Device for Cryoablation of Tumors in Soft Tissue

DESIGN PROJECT 3 | IDP 603

Pooja B.Kulkarni
156130008

Guided by **Prof. Purba Joshi**
Co-Guided by **Prof. Milind Atrey** and **Prof. V. P. Bapat**

DECLARATION

The written submission is a part of my report, '**Design of a device for cryoablation of tumors in soft tissue**', is done as Project three for Post Graduate Program at IDC School of Design, IIT Bombay, under the guidance of **Prof. Purba Joshi, Prof. Milind Atrey and Prof. V. P. Bapat**

I hereby declare that the thoughts, ideas and words in this document are original and appropriate references are cited wherever due. I understand that the violation of the above can cause disciplinary action by the Institute.

Pooja B. Kulkarni
156130008
Industrial Design Centre,
Indian Institute of Technology, Bombay

APPROVAL

The project titled, ' **Design of device for cryoablation of tumors in soft tissue**' by Pooja Bhuvanesh Kulkarni, is approved for partial fulfillment of the requirement for the degree of 'Master of Design' in Industrial Design.

Guide:
Prof. Purba Joshi

Co Guide:
Prof. Milind Atrey

Co Guide:
Prof. V. P. Bapat

Chairperson:

Internal Examiner:

External Examiner:

Date: 27.04.2017

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to **Prof. Purba Joshi, Prof. Milind Atrey and Prof. V. P. Bapat** for guiding me through the project and constantly encouraging me to push my boundaries.

I would also like to thank the **professors and staff at IDC** and the for their valuable inputs during the course of the projects.

To my **classmates and batch mates** for their critical feedback, motivation and support. Also to **Dr. Trimbak Kavdikar, Chetan Pakhare, Sanket Pai and Ashish Shukla** for their contributions and timely and critical inputs regarding the project.

A special acknowledgement to **Dr. Hemant Bhansali, Dr. Rakesh Neve, Dr. Hrishikesh Kulkarni and Dr. Utkrant Kurlekar and Dr. Aparna Kulkarni** for their expert inputs and insights in the project.

Most importantly, I would like to thank my **family and friends** in their unwavering support and encouragement.

ABSTRACT

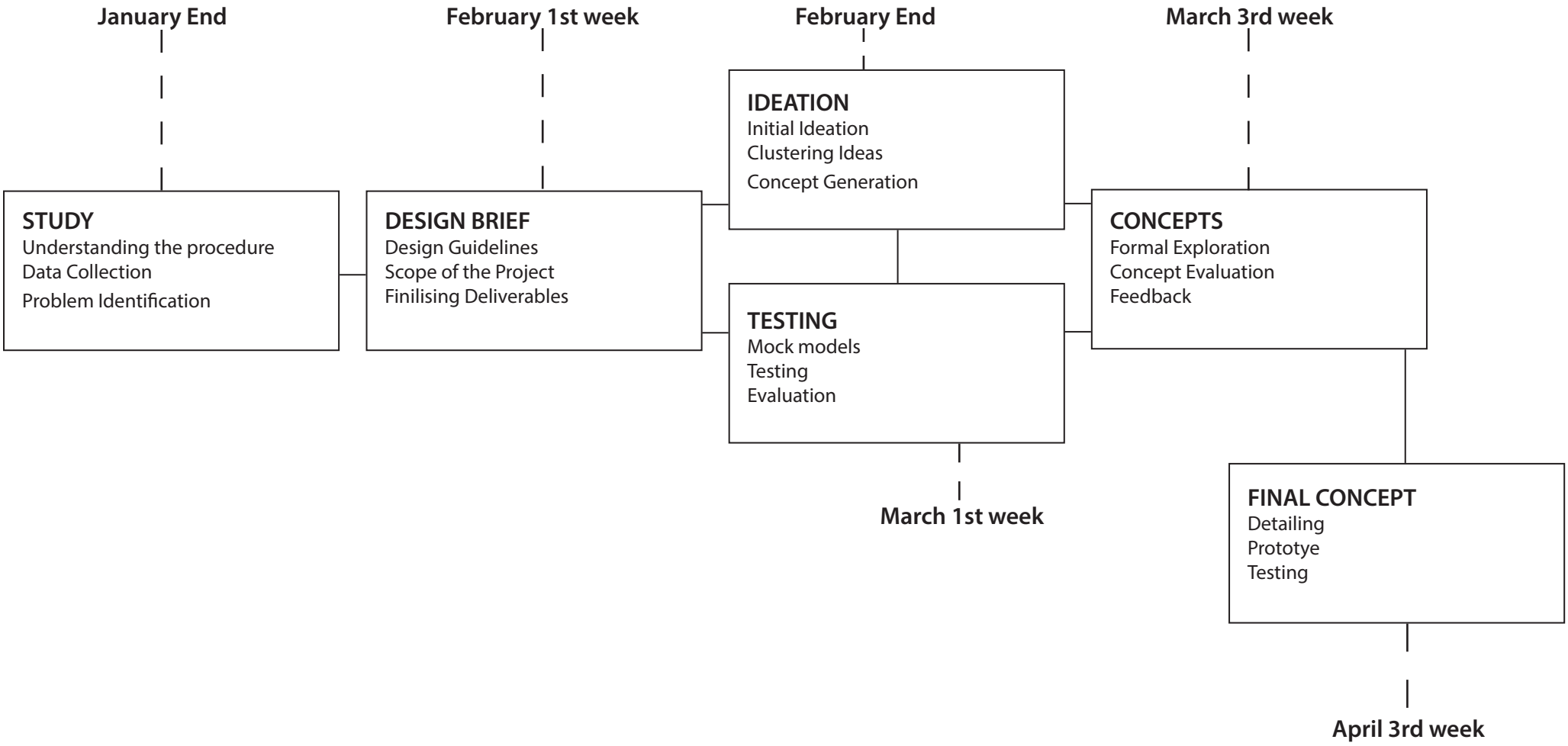
In the past two decades, major development has been happening in finding alternate cure methods for Cancer. Cryosurgery is one such promising technique, that uses extremely low temperatures to kill cancer cells. As this procedure can be performed with minimal invasion, it has huge benefits over the traditionally performed surgeries. Research and development has been happening in developing devices for curing breast cancer using cryosurgery.

Abdul Mateen A. G. Shaikh, Prof. Atul Shrivastava and Prof. Milind Atrey have designed a liquid nitrogen cryoprobe and tested it for ice formation. This device needs design intervention to make it usable. There is a scope to innovate and come up with a product that can change the cancer research scenario worldwide.

The project aims to design an ergonomic probe for cryosurgery for breast cancer, which can later be scaled to incorporate other organs and also propose a system for the same. The primary aim of the project is to design an ergonomic probe keeping in mind the design constraints for a class II device and also for a cryogenic device. An operative process that requires less time compared to the current operative processes, and is minimally invasive has also been proposed.

CHAPTERS

PROJECT TIMELINE



A | INTRODUCTION

A.1 Structure of a cell

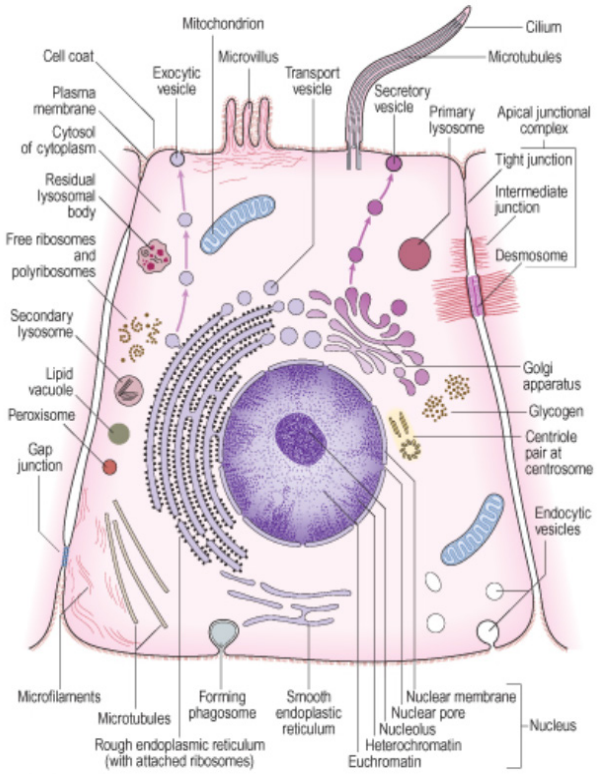


Fig. A.1 shows the cell structure.

Source: [2]

A cell is the smallest structural and functional unit of a living body or an organism. It can be defined as a mass of protoplasm containing nucleus or nuclear material. The cells are of multiple types according to the function of the organ that they form. The cells have a definite structure, which consists mainly a cell wall, a cell membrane, cytoplasm and a central nucleus.

A typical cell has a nucleus surrounded by cytoplasm. The nucleus is bounded by a double layered nuclear membrane, and contains the chromosomes which are made of DNA and protein. One or more nucleoli, made of protein, RNA and DNA maybe present, these are sites of ribosome formation. [1]

In a healthy functional body the cells are constantly dividing, growing and dying. This process continues throughout our lifespan. The dead cells are excreted by the body.

A.2 Cancer

Cancer is a group of diseases that cause cells in the body to change and grow out of control. Most types of cancer cells eventually form a lump or mass called a tumor, and are named after the part of the body where the tumor originates. [3]

Sometimes due to some external irritants the cells of the body undergo a change in the nucleic structure. These cells do not follow the divide, grow and die pattern. They do not follow a programmatic death pattern and grow uncontrollably. This leads to an abnormal mass known as a tumor, except in the case of blood cancer where the cells flow in the blood stream. The cancer is named according to area of the body that has been affected.

The cancer cells deprive the surrounding healthy cells of nutrition and grow like a parasite. This uncontrolled growth can result into spread of the cells into the body leading to organ failure and eventual death of the affected human if not treated in time.

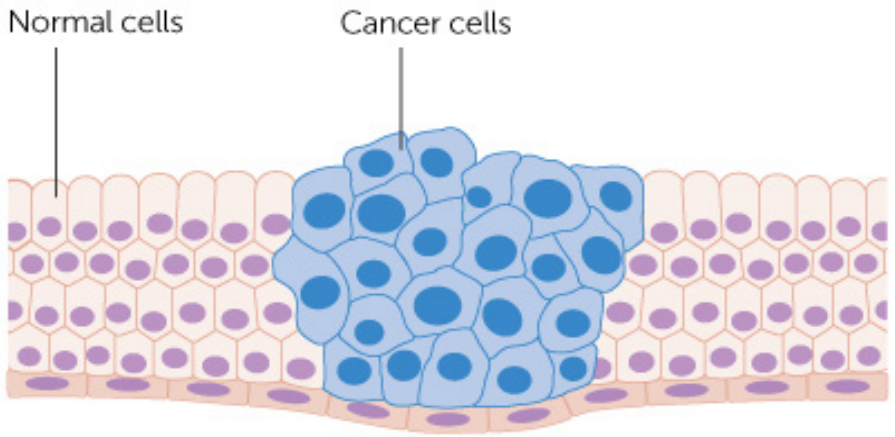


Fig. A.2 Growth of cancer cells
Source: [4]

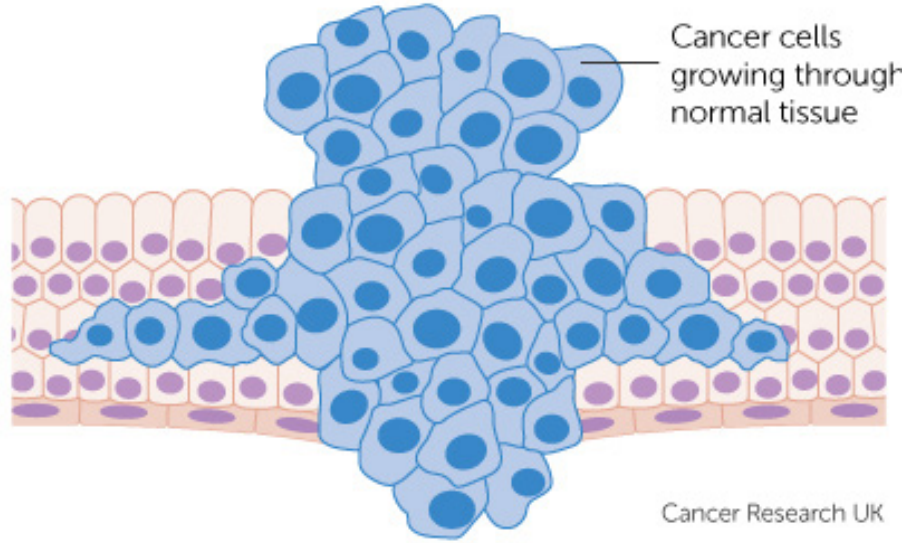


Fig. A.3 Growth of cancer cells
Source: [4]

A.3 Breast anatomy

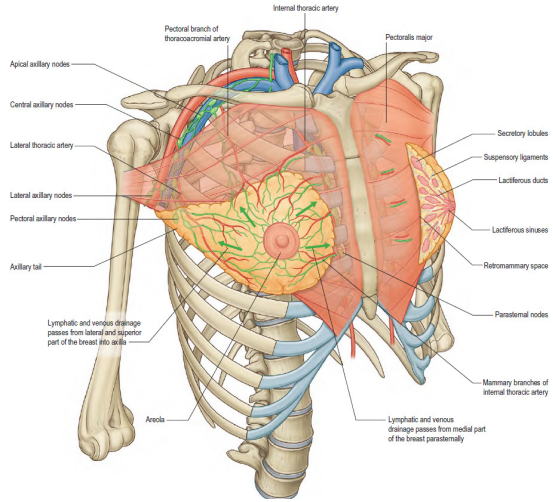


Fig. A.4 Anatomy of a breast
Source: [2]

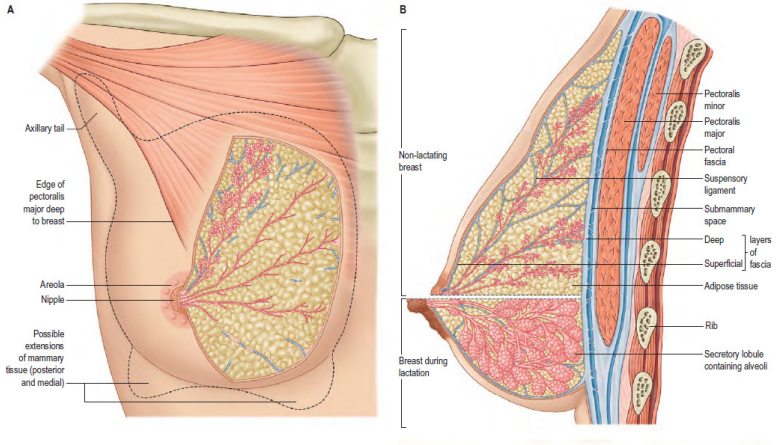


Fig. A.5 Anatomy of a breast
Source: [2]

To understand the breast cancer and the tumor location it is essential to understand the anatomy of the breast.

The breast is the tissue overlying the chest (pectoral) muscles. Women's breasts are made of specialized tissue that produces milk (glandular tissue) as well as fatty tissue. The amount of fat determines the size of the breast.[5]

The breast is composed of the adipose tissue, the milk producing parts organized in 15-20 sections called as the lobes, which branch out into lobules, ducts that store the milk, nipple through which the milk comes out, connective tissue, ligaments to provide support to the breast, nerves, blood vessels, lymph vessels and lymph nodes.

A.4 Breast cancer

Breast cancer is the most common type of cancer in female and the second most common type of cancer overall. The cancer affecting the breast is known called breast cancer. The cells affect the adipose tissue in the breast region leading to a tumor.

The vast majority of breast cancers begin in the parts of the breast tissue that are made up of glands for milk production, called lobules, and ducts that connect the lobules to the nipple. [3]

The cancer can be classified according to the site and the extent of its spread and the site or origin:

Invasive breast cancer

Invasive lobular breast cancer

Triple negative breast cancer

Ductal carcinoma in Situ (DCIS) [Fig no. A.6]

Lobular carcinoma in Situ (LCIS) [Fig no. A.7]

Male breast cancer

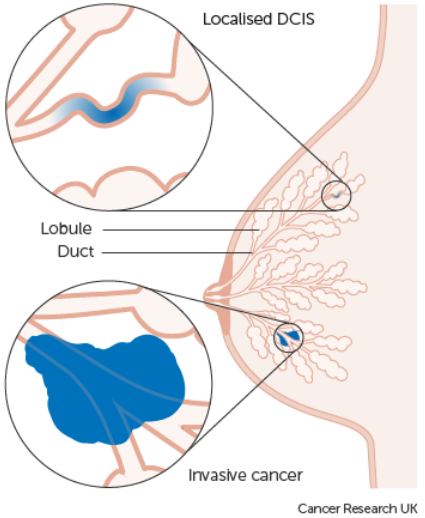


Fig. A.6 Ductal carcinoma in Situ
Source: [4]

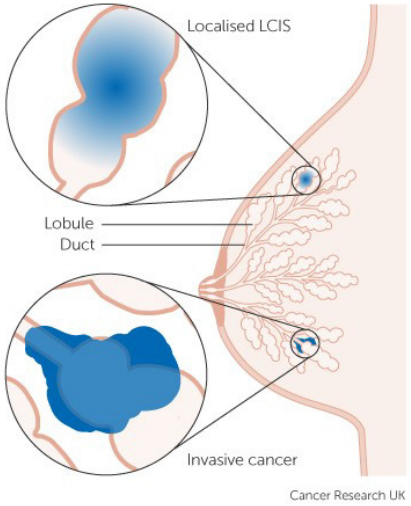


Fig. A.7 Lobular carcinoma in SItu
Source: [4]

A.5 Breast cancer treatment:

Current techniques

Depending on what stage the cancer is in the cure is decided. Some of the commonly preferred treatments are:

Surgery

There are two traditional types of surgeries performed to remove the tumor from the breast tissue.

