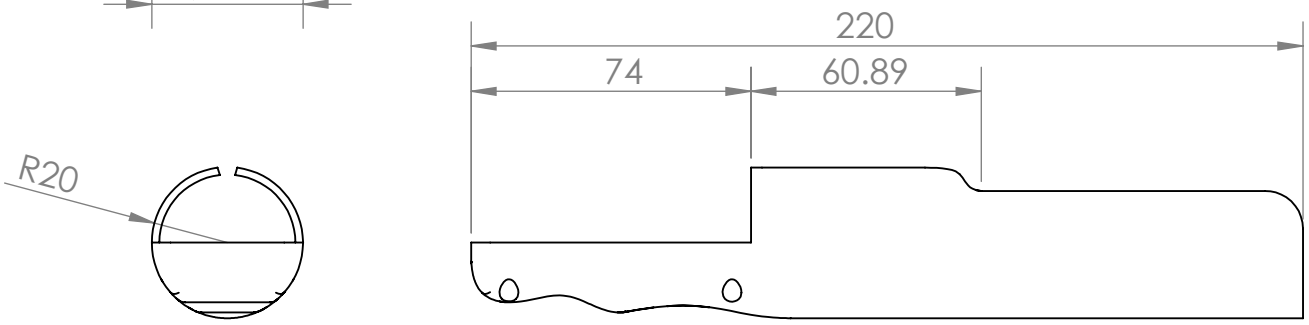
TU Delft	DATE: 19-11-2018	MATERIAL: E-shell 600 photopolymer	Units: mm
NAME Josette Kuipéri		Shell top	A4
			Scale: 1:1

Top view:

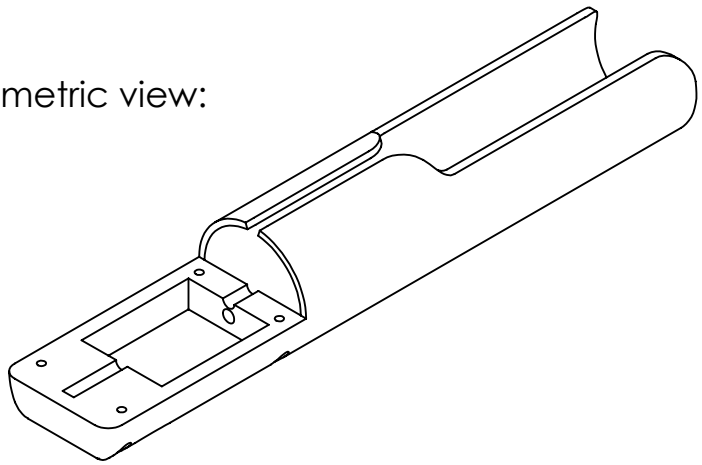


Bottom view:



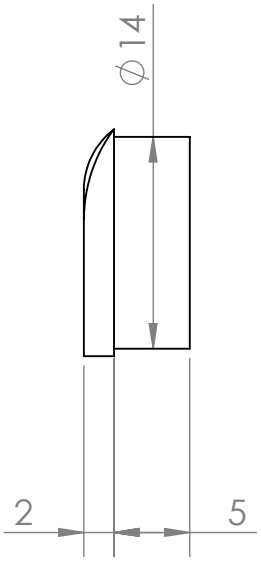


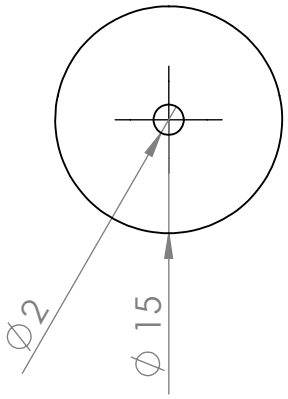
Isometric view:



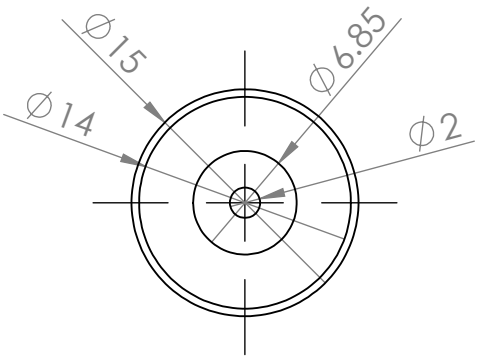
TU Delft	DATE: 19-11-2018	MATERIAL: E-shell 600 photopolymer	Units: mm
NAME Josette Kuipéri		Shell bottom	A4
			Scale: 1:2

Front view:

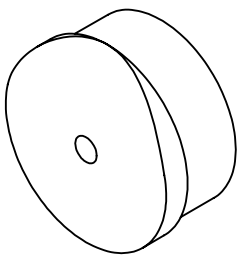




Back view:



Isometric view:



TU Delft	DATE: 19-11-2018	MATERIAL: Bronze	Units: mm
NAME Josette Kuipéri	Cannula cap	A4	Scale: 2:1