Lumpectomy

Partial removal of the breast tissue to remove the tumor.

Mastectomy

Removal of the entire breast tissue including the nipple.

Radiotherapy

Use of high energy rays like x-rays to kill breast cancer.

Chemotherapy

Chemotherapy uses cytotoxic drugs to kill the cancer cells. These drugs are circulated through the blood stream.

Harmone therapy

Hormone therapy is used to lower or block the effects of estrogen and progesterone . This therapy is used only if the cancer cells have estrogen receptors (ER).

Biological therapy

Biological therapy uses drugs to change the way the cells work and help the bod to control the growth of cancer. Some seek to destroy the cancer cells while others help the body to fight cancer.

A.5 Breast cancer treatment:

New techniques

With the advancement in the medical field, new ways are coming up to kill the cancer cells without much damage to the surrounding healthy tissue. The physical and psychological impact of the traditional cancer treatment is damaging to the patients and thus research is carried out to come up with new techniques and drugs that are effective in killing cancer while not being harsh on the body. A lot of research is going on in developing techniques that are minimally invasive to reduce the damage caused to the body.Apart from cryoablation, the following are the other new minimally invasive techniques used to treat cancer currently:

Radiofrequency ablation (1990)

Alternating electric current operated in the range of radiofrequency can produce a focal thermal injury in living tissue. Shielded needle electrodes are used to concentrate the energy in selected tissue. The tip of the electrode conducts the current, which causes local ionic agitation and subsequent frictional heat. Temperatures in excess of 50°C produce coagulative necrosis (death of a tissue). A 50 mm spherical injury can be produced with each ablation. [6]

Ethanol ablation

This treatment is generally used for treating primary malignant hepatic tumors. It is one of the most inexpensive treatment available.

Microwave ablation (1986)

In microwave coagulation therapy or ablation, molecular dipoles are vibrated and rotated, resulting in thermal coagulation of the target tissue. The basic mechanism of heat generation in living tissue consists of rotation of water molecules. The rotation follows the alternating electric field component of the ultra-high-speed (2,450-MHz) microwaves. Microwaves emitted from the distal segment of a percutaneous probe cause the thermal coagulation of the adjacent tissues.

Laser ablation (1983)

Portable solid state lasers with a power output of 30W are used. This energy is delivered through fibers over 10 m in length with the great advantage of being fully compatible with MR imaging.

Chemoembolization

This treatment is still in the experimental stage and is generally used for patients with either primary or metastatic malignant hepatic tumors. The drugs are directly delivered into the portal vein rather than through the traditional technique. This increases the drug concentration in the liver tumors to hundred fold compared with systemic infusion, while simultaneously embolization prolongs the dwell time of the drug from hours to weeks.

A.6 Tumor Detection

Fig. A.8 Magnetic Resonance Imaging

Source: [9]

Fig. A.9 Ultrasound and biopsy

Source: [10]

While performing a minimal invasive surgery it is essential to visualize the area that is being performed on. This helps the surgeon to visualize the area and the path of the devices that are being introduced.

Some of the techniques used to visualize are:

CT Scan

X Ray

MRI (Magnetic Resonance Imaging)

Ultrasound

Laparoscopy

Mammography for breast cancer

A.7 Minimal invasion surgery

Minimal invasive surgery is a surgical procedure where the surgery is performed through small incisions made on the body to insert the instruments. The area to be operated is visualized on the monitor by either laparoscope, ultrasound, MRI, CT Scan etc.

It has multiple advantages over the open surgery. Primarily the wound size is small thus it reduces the chance of infection, the recovery time and also has cosmetic advantages. Secondly the surgery is localized and thus the chance of accidental damage to the surrounding organs is less.

These days a lot of surgeries are performed this way and that has changed the medical scenario multifold. Diagnosis and surgery time has reduced and the detection of disease and treatment has become faster and less painful.

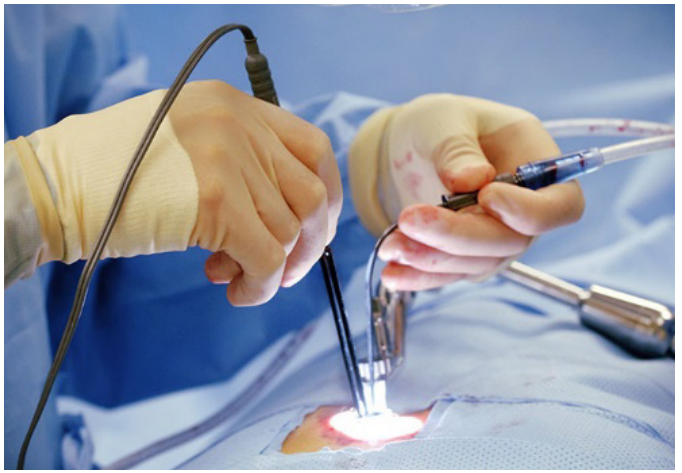


Fig. A.10 Minimally invasive surgery
Source: [7]

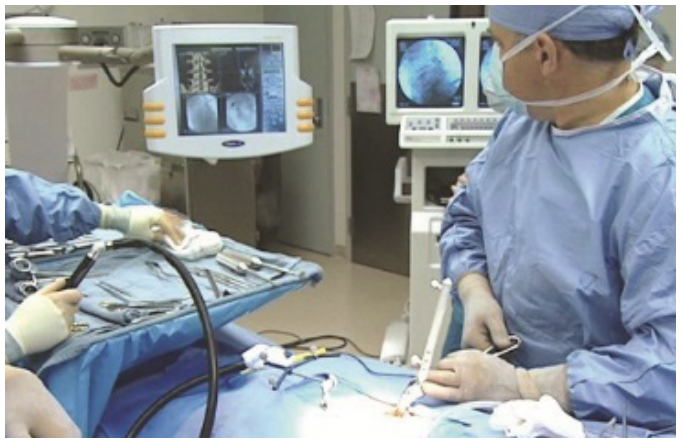


Fig. A.11 Minimally invasive surgery
Source: [8]

A.8 Cryoablation:

What is cryoablation?

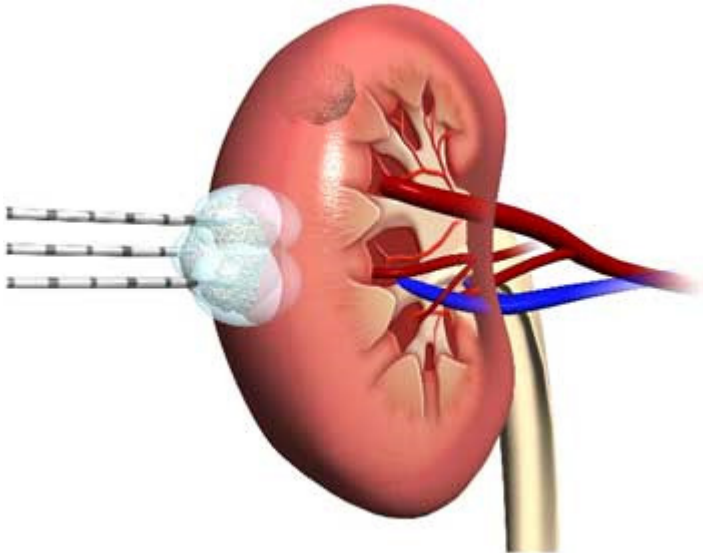


Fig. A.12 Cryoablation on a kidney
Source: [13]

Fig. A.13 Ice ball formation
Source: [6]

Cryo= Ice and Ablation=Killing the dead cells.

Cryoablation is the technique of killing the cells using low temperatures. The cells are subjected to extremely low temperatures for a certain duration of time freezing the cellular fluid, forming ice. This leads to the cell membrane rupturing and in turn leads to cell death. Generally a cycle of cooling and heating is used to ensure cell necrosis.

Cryosurgery is still at a stage where art overshadows science. Most cryotherapy devices are bulky and somewhat complex to handle outside of a standard operating room. The ideal device would be small and compact. It should interface with the stereotactic biopsy table and ultrasound devices. Debate continues as to numbers and duration of freeze thaw cycles needed to maximize the probability of cell destruction. [11]

Cryoablation is widely used for external applications, warts, skin cancer and also for cervical cancer. There are experiments going on for the use of cryoablation technique for internal applications. Device development has been going on to adopt this technique for curing breast cancer, it is still in the Clinical trial phase.

A.8 Cryoablation:
History of cryoablation

1986
A 77 year old woman with a 1 by 2 cm sized palpable mass underwent cryosurgery under US guidance, and the tumor was resected is the first patient to go for a cryosurgical treatment. After the histopathology analysis it reveled no viable tumor cell. (No cancer)

1997
A 76 year old woman with percutaneous carcinoma, received cryosurgery. At the 4th and 12th week follow up post surgery, tissue necrosis, inflammatory cells and cellular debris were observed but the tumor was absent.

As of 2012, this is the only example of the natural history of cryoablated breast carcinoma because nearly all ablation studies are coupled with post procedure resection.

2012
In Fuda Cancer Hospital Guangzhou, Niu et al. had treated 27 patients with small solitary invasive breast cancers using US-guided cryoablation. Tumor proven by core biopsy had median of 13 mm with range of 8-25 mm in size. All 27 patients underwent lumpectomy an average of 14 days after the cryoablation (8-35 days).

Currently cryoablation is used to reduce the tumor and kill the tissue, post this a lumpectomy is performed to remove the dead cells.

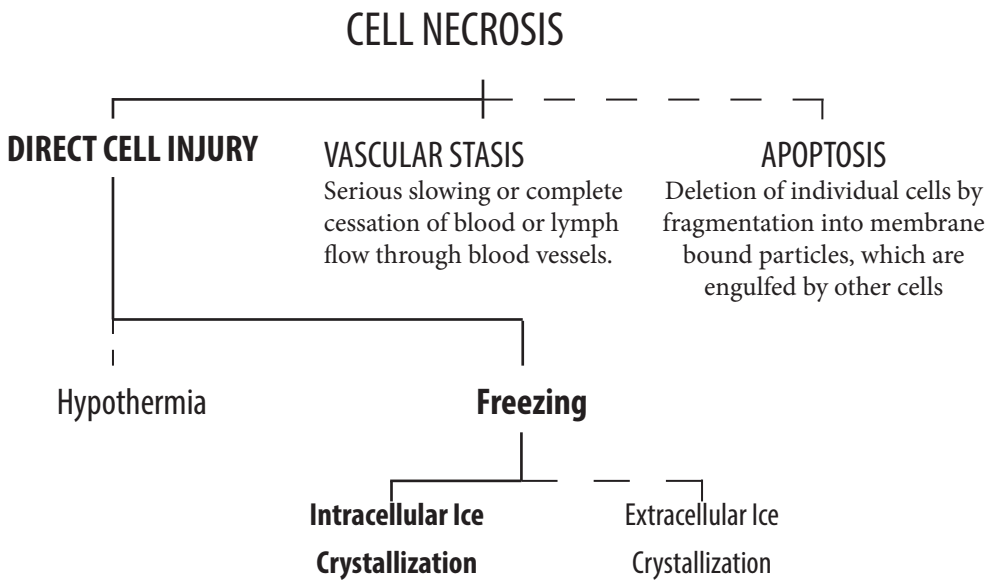
For advanced breast cancer, cryosurgery can improve patient's condition and prolong survival. Korpan showed 52 patients with breast cancer, including 10 primary advanced and 42 recurrent, who underwent cryosurgery. Three- and four-year survival were 40%. This figure is not disappointing given the patients' severe condition.

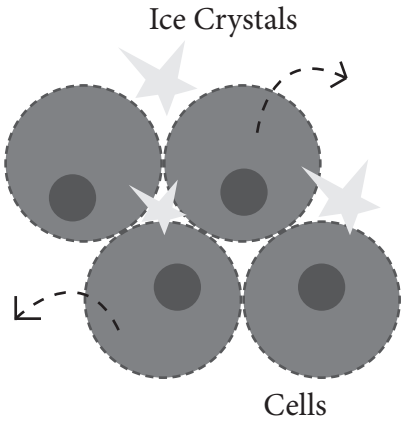
Source: Cryosurgery for Breast Cancer, Lizhi Niu, Liang Zhou, Kecheng Xu
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4115688/#r17; 17.02.2017 1.35PM

A.8 Cryoablation:

Intracellular and Extracellular ice formation

Cell necrosis is a form of cell injury that results in premature death of the cell in the living tissue. Necrosis can be caused due to the following reasons:





EXTRACELLULAR ICE CRYSTALLIZATION

Extra celullar crystals form at -20°C

Water is drawn out from the cells due to osmotic pressure

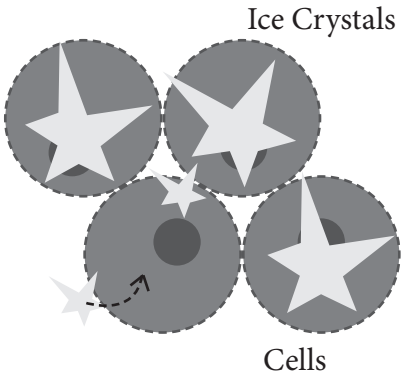
Increase in concentration of solutes and dehydration of cells leading to death due to the solution effect

INTRACELLULAR ICE CRYSTALLIZATION

At high cooling rates water cannot leave the cells resulting in IIF (Intracellular Ice Formation)

Also extracellular ice may enter the cells through the micropores in cell membrane

Once formed the IIF kills the cell in most certainty



A.8 Cryoablation:
Design of a cryoprobe

A cryoprobe is a device used in cryosurgery along with a monitoring device like an ultrasound or an MRI device. Generally liquid nitrogen or argon gas is circulated through an internal tubing. This is encompassed in a vacuum chamber. A cryo needle is attached to the probe and inserted into the body for localized freezing.

The images show the traditionally used probes for cryosurgery. The needles have insulated jackets to ensure that there is localized freezing of the tissue and the healthy tissue remains intact.

Cryosurgery for breast cancer is still in its early phase and thus not much development has happened in terms of the device. Surgeries for hepatic and renal tumors are being performed, but not a larger extent. In this case, as there is space available in the abdominal cavity accidental damage caused to the surrounding healthy tissue is not a major concern. These surgeries are performed laparoscopically.

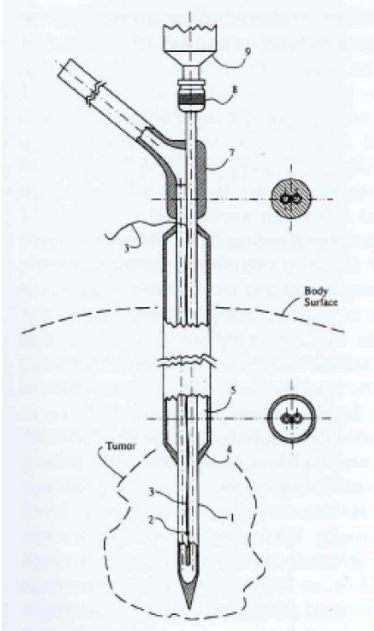


Fig. A.14 Design of a cryoprobe
Source: [12]

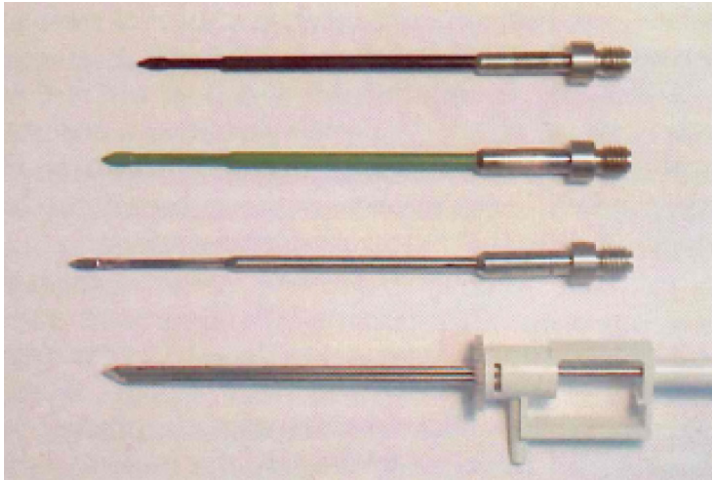


Fig. A.15 Cryoneedles
Source: [12]

A.8 Cryoablation:

Advantages and Disadvantages

Advantages

1. Ablated tissues remain in the breast for resorption over time, improving the cosmetic outcome and increases the recovery time.

2. Reduced reoccurrence rate of the tumor.

3. Due to the cooling temperatures there is an anesthetic effect and reduced pain.

4. The technique does not damage native tissue, making it less disruptive to the contour of the breast.

5. Works better for tumors in the initial stages and in cases of later stage tumors cryosurgery helps in improving the patients condition and prolong survival.

6. For prevention of skin injury, at least a 10-mm separation of the tumor edge and the skin surface is required. With cryoablation, it is possible to inject saline (while monitoring with real-time ultrasound) between the tumor and the skin, increasing their separation. This allows for the treatment of tumors close to the skin

7. During cryoablation, ultrasound shows the proximal edge of the ice-ball appearing as a clearly visible hyperechoic rim, provides an excellent guidance at the boundary between frozen and unfrozen tissue.

Disadvantages

1. It is not widely used and thus not much device development is seen.

2. The cost of the surgery is high currently.

3. There is a possibility of hemorrhage due to accidental freezing of the blood vessel, increasing the pressure and leading to rupture.

4. Use of cryosurgery for larger tumors is still not been explored and is currently confined just to the tumors below 20mm dia.

5. It does not provide tissue for pathological examination. As a consequence, one cannot be certain that the entire lesion is ablated. Moreover, some tumor characteristics like the microscopic size, grade, hormonal receptor status and margin status are not available.

B | STUDY

B.1 New generation probe design

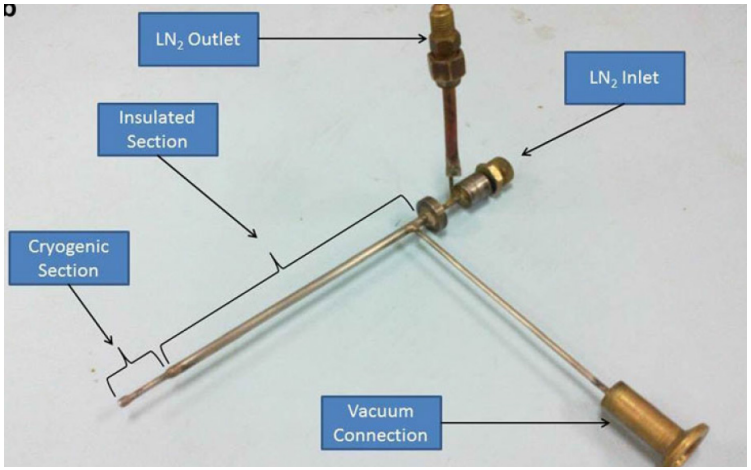


Fig. B.1 Next generation cryoprobe
Source: [15]

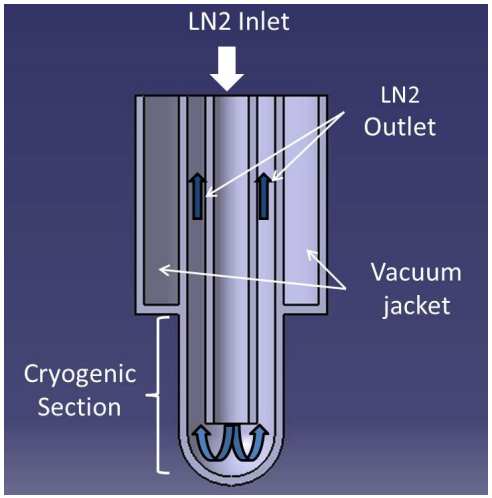


Fig. B.2 Next generation cryoprobe
Source: [15]

Abdul Mateen A. G. Shaikh, Atul Shrivastava and Milind Atrey have designed a Liquid Nitrogen Cryoprobe. This has been published in OMICS, A journal of Integrative Biology, Volume 19, Number 2 in 2015. There was a need to integrate the technique that they have developed into a device. Thus to understand the process and the process and device associated problems better it was necessary to carry out a through study of this technique.

Two concentric hollow tubes are used to circulate liquid nitrogen. Liquid nitrogen enters through the inner tube through one end and is released in the annular space between the two tubes where it gains heat from the surrounding tissue and changes phase. The resulting two phase mixture then passes through the annular space and is released into the atmosphere. Another concentric tube or the vacuum tube envelopes the outer tube except at a certain length at the tip of the cryoprobe (cryogenic section of the cryoprobe). The annular space covered between the vacuum tube and the outer tube is vacuum insulated to prevent damage to the surrounding healthy tissue. [15]

Design Intervention

The device developed has been tested and it has proven ice formation. There is a need to make the device usable and to come up with a simple and easy to use device design.

B.2 Literature review

A patent study was carried out to understand the probe development and the criticalities involved with the design. Also it was essential to go through research articles regarding cryosurgery ad it is still in the developmental stage.

The table contains a few of the patents studied. There is a reference list at the end for the papers that have been studied.

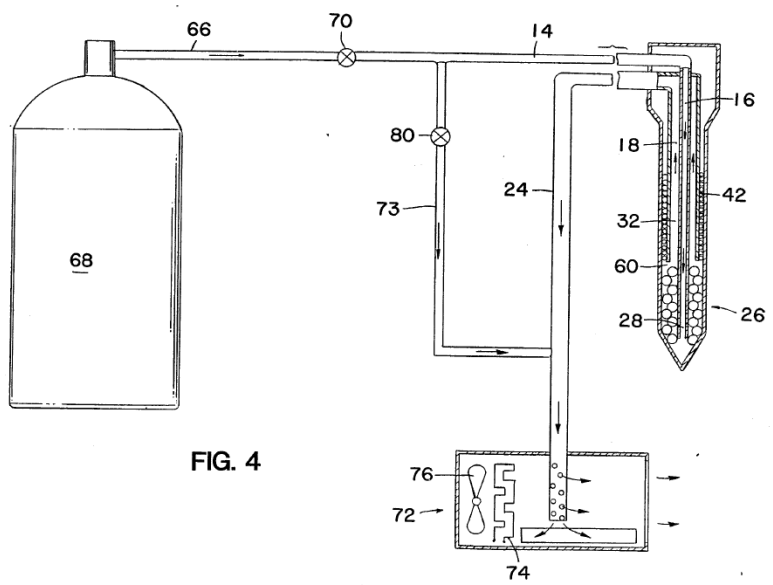
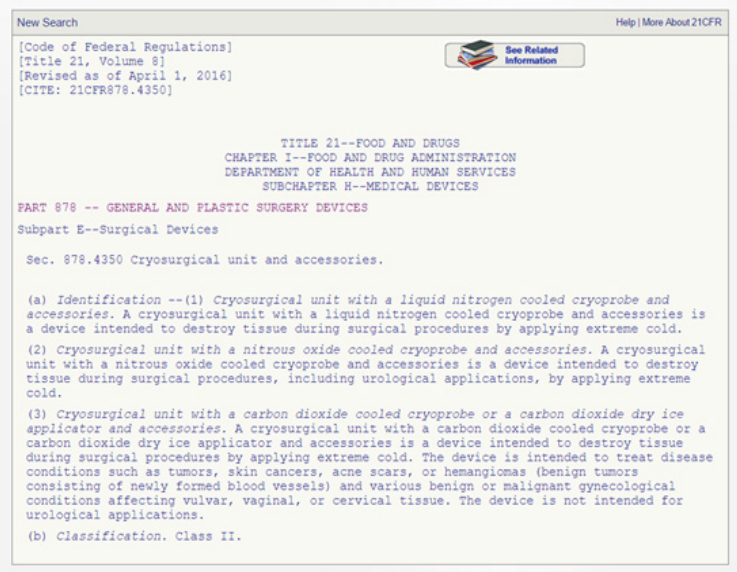


Fig. B.3 Setup for cryosurgery
Source: US4946460

No.	Patent No.	Name	Relevance	Source
1.	US5899897	Method and apparatus for heating during Cryosurgery	Heating device	United States Patent
2.	US5674218	Cryosurgical Instrument and System and Method of Cryosurgery	Process understanding	United States Patent
3.	US4946460	Apparatus for Cryosurgery	Setup	United States Patent

B.3 Device classification standards



New Search | Help | More About 21CFR

See Related Information

[Code of Federal Regulations]
[Title 21, Volume 8]
[Revised as of April 1, 2016]
[CITE: 21CFR878.4350]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER H--MEDICAL DEVICES

PART 878 -- GENERAL AND PLASTIC SURGERY DEVICES

Subpart E--Surgical Devices

Sec. 878.4350 Cryosurgical unit and accessories.

(a) *Identification* --(1) *Cryosurgical unit with a liquid nitrogen cooled cryoprobe and accessories.* A cryosurgical unit with a liquid nitrogen cooled cryoprobe and accessories is a device intended to destroy tissue during surgical procedures by applying extreme cold.

(2) *Cryosurgical unit with a nitrous oxide cooled cryoprobe and accessories.* A cryosurgical unit with a nitrous oxide cooled cryoprobe and accessories is a device intended to destroy tissue during surgical procedures, including urological applications, by applying extreme cold.

(3) *Cryosurgical unit with a carbon dioxide cooled cryoprobe or a carbon dioxide dry ice applicator and accessories.* A cryosurgical unit with a carbon dioxide cooled cryoprobe or a carbon dioxide dry ice applicator and accessories is a device intended to destroy tissue during surgical procedures by applying extreme cold. The device is intended to treat disease conditions such as tumors, skin cancers, acne scars, or hemangiomas (benign tumors consisting of newly formed blood vessels) and various benign or malignant gynecological conditions affecting vulvar, vaginal, or cervical tissue. The device is not intended for urological applications.

(b) *Classification.* Class II.

Fig. B.4 Device classification
Source: [17]

Device Classification

According to this the device is a Class C CDSCO device and a Class II FDA device. The device classification can be checked on the FDA website.
Website link: [16] and [17]

The classification of the medical devices is according to the design and complexity of use. There are governing bodies that classify and regulate the use of these devices. Special license could be a prerequisite for the complex devices.

Until a few years back India did not have a regulatory body for medical devices, but now **CDSCO: Central Drug Standards Control Organization** is responsible for the same. According to this the devices are classified as Class A (low risk, eg.thermometers), Class B (Low moderate risk, eg. hypodermic equipment, Class C (Moderate high risk, eg. lung ventilator) and Class D (High risk, eg. heart valves).

Depending on the country where the device will be used the device needs to be registered and needs the approval for use on the patient. **FDA: U.S. Food and Drug Administration** is responsible for device regulation in the United States. The classifications being Class I (General controls, eg. elastic bandages), Class II (General controls and special controls, eg. infusion pumps) and Class III (General controls, special controls and premarket approval, eg. automatic external defibrilators) Similarly, Canada, Europe and Australia have their own regulatory bodies.

B.4 MSDS for Liquid Nitrogen

MSDS stands for Material Safety Data Sheet.

A Material Safety Data Sheet (MSDS) is a document that contains information on the potential hazards (health, fire, reactivity and environmental) and how to work safely with the chemical product. It contains information on the use, storage, handling and emergency procedures all related to the hazards of the material. [16]

The MSDS is prepared by the supplier and manufacturer of the chemical.

The MSDS for Liquid nitrogen was studied to better understand the material and safety concerns and to incorporate them in the design.

The following are the safety guidelines for Liquid Nitrogen:

Safe handling: When Liquid nitrogen is held in any closed vessel or space, there must be an appropriate pressure relief device because of the large pressure increases that can occur as the liquid nitrogen is vaporized. Use only containers designed for cryogenic liquids. Do not use any stopper or other device that will interfere with venting of gas. Unauthorized modification to these liquid containers is forbidden.

Storage: Store in a cool and well ventilated area. If containers are stored outside, provide shelter to protect against extreme weather conditions. Excessive exposure to any heat could cause the internal pressure to increase significantly with the consequent loss of liquid product that has vaporized. Keep out of reach of children.

Personal Protective Equipment: Wear face shield; leather gloves and leather apron when using or decanting liquid nitrogen. Do not put hands (even in the best gloves) in the cryogenic liquid. Wear safety boots and overalls.

Referrence: MSDS for Liquid Nitrogen
http://www.afrox.co.za/internet.global.corp.zaf/en/images/Liquid%20Nitrogen266_92254.pdf?v=.

B.5 User Study

It was crucial to understand the doctor's perspective about cryosurgery and breast cancer to develop a better system. Currently in India, cryosurgery is not used to treat breast cancer. Thus there was no direct feedback regarding cryosurgery, but some valuable insights were obtained regarding problems associated with breast cancer and tumor eradication.

A telephonic interview was carried out with two renounced oncologists in Pune. **Dr. Utkrant Kurlekar** who is an **Oncosurgeon** with **Deenanath Mangeshkar Hospital and Research Centre** and **Dr. Rakesh Neve** who is associated with **Ruby Hall Cancer Centre in Pune** helped in coming up with valuable insights into the current problems associated with breast cancer.

Dr. Hemant Bhansali who is a **senior laparoscopic surgeon** was also consulted for his views on cryosurgery.

Dr. Hrishikesh Kulkarni who is a **specialist in internal medicine**, and associated with hospitals **Edward W Sparrow Hospital, Ohio** was consulted.

Insights

Currently lumpectomy and mastectomy are regularly performed to cure cancer. Cryosurgery is not used in India.

The tumor biopsy is carried out first and then it is removed from the body using cauterization or lasers. This causes a visible scare and larger incision.

Cryosurgery is not used due to the unavailability of the setup and also due to the higher costs and confusion about the advantage and risks involved.

Cryosurgery is used widely for external applications, to treat skin cancer and warts, and for cervical cancer since two decades.

Cryosurgery has been used for applications where the tissue to be killed is visible.

B.6 Task Analysis

Task Analysis is used to derive insights that will guide to frame the brief for the probe and system design. Currently there is no specific device that is used for cryoablation of breast cancer tumors, thus the task analysis has been done taking referrences from cryoablation surgery for hepatic tumors and a lumpectomy.

Fig. B.5 is of a cryosurgery performed on a renal fibroid and Fig. B.6 is a traditional lumpectomy.

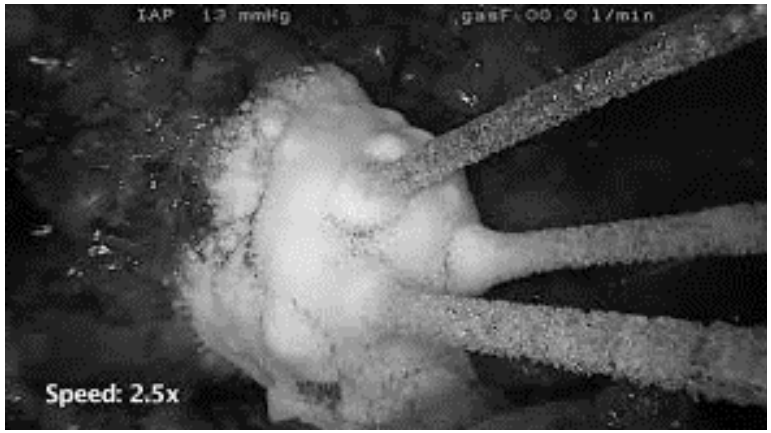


Fig. B.5 Cryosurgery for renal fibroid
Source: [19]

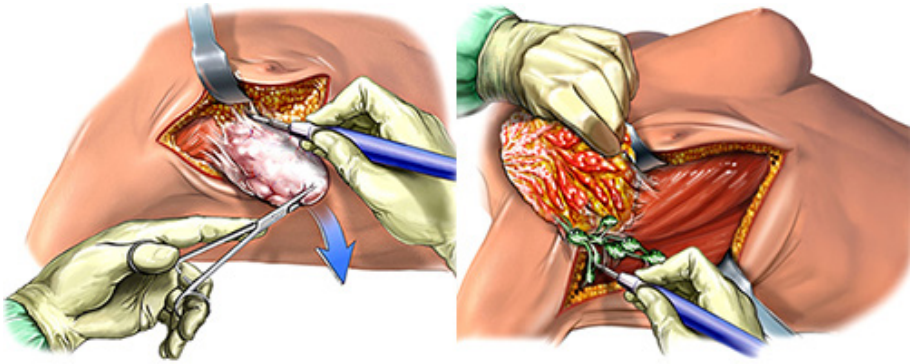


Fig. B.6 Lumpectomy
Source: [20]

Pre operative

1.Patient Preparation: This step involves the physical and mental preparation of the patient prior to the surgery. The fitness and other parameters are monitored for a certain duration to decide whether the patient is eligible for cryosurgery.

2. Operation theatre Preparation: The OT is cleaned and steralized. The devices are checked. The equipment is steralized and arranged on the trays.

3. Device Preparation: The levels for liquid nitrogen are checked. The probe is steralized and the device is setup for the surgery. Simultaneously the ultrasound device is also setup.

4. Mammogram: Prior to the surgery a mammogram is taken to locate the tumor. This is the major guidance factor for the tumor location.

Operative

1. Tumor location mapping: The tentative tumor location is mapped on the breast, from the mammograms available. The ultrasound is also used as a guide.

2. Tumor Visualization: The tumor is visualized using the ultrasound device, on the monitor screen placed in front of the surgeon.

3. Incision: An incision is made on the breast using a surgical blade. the depth of the incision is monitored using the ultrasound.

4. Probe insertion: The probe is inserted through the incision. After checking the probe location from all different angles on the ultrasound monitor the freezing cycle is started.

5. Freezing and thawing cycles: To ensure that the tumor cells are dead a freezing and thawing cycle is used. The cells are rapidly frozen to temperatures below -50°C. The frozen zone is monitored. A prolonged thaw cycle ensures that the cells defreeze after the freezing cycle. This is repeated to ensure tissue necrosis.

6. Removal of the probe: After the second thaw cycle is complete the probe is removed from the tissue.

Post operative

1. Sutures: If the incision width is more than 3-5mm a suture is used to close the incision.

Follow up

1. The patient is monitored regularly for relapse. If even a sligth unwanted growth is observed the process can be repeated.

Insights

1. Ultrasound is used currently to monitor the iceball growth. In comparision to a mammogram and a MRI this technique is less accurate. Also the tumor can be visualized from one angle at a time and the probe needs to kept moving to get a good sense of ice ball formation.

2. The current incision size is about 8mm for the New generation probe and a prior incision is required.

3. The form of the tumor is varied and thus multiple incisions could be required to freeze the entire cancerous growth.

4. The probe needs to held manually in the same position for about15-20 mins (entire duration of the surgery).

B.7 Posture Study

A guideline for validation of concepts for their ergonomic efficiency needs to be defined ad that the user is not under much stress while opearting.

To prevent MSDs (Musculoskeletal Disorders),injuries and fatigue the most imporatant principle is to maintain a neutral posture.

A neutral posture is achieved when the muscles are at their resting length and the joint is naturally aligned. For most joints the neutral posture is associated with the midrange of motion

Principles for Neutral Posture:
1. Maximum muscle force produced in a neutral posture is greater than the maximum muscle force produced in an akward posture.

2. Fatigue occurs sooner while working in an akward posture.

3. Working in extreme akward postures (near extreme ranges of motion) causes stress on muscles and joints.

Source: [21]

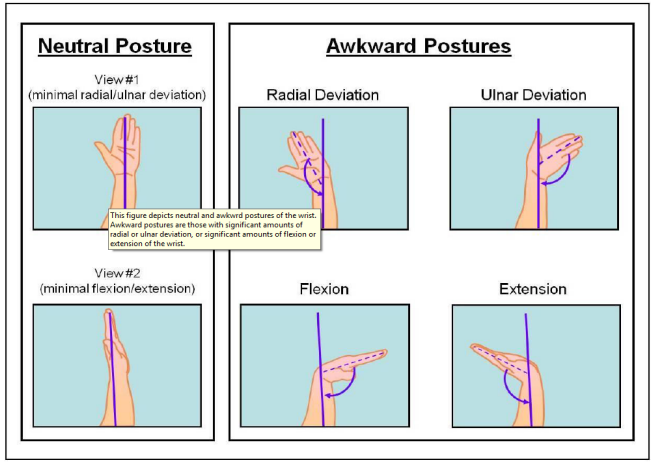


Figure 1. Neutral and awkward wrist postures.

Fig. B.7 Posture study for hand
Source: [21]

The probe requires a precise controlled grip for piercing the tissue. Also some amount of force is required to penetrate throught the adipose tissue.
Higher precision is achieved when the distance of the fingers from the tip is minimum. Also this ensures a greater control and precise force application on the device and the chance of error is less as compared to any other grip.
With this essential of maintain a neutral posture while operating.

For the system it is essential to maintain a neutral posture while carrying out the tasks. Reach and clearance criteria and the dimensions need to be according to the anthropometric data.

The posture analysis and the anthropometric data has been further explained with the system and probe concepts.

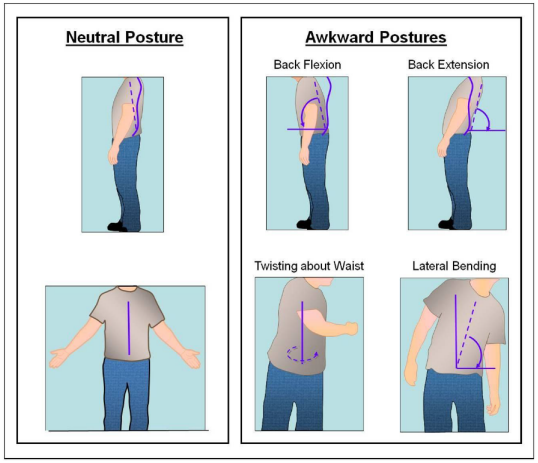


Figure 4. Neutral and awkward back postures.

Fig. B.8 Posture study for posture
Source: [21]

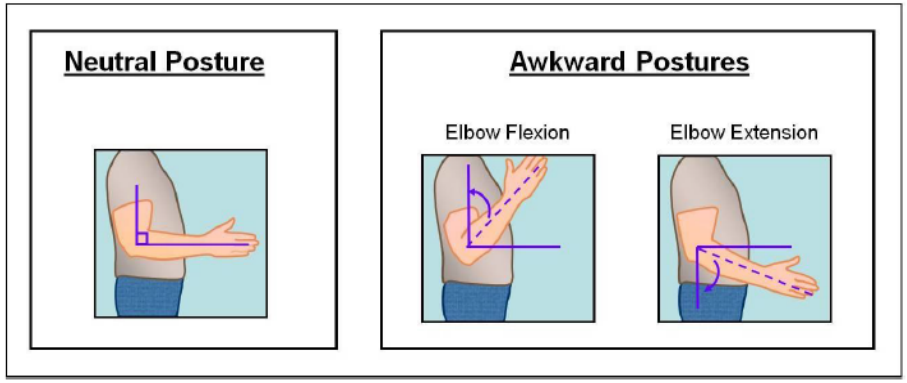


Figure 2. Neutral and awkward elbow postures.

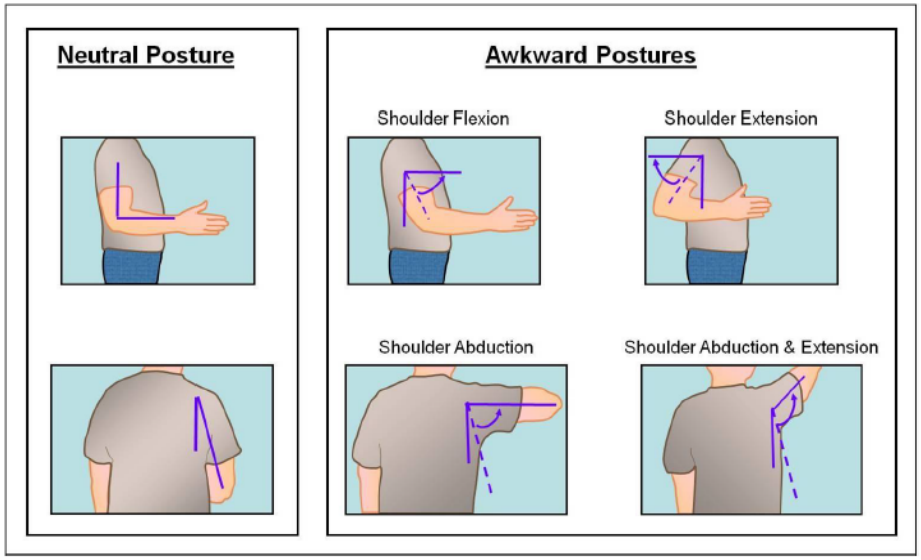


Figure 3. Neutral and awkward shoulder postures.

Fig. B.9 Posture study for posture
Source: [21]

C | DESIGN BRIEF

To design a probe for cryoablation of tumors in breast tissue.

Probe

1. The probe should cause minimum damage to the healthy tissue.

2. The probe should be held in the same position for a certain time duration ranging from 10 to 30 mins.

3. The probe should have an ergonomic handle.

4. The probe should be made using biocompatible materials.

5. The device should be easy to set up and use.

6. The probe should be able to withstand appropriate sterlization procedures.

7. The number of steps required to setup the device should be less.

8. There should be minimum frosting on the probe.

D | PROBE

D.1 Insights from the study

1. Minimum damage to healthy tissue

Brainstorming for this problem has been carried out.

2. Ergonomic handle

Posture study and feedback

3. Stabilize the probe

Brainstorming for this problem has been carried out.

4. Biocompatible materials

Its is essential to use materials that are biocompatible for the probe. As an additional requirement for this device it is essential that the materials will be able to sustain cryogenic temperatures.
A few materials that satisfy both the criteria are SS304 and SS 316. (Medical grade stainless steel), titanium, silver and some copper alloys.
Some regularly used biocompatible plastics are Polyethylene, polypropylene, PVC (Poyvinyl chloride), PEEK (Polyethyl Ethyl Ketone), Polycarbonate and Polyurethane.
Glass and ceramics are biocompatible and are good insulators.

5. Sterlization procedures

Sterlization of the surgical instruments is essential to prevent contamination. A few sterilization procedures currently used are, rinsing, ultrasonic cleaning, autoclaving, cold strilization.
The cryoprobe falls under the 'Critical items' category and thus the treatment required is different.
Most of the items in this category should be purchased as sterile or be sterilized with steam if possible. Heat-sensitive objects can be treated with EtO, hydrogen peroxide gas plasma; or if other methods are unsuitable, by liquid chemical sterilants.[22]

6. Easy to use

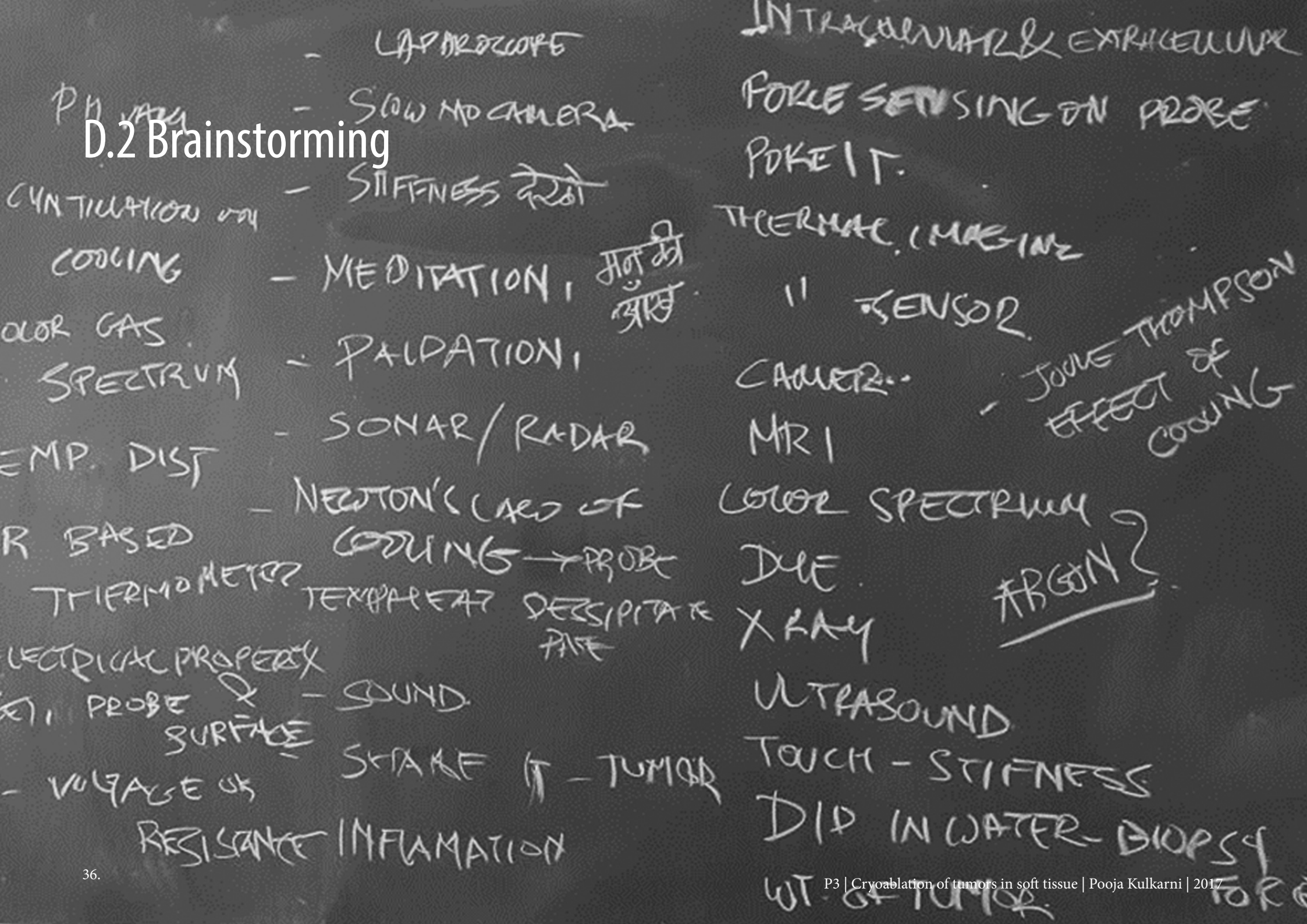
Task Analysis to test the number of steps involved.

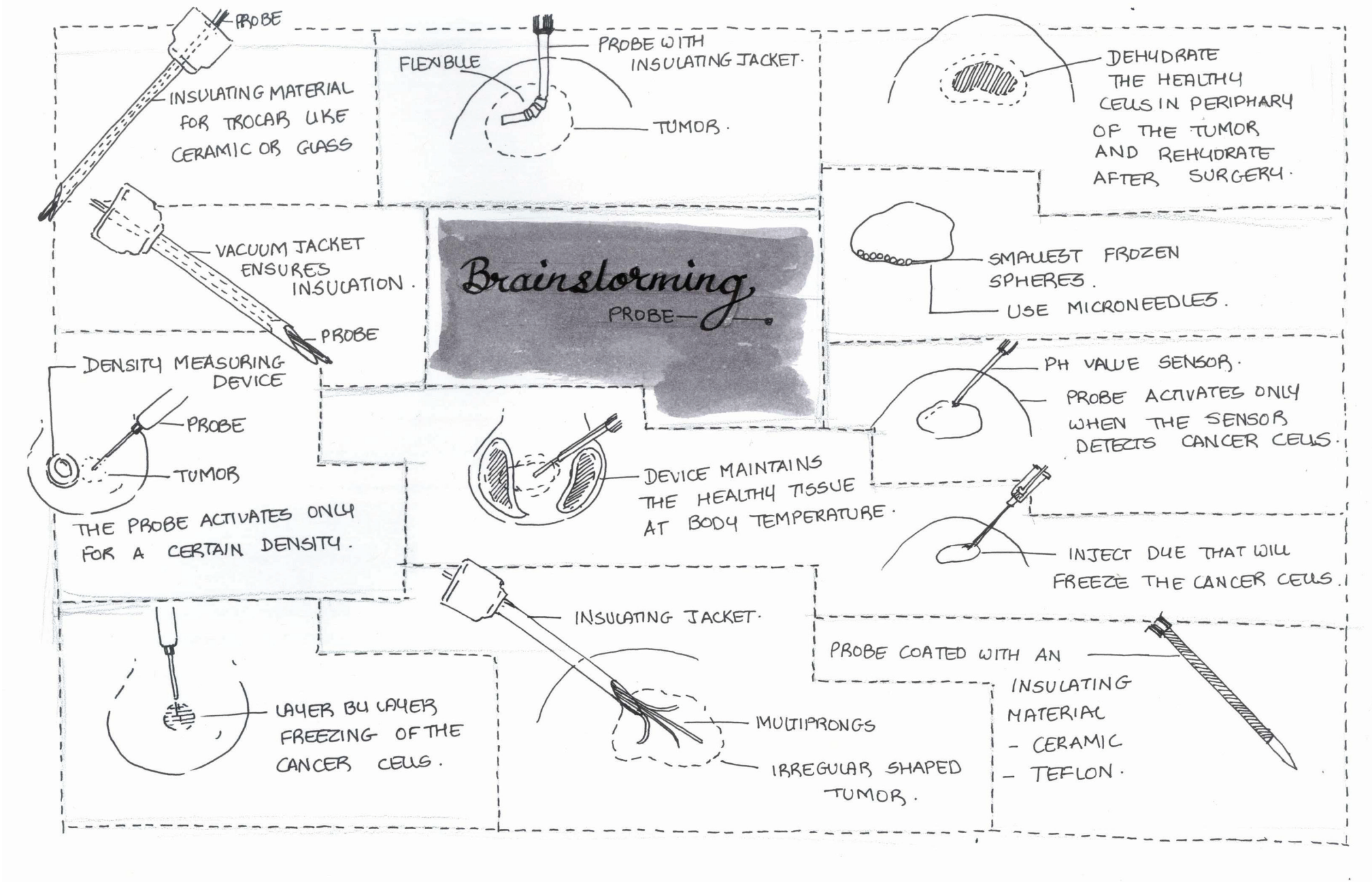
7. Reduced setup time

8. Minimum frosting

To ensure minimum frosting the probe should not be exposed to humidity.

D.2 Brainstorming




PROBE
INSULATING MATERIAL FOR TROCAR LIKE CERAMIC OR GLASS
FLEXIBLE
PROBE WITH INSULATING JACKET.
TUMOR.
DEHYDRATE THE HEALTHY CELLS IN PERIPHARY OF THE TUMOR AND REHYDRATE AFTER SURGERY.
VACUUM JACKET ENSURES INSULATION.
PROBE
Brainstorming
PROBE
SMALLEST FROZEN SPHERES.
USE MICRONEEDLES.
DENSITY MEASURING DEVICE
PROBE
TUMOR
THE PROBE ACTIVATES ONLY FOR A CERTAIN DENSITY.
PH VALUE SENSOR.
PROBE ACTIVATES ONLY WHEN THE SENSOR DETECTS CANCER CELLS.
DEVICE MAINTAINS THE HEALTHY TISSUE AT BODY TEMPERATURE.
INJECT DYE THAT WILL FREEZE THE CANCER CELLS.
INSULATING JACKET.
LAYER BY LAYER FREEZING OF THE CANCER CELLS.
MULTIPRONGS
IRREGULAR SHAPED TUMOR.
PROBE COATED WITH AN INSULATING MATERIAL
- CERAMIC
- TEFLON.

D.3 Initial Ideation

Ideation

The ideation was done for multiple aspects of the problem. The ideas form the brainstorming were combined together and developed further.

It was decided to go ahead with a single probe concept.

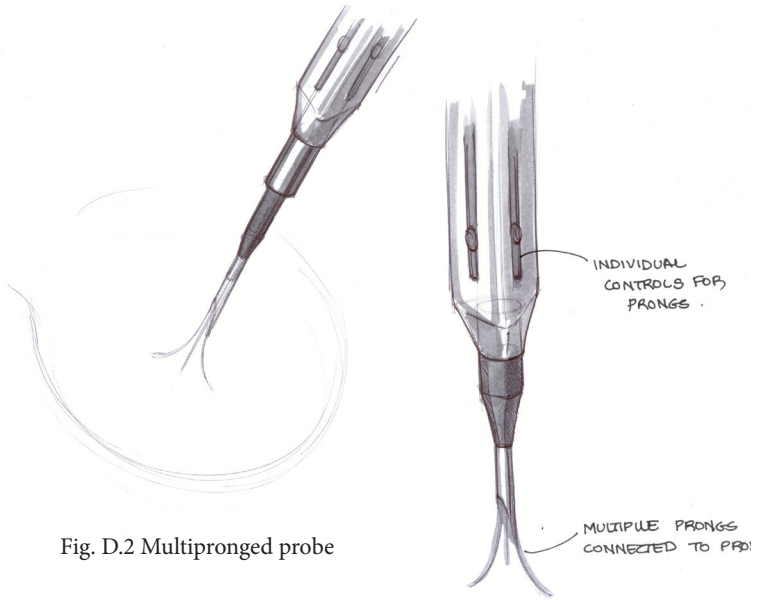


Fig. D.2 Multipronged probe

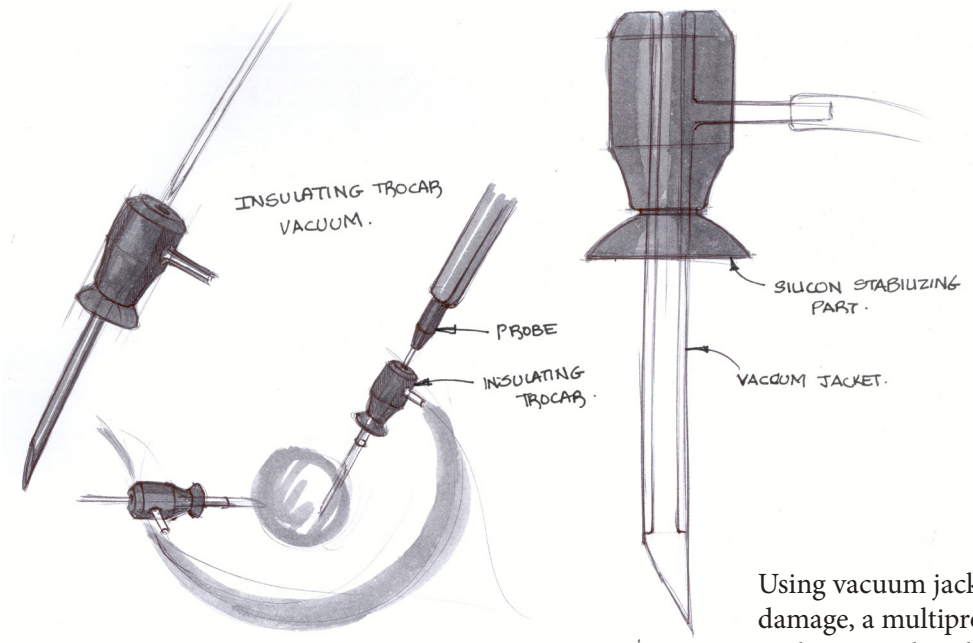


Fig. D.1 Vacuum jacket trocar

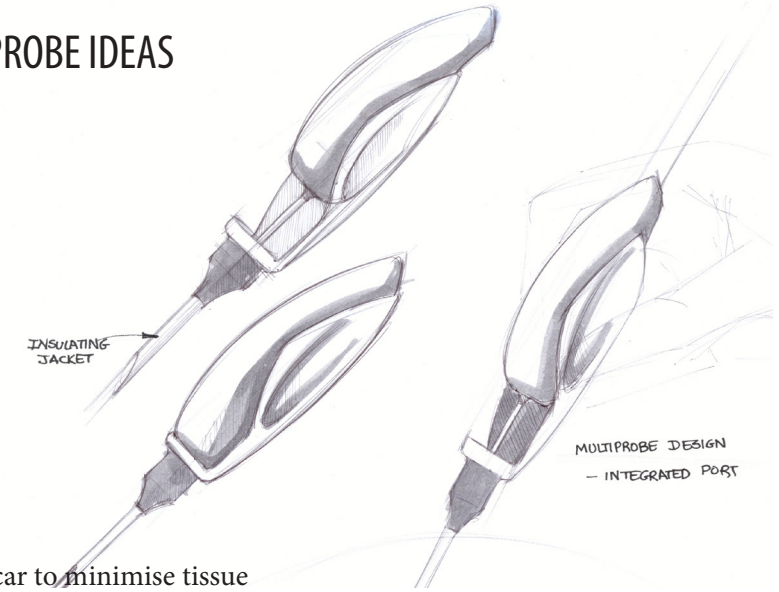


Fig. D.3 Integrated probe and trocar

Using vacuum jacket trocar to minimise tissue damage, a multiprobe idea for mounting, and a multipronged probe

PROBE IDEAS

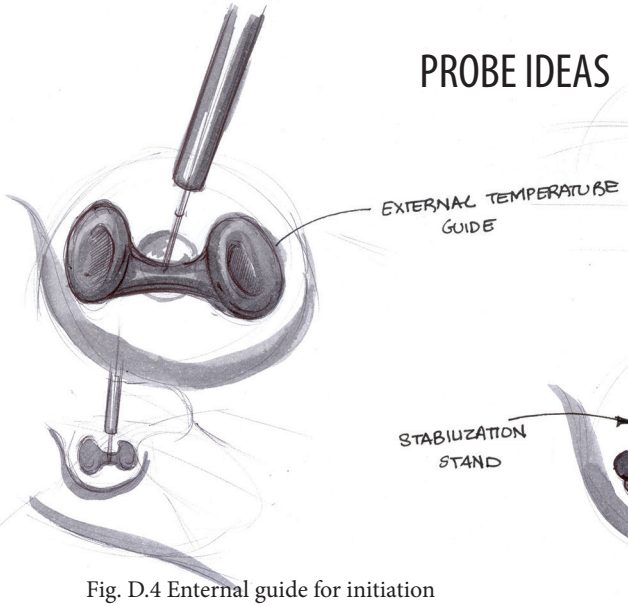


Fig. D.4 Enternal guide for initiation

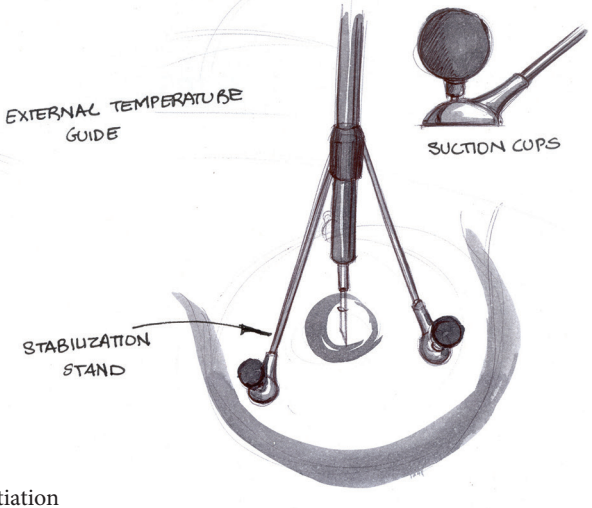


Fig. D.5 Stabilization of probe

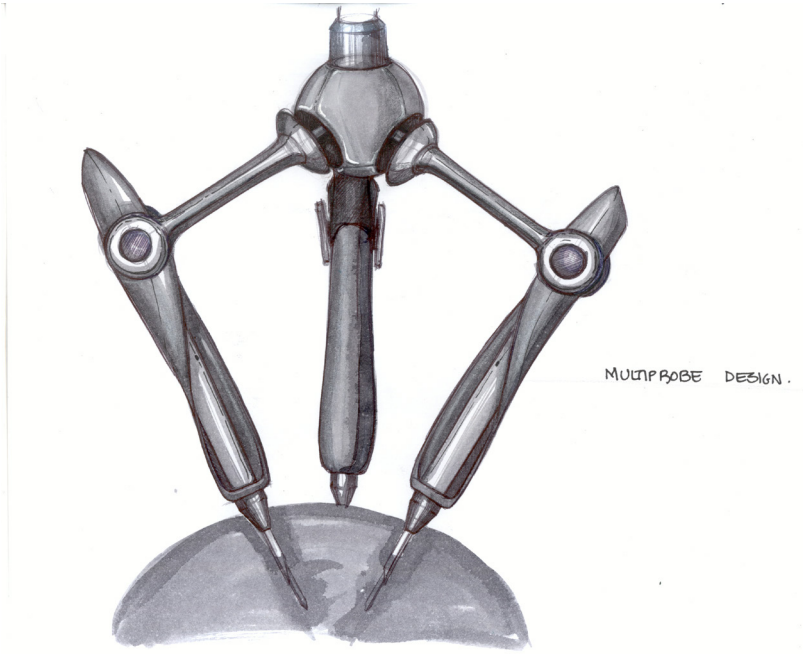


Fig. D.7 Multiprobe design

The idea sketches are for using an external guide to initiate freezing, stabilizing concepts, multiprobe ideas and combining the trocar and probe.

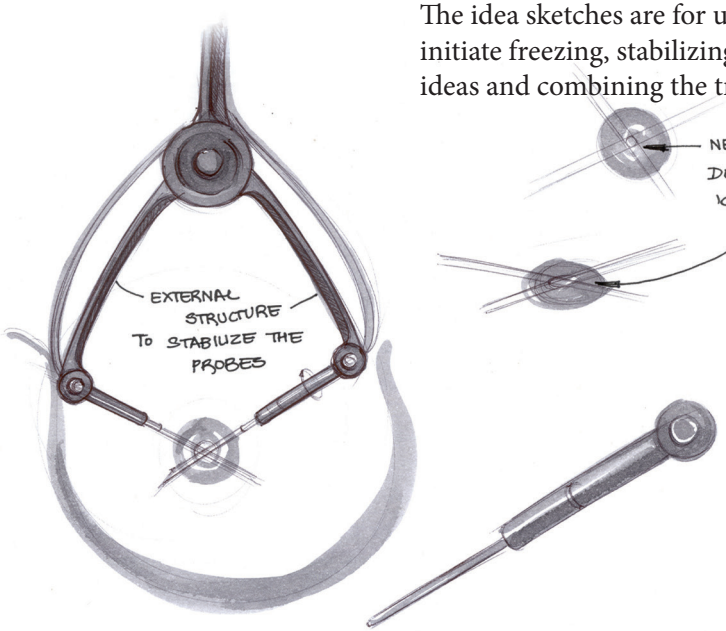


Fig. D.6 Intersection of probes defines the ice growth

PROBE DETAILING

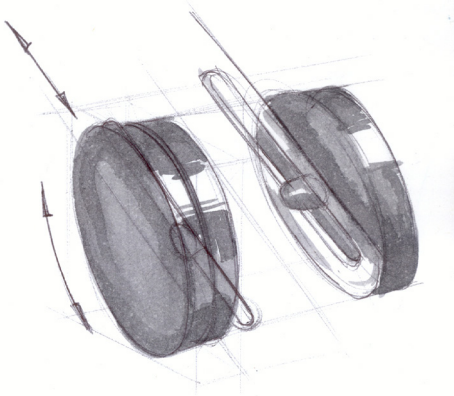


Fig. D.8 Hinge detail

D.4 Concepts

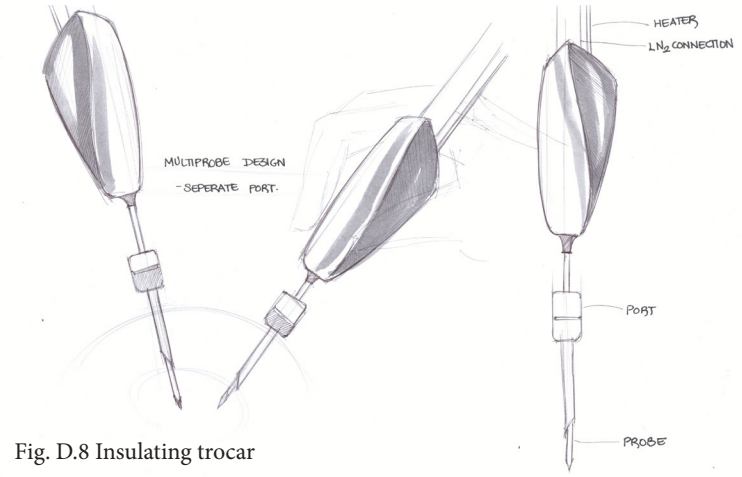


Fig. D.8 Insulating trocar

Concept 1:

A seperate insulating trocar made of insulating materials is used. The cryoprobe goes through it. A seperate incision is avoided.

Merits:
Separate trocars thus it is easier to locate and insert the tumor
No separate incision required as the trocar has a sharp tip that creates the incision
Demerits:
Incision width above 4mm due to the minimum thickness of the material
Brittle materials thus possibility of it breaking inside the body and causing damage
Insulating capacity of the materials needs to be tested for cryogenic temperature
Possibility of damage or loss of trocars

Concept 2:

An allintegrated design using vacuum as an insulating jacket to minimise tissue damage.

Merits:
It is an all integrated device making it easy to use and store
Quick to install and operate
No seperate incision is required and the incision width is 3.5mm
Demerits:
Sterlizing the device is a major concern
Frosting will occur in the areas where the tip is exposed to the moisture in the atmosphere

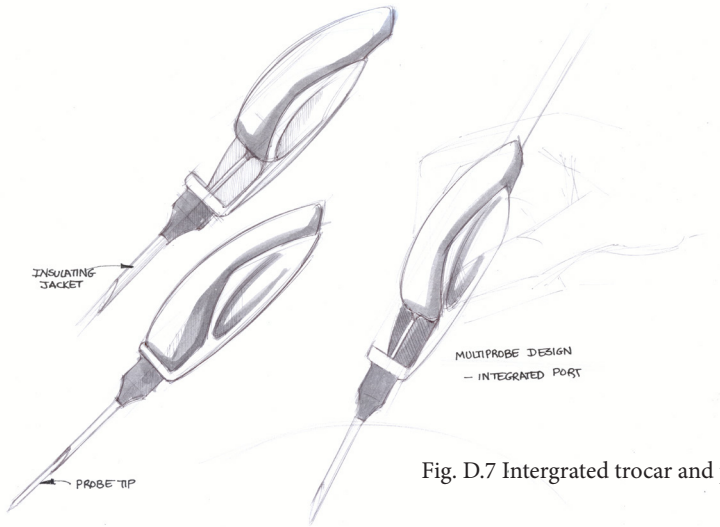


Fig. D.7 Intergrated trocar and probe

Fig. D.8.i Variation 1 for concept2

Fig. D.8.ii Variation 1 for concept2

Concept 2 variations

Design alterations were made to concept 2 to reduce the frosting and to increase the efficiency of the probe.
The insulating jacket and the tip will be detachable and disposable to minimise the contamination and to reduce chance of infection.
A triangular form for the grip will be the easiest to hold comfortably.

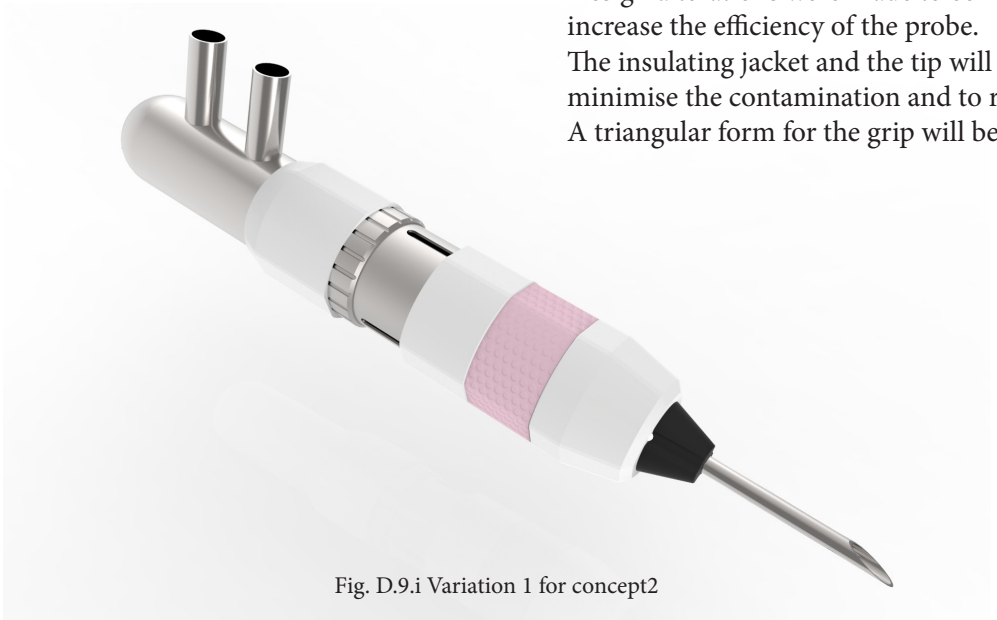


Fig. D.9.i Variation 1 for concept2

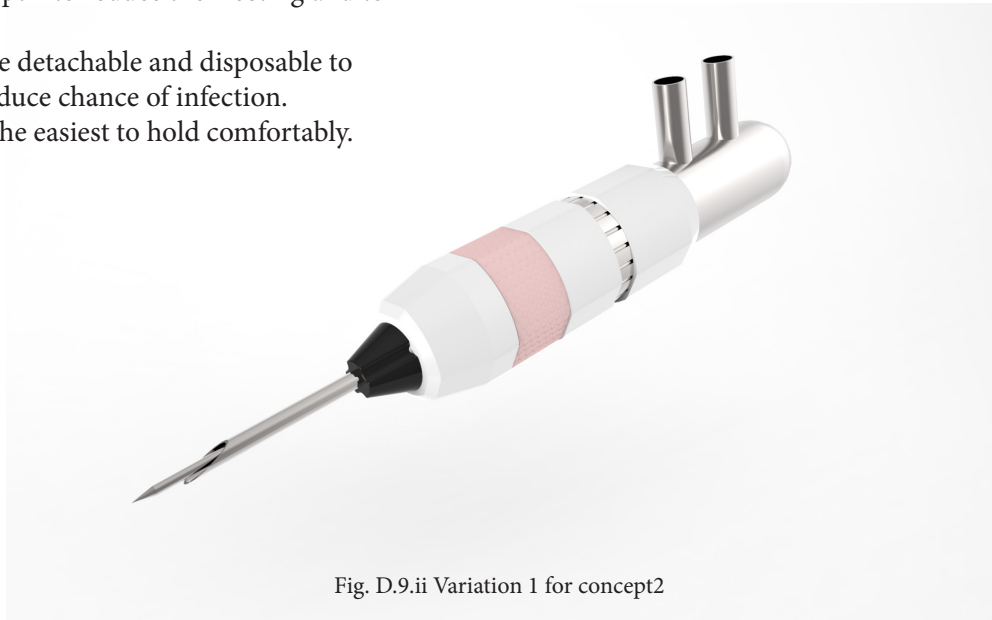


Fig. D.9.ii Variation 1 for concept2

D.5 Ergonomic Analysis for the grip

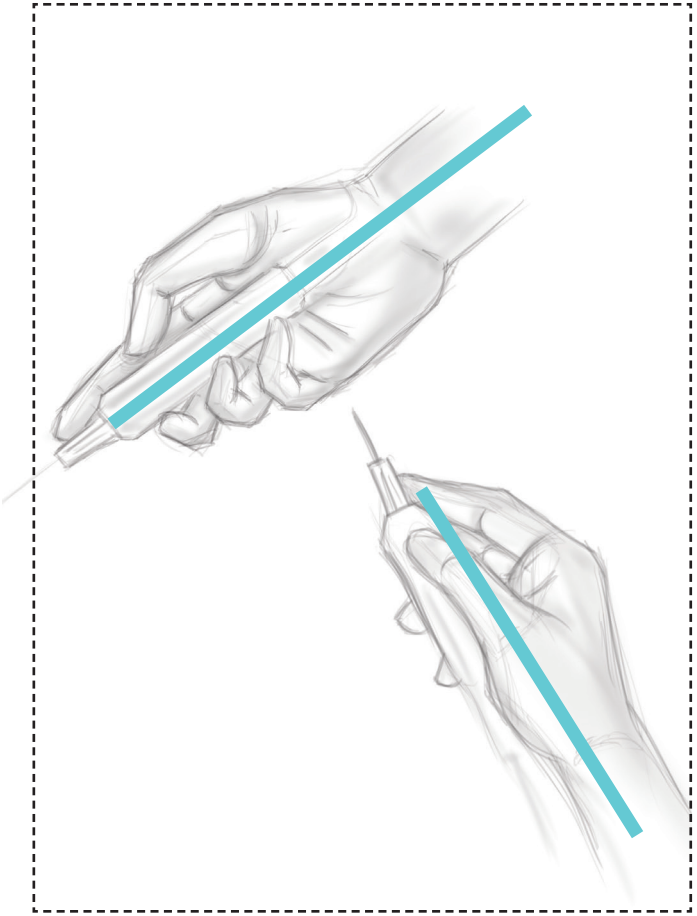


Fig. D.10 Grip 1

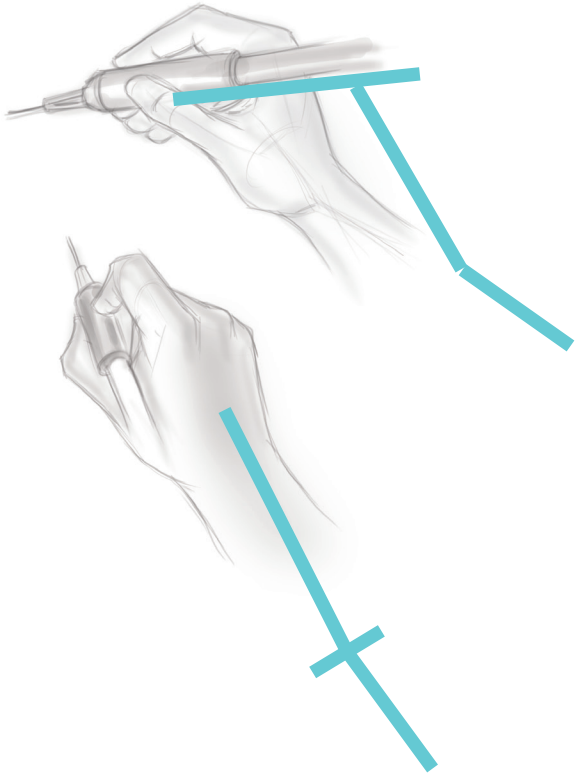


Fig. D.11 Grip 2

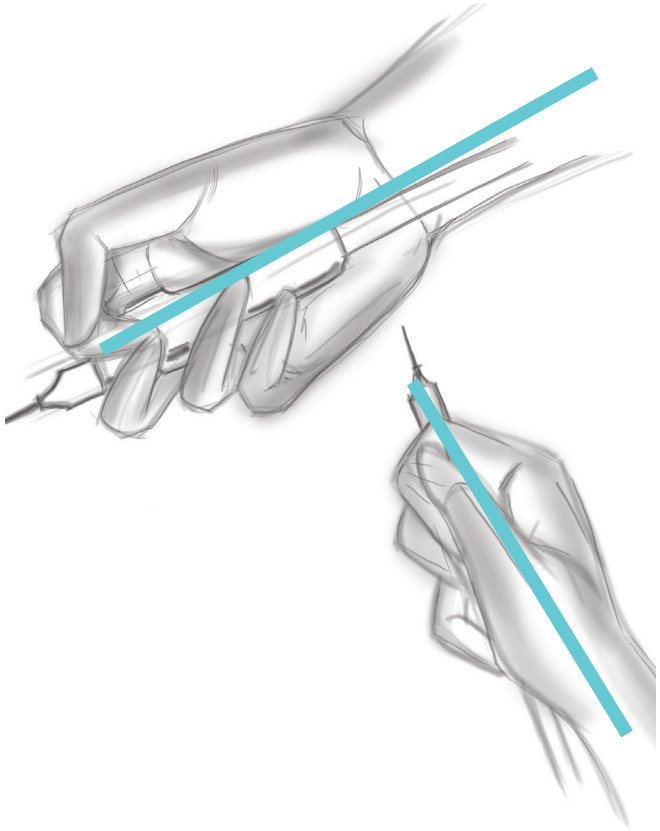


Fig. D.12 Grip 3

Grip Posture

The grip for the probe should have good precision grip and also a should enable the user to exert enough force to pierce the tissue.

According to these requirement the following grips could be used.Refer Fig. D. , Fig. D. and Fig. D. .Grip 1 and grip 3 are the most appropriate grips for the probe. It maintains the natural wrist position and thus prevents injury and fatigue. Grip 1 has better accuracy as the pointing finger acts as the guide for piercing.

Dr. Bhansali was asked for his reviews about the device grip and he demonstrated that grip 1 is the appropriate grip for the probe.

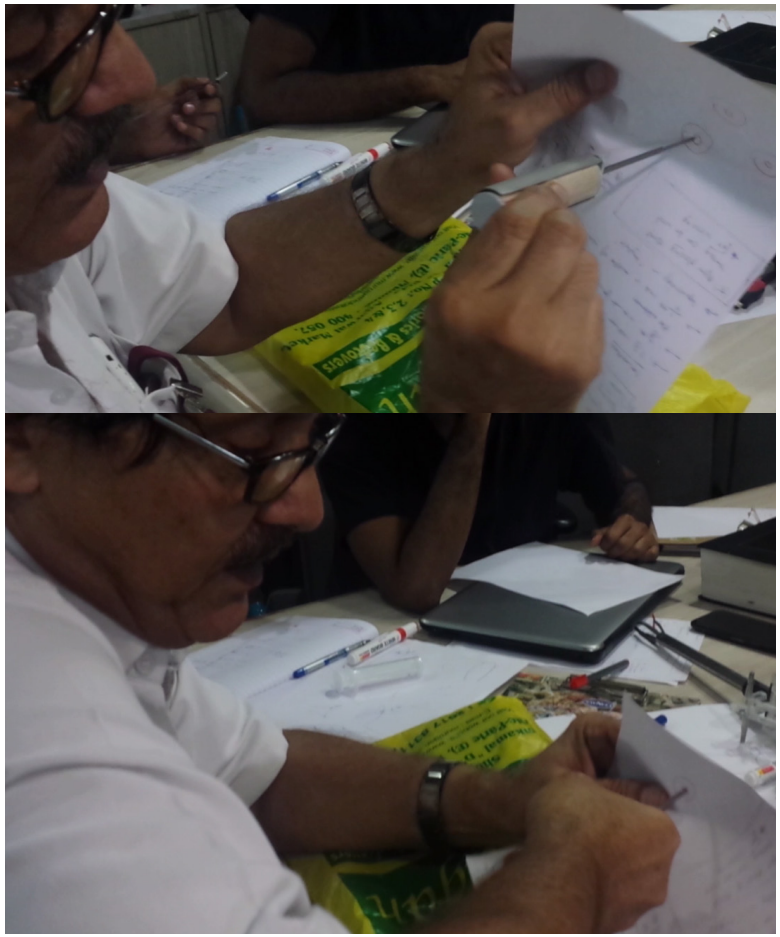


Fig. D.13 Interaction with Dr. Bhansali

D.6 Mock models

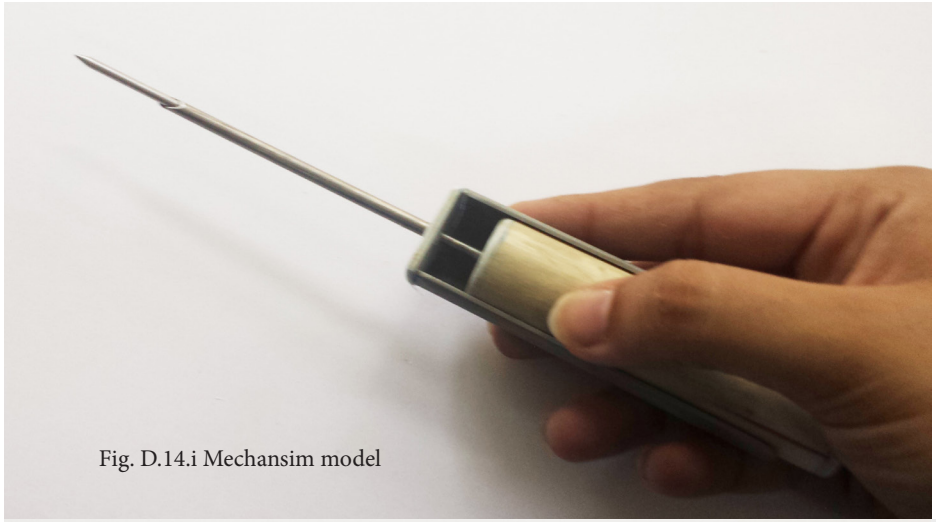


Fig. D.14.i Mechansim model

Mock for the mechanism

The mock was made to test the concept and to understand and analyse the problems with the usability of the probe.
It helped in understanding that there should be no gap between the main probe and the insulating jacket as this can aid in frosting and comprimising the procedure.

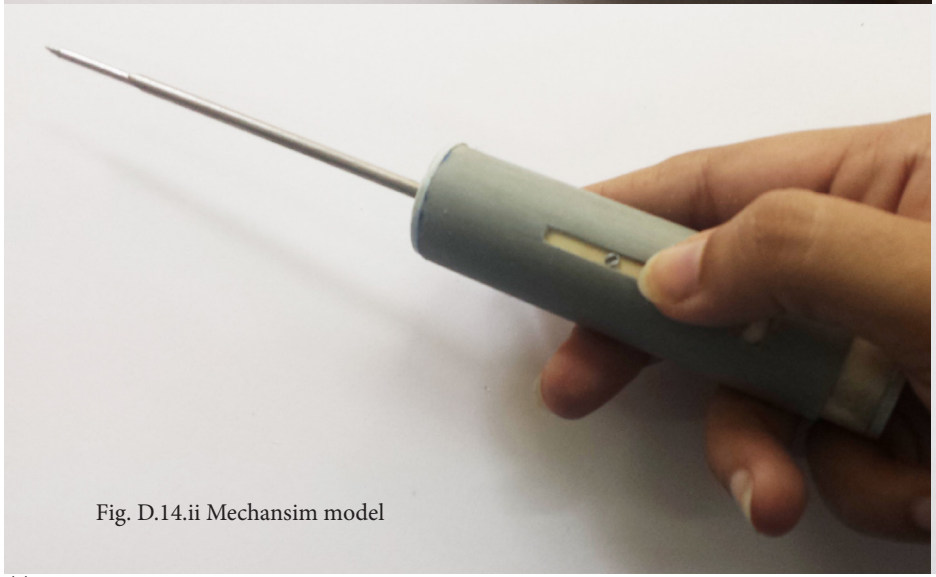


Fig. D.14.ii Mechansim model

Fig. D.14.iii Mechansim model

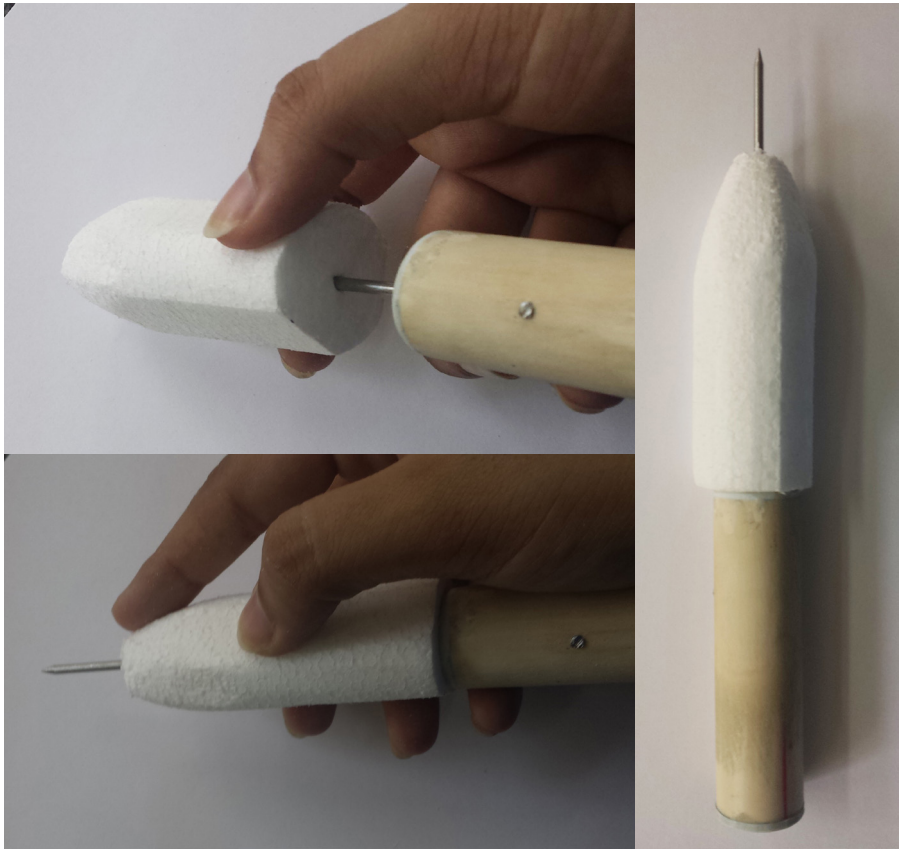


Fig. D.15 Form mockup with a simple triangular cross section

Form mock ups

Quick mock models in soft material were made to test the form. A trianguar cross section has a good grip.

Form selection

The form from Fig. D.15 was chosen as it has a comfortable grip and works well with the circular cross section of the internal probe.

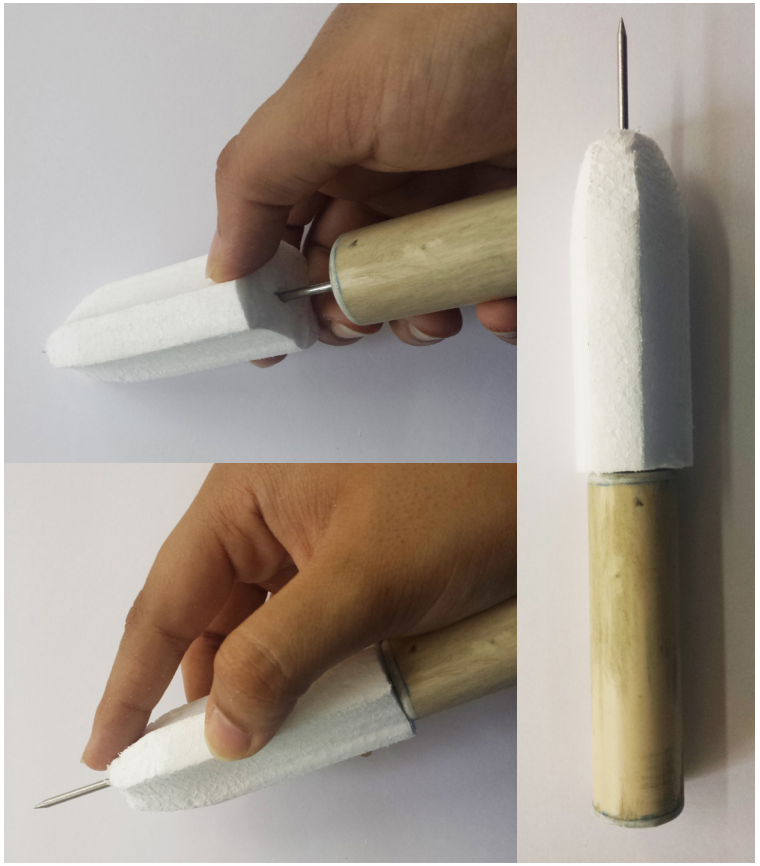


Fig. D.16 Form mockup with a simple triangular cross section

D.7 Inspiration Board

https://s-media-cache-ak0.pinimg.com/736x/87/0b/16/870b160906a-04c567950a77829932de7.jpg

http://mediaroom.carestreamdental.com/wp-content/uploads/2013/10/CS+3500+Main+2.jpg

http://heldundteam.de/wp-content/uploads/2013/06/130614_Starlab_Pipette1_prev.jpg

https://technabob.com/blog/wp-content/uploads/2011/08/on-air-cam-concept-by-lee-jung-hoon-3-600x500.jpg

https://s-media-cache-ak0.pinimg.com/564x/02/7c/0f/027c0f8d-f868086cc22a5708ca696e.jpg

http://www.design-concepts.com/assets/slideshow-images/06-Work-Case_Study-Boston_Scientific-Lotus_Valve-Hero1-1186x667.jpg

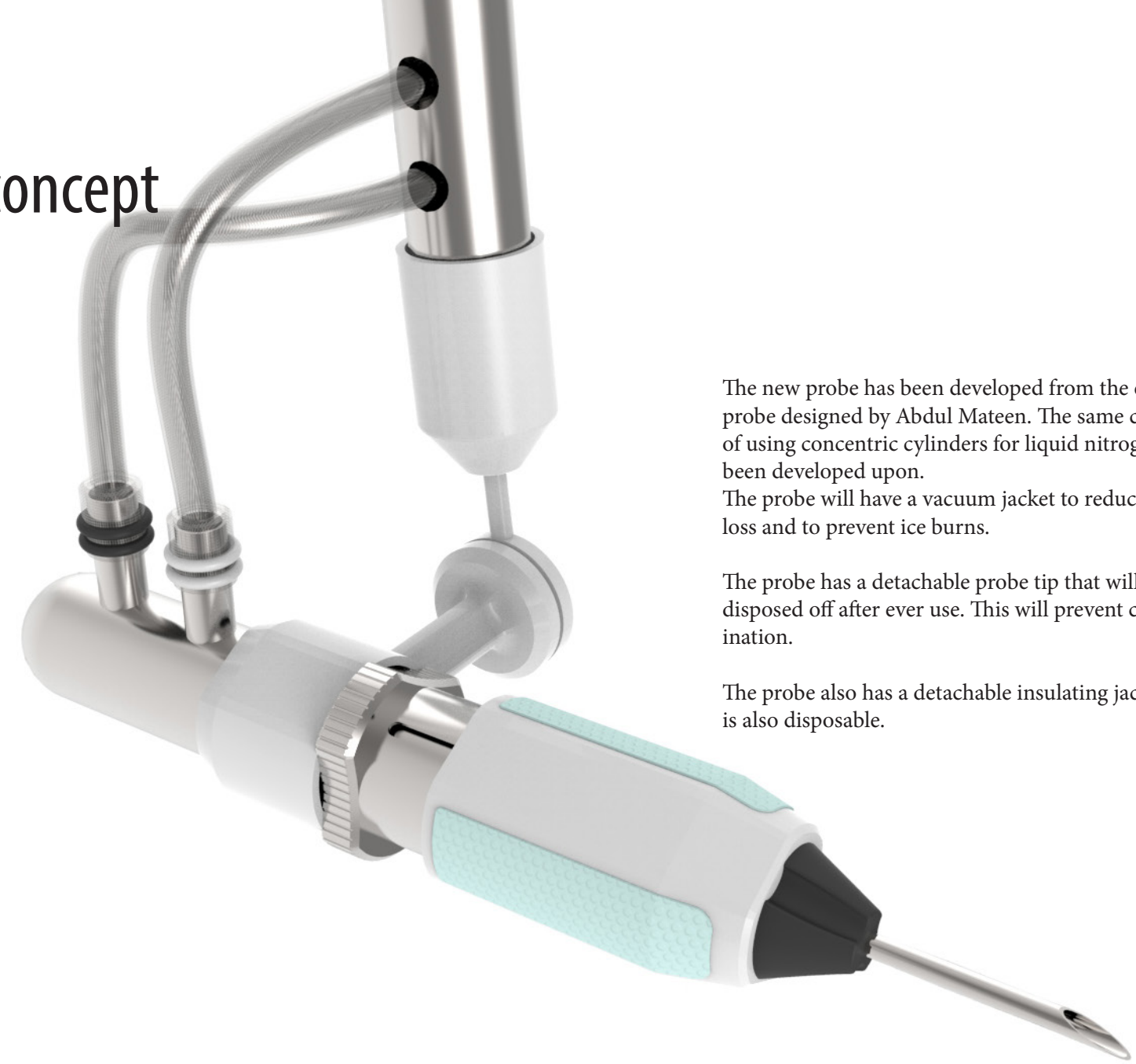
https://s-media-cache-ak0.pinimg.com/736x/d5/[illegible]/b7/d598b796a3c44478cb0c5561001b67c3.jpg

https://lh3.googleusercontent.com/NUEJ8Oe284dosqD_K-UB9ngtNuB-wNb8sKW1x5eV4gBxJl23VQVDLHRwUpvKrqlqWcOdX=s132

https://s-media-cache-ak0.pinimg.com/736x/be/7b/97/be7b97c-20c56d294f7ac14b81[illegible]9dc.jpg

http://storage.weimag.cn/imgs/M00/0F/59/Cr6JoVSs7WaAXv1ZAABzb1DfCJ8473.jpg

D.8 Final concept



The new probe has been developed from the earlier probe designed by Abdul Mateen. The same concept of using concentric cylinders for liquid nitrogen has been developed upon.
The probe will have a vacuum jacket to reduce heat loss and to prevent ice burns.

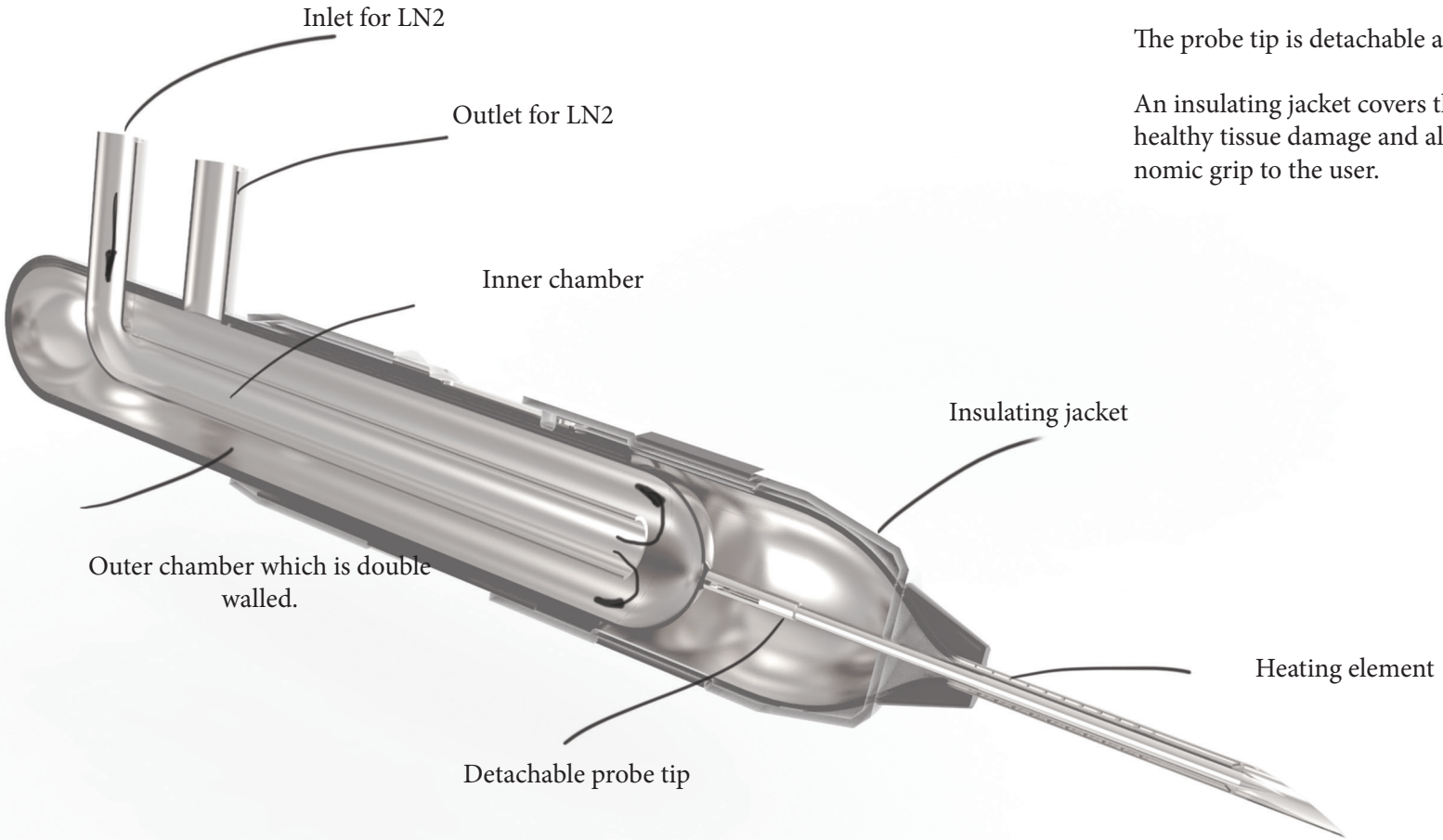
The probe has a detachable probe tip that will be disposed off after ever use. This will prevent contamination.

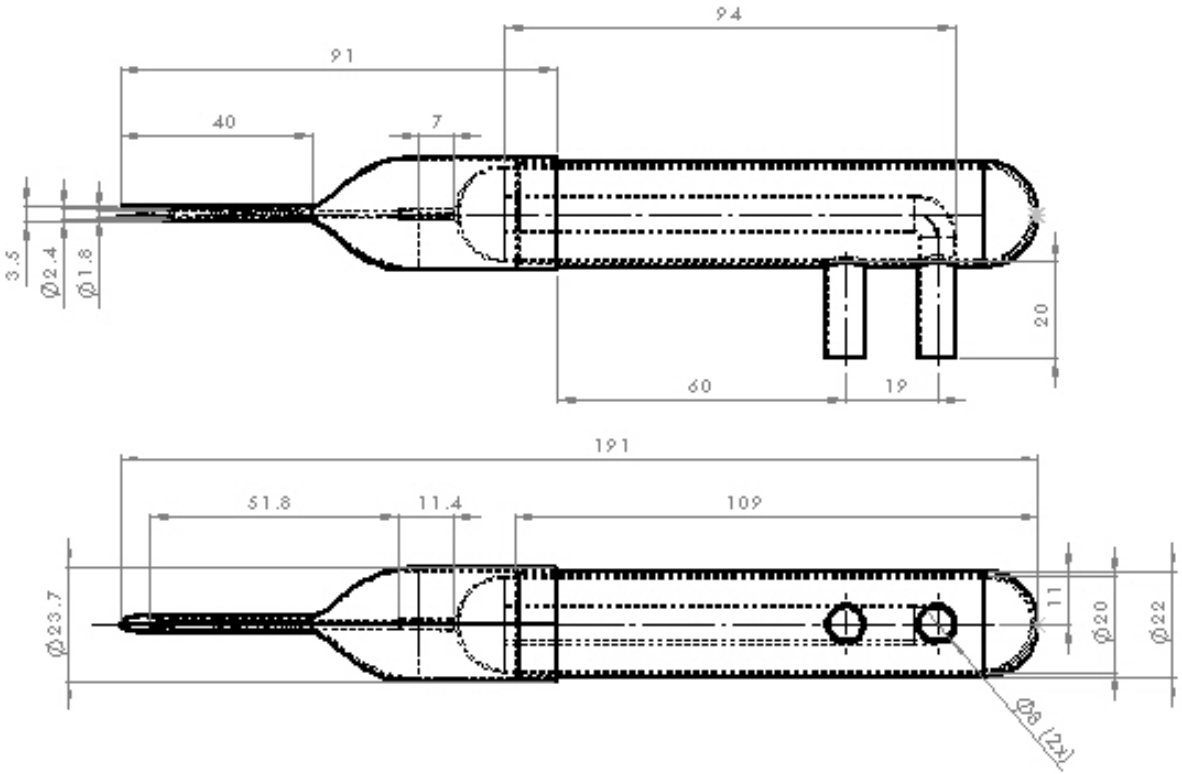
The probe also has a detachable insulating jacket that is also disposable.

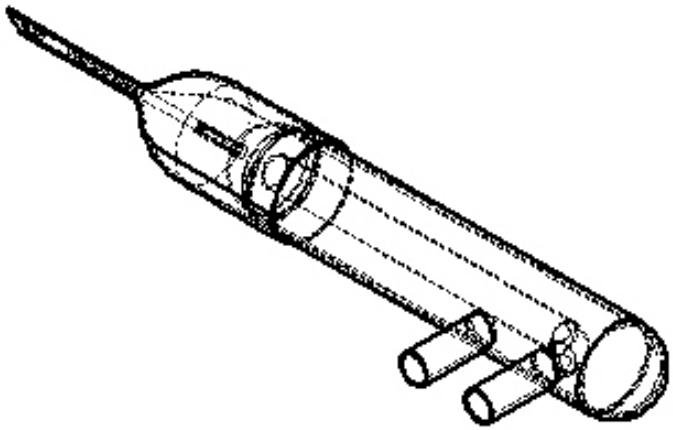
Liquid N2 flows from the inner chamber and comes out from the outer chamber, after exchanging the heat at the probe tip. This is encompassed in a vacuum jacket.

The probe tip is detachable and disposable.

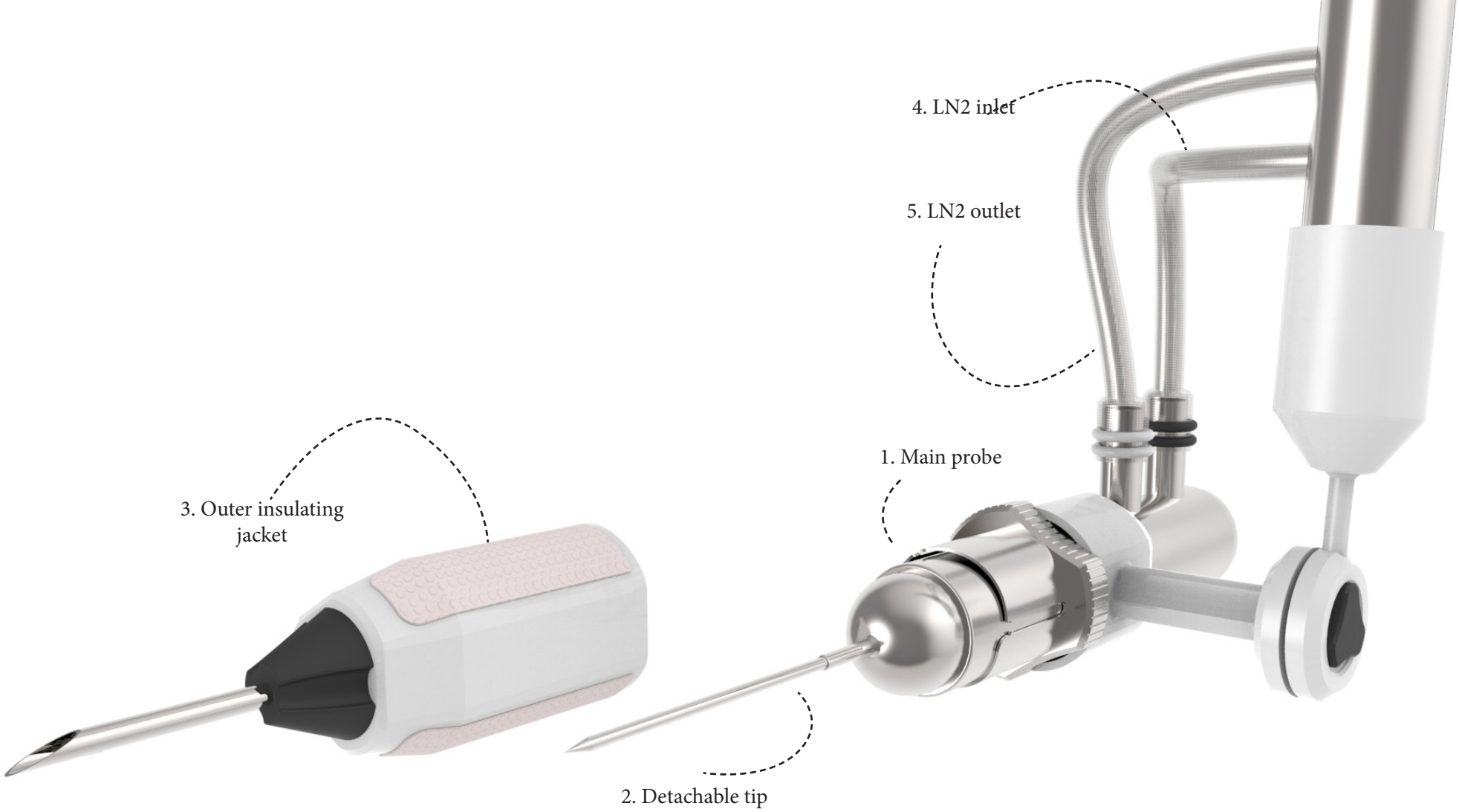
An insulating jacket covers the probe to prevent healthy tissue damage and also to give a good ergonomic grip to the user.





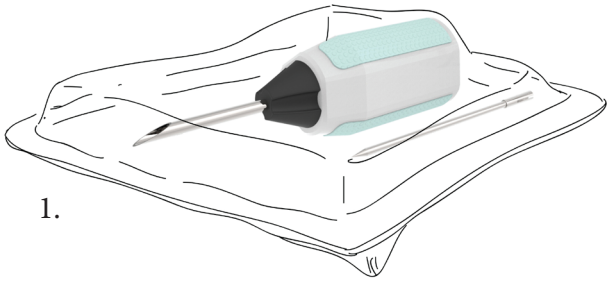


Dimension drawing for the probe: The probe is based on the previous design, with an increase in diameter and a change to minimise heat loss.

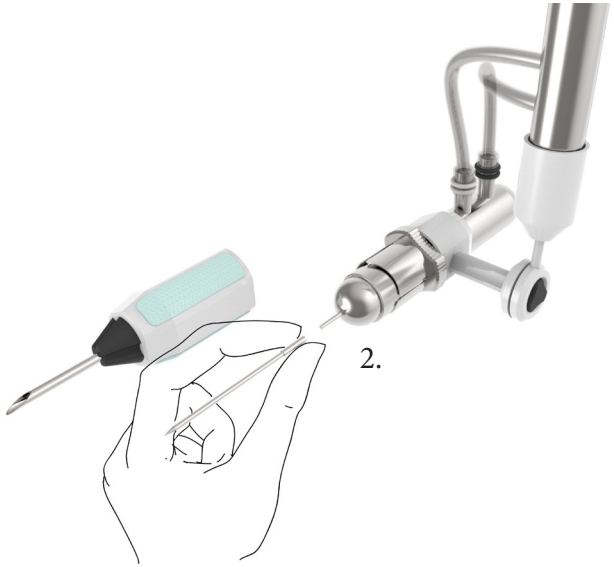


Probe detailing and parts:

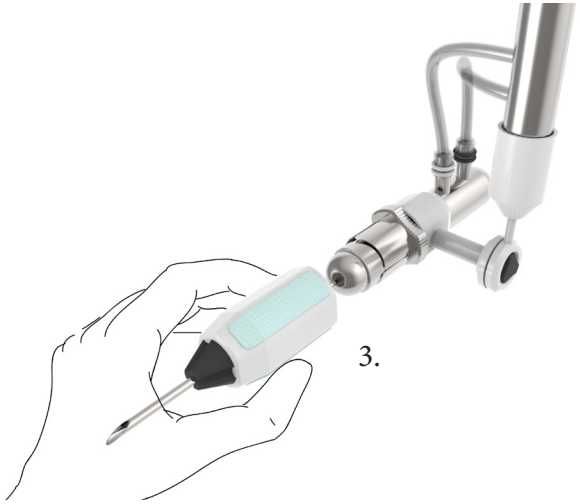
1. Main probe
2. Probe tip
3. Insulating jacket
4. LN2 inlet
5. LN2 outlet



1.



2.



3.

4.

The grip for each step involved with the probe:

1. The disposable parts come in a sterile pack
2. Attaching the probe tip
3. Attaching the insulation jacket
4. Inserting the probe in the tissue

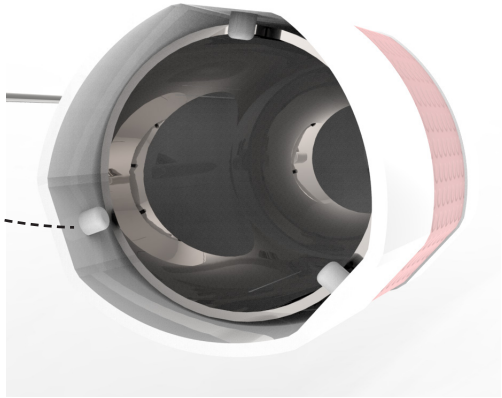
Hinge: Injection molded in HDPE

Insulating jacket: HDPE (High density Polyethylene)
Injection co-molding and ultrasonically welded to the stain-
ess steel jacket

Grip to push the probe in once the jacket is in place.

The attaching detail for the insulating jacket is simple. A small stopper holds the jacket in place.

Main probe material: Stainless steel 304
The tubes will be welded, grove is milled.



E | SYSTEM

E.1 Insights from the study

1. System components

1.Cryoprobe
2. Ultrasound device and monitor
3. Liquid nitrogen cylinder
4. Control panel
5. Power supply for heater

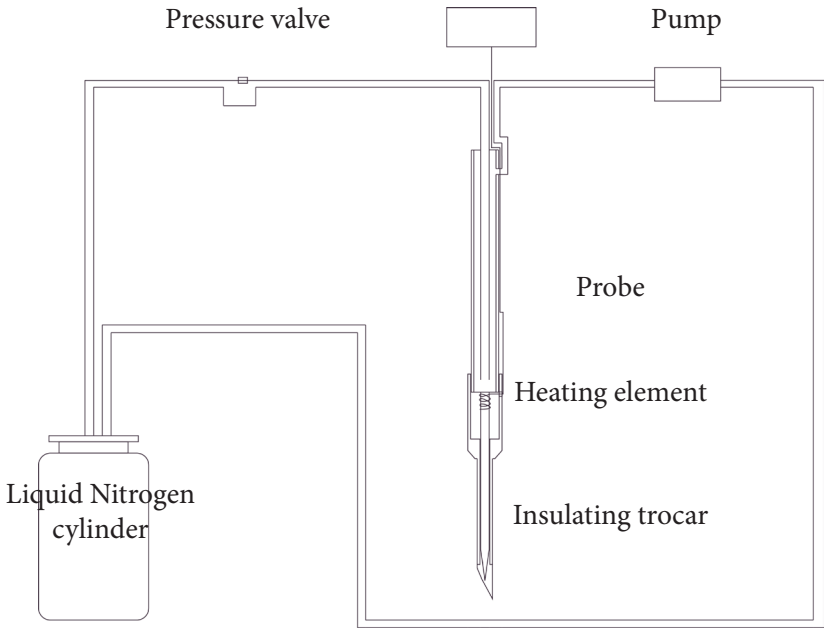
2. System Ideation

Tyes of systems, basic requirementss and system specifications

3. Volumetric study for the components

For a 10 min of cooling of the probe about 6-8 lit. of LN2 is required, thus the system should have a 10 lit. cylinder or a closed system (explained further). As the open system is used widely and is easier to setup it has been used. The cylinder size is approximately 13 inches diameter and 24 inches height.
The Operation theatre bed height is adjustable from 730mm to 900mm.

E.2 System ideation



Closed System

In this system the liquid nitrogen is recirculated and reused. This is reduces the amount of liquid nitrogen used and in turn helps reduce the size of the device.

This system requires a pump to compress the LN2 after heat exchange to let it back into the cylinder.

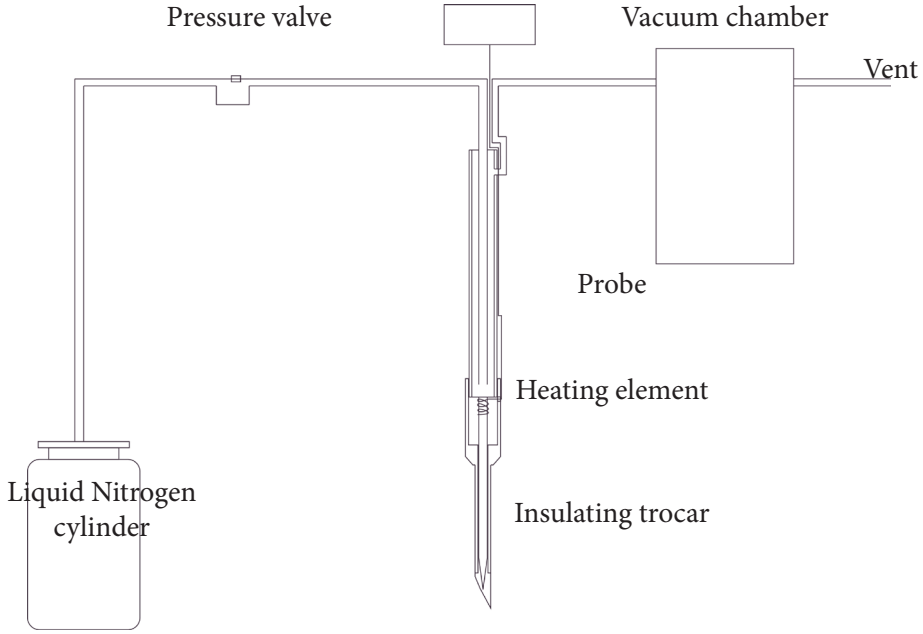
The cost and complexity of the system is higher and thus it will require a through development and testing before it is useful. If it can be developed the device size will be considerably smaller and could be made handheld and portable.

Open System

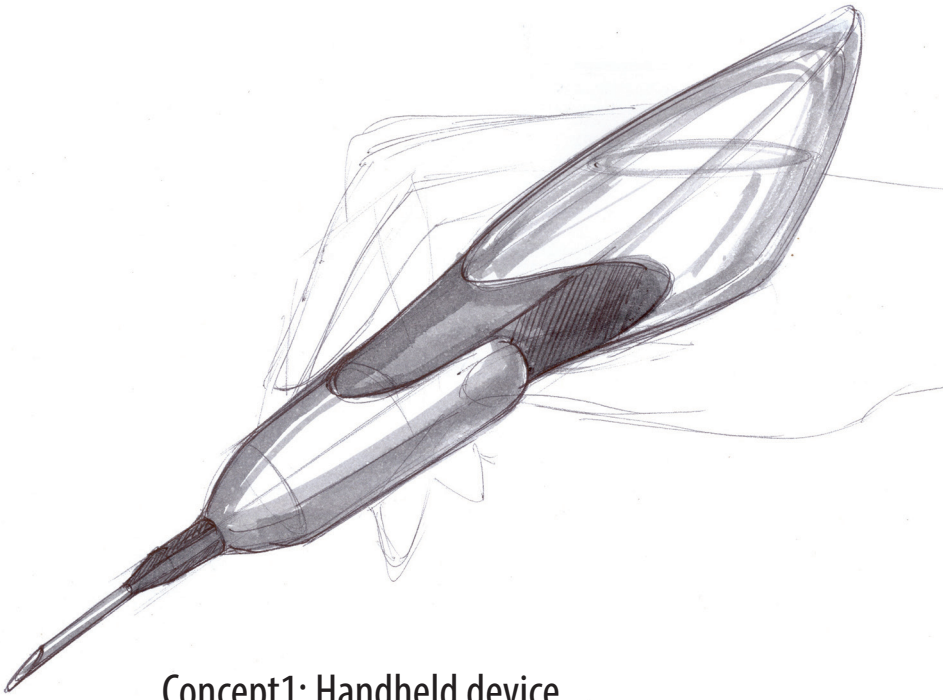
In this system the liquid nitrogen is used to cool the probe and then released into a vacuum chamber where it expands and is then released into the air, or directly released.

The system is comparatively cheaper to manufacture as it doesnot require a pump and is also used currently.

As technological development is still going on, this system is easier to setup and maintain



E.3 System concepts



Concept1: Handheld device

A small handheld device with a closed system to recirculate the LN2.

It will be portable and easy to use and carry around.

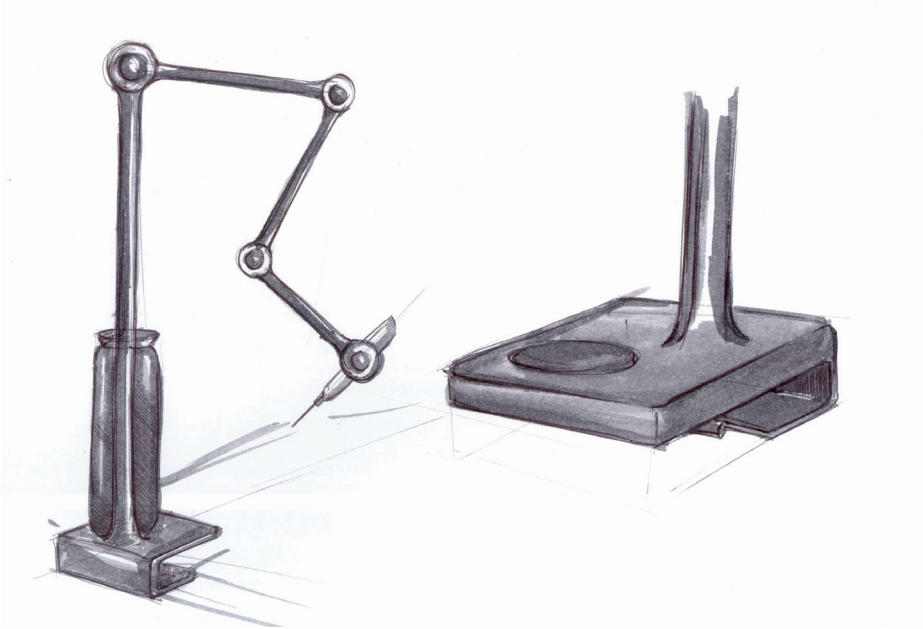
The hospital will have a small cartridge refilling station.

Concept2: Bed attachment

The device has a small cylinder and a closed system. It will have a stand to mount the probe on and will be attached to the operation table.

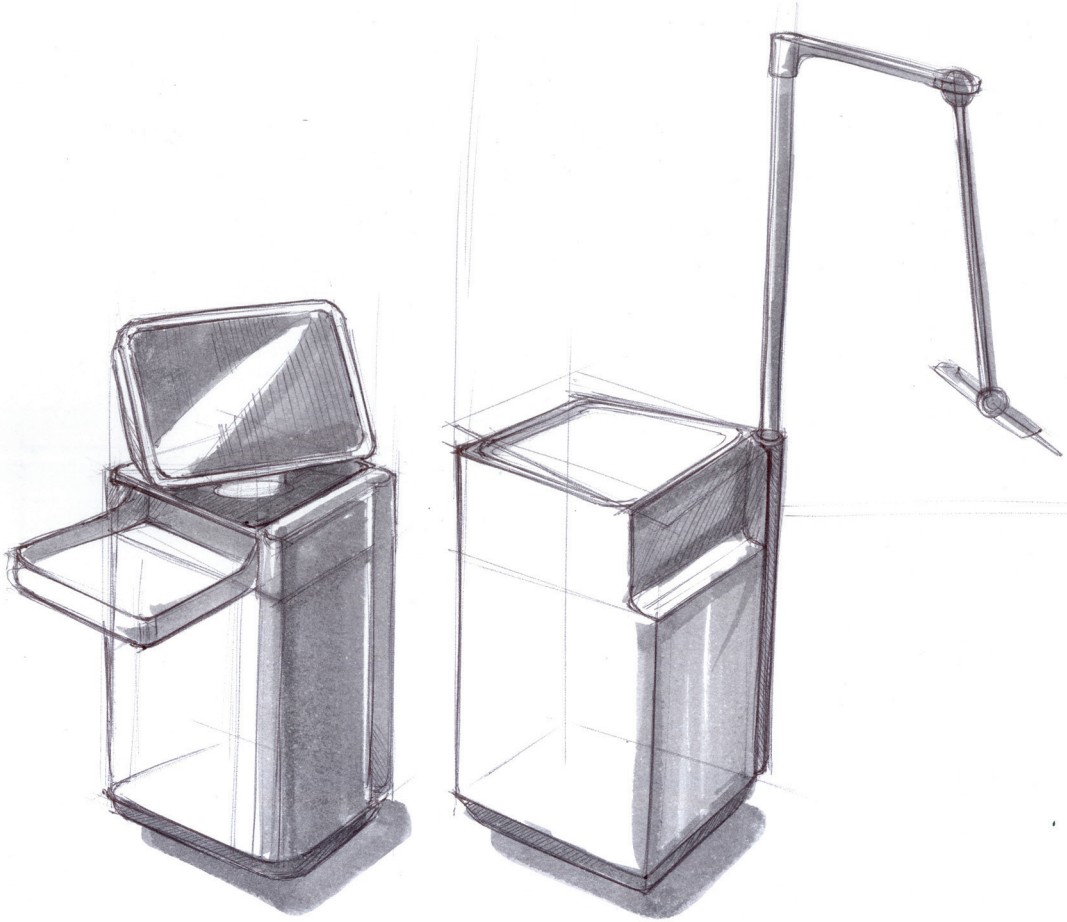
Its compact and portable.

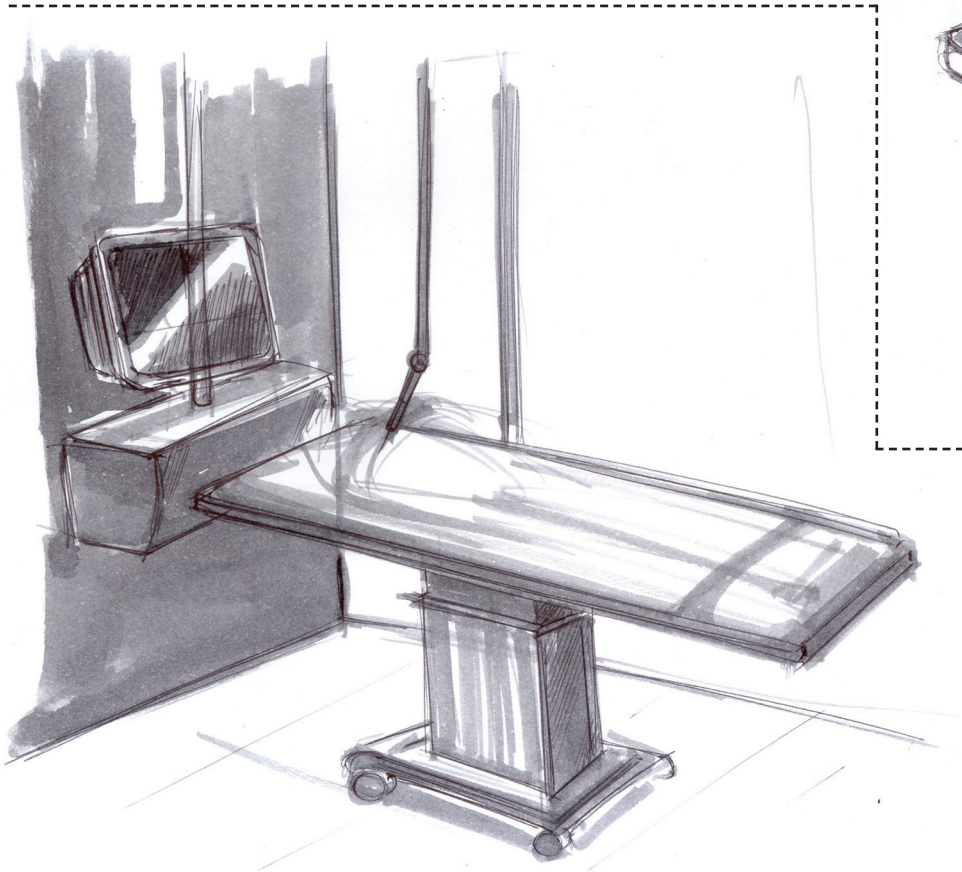
The cylinders can be filled from the main supply.



Concept 3: Portable system

The device will be a portable trolley system that can be carried around. It will have a cylinder of 10 lit capacity, and a provision to attach the monitoring device.





Concept 4: Inbuilt system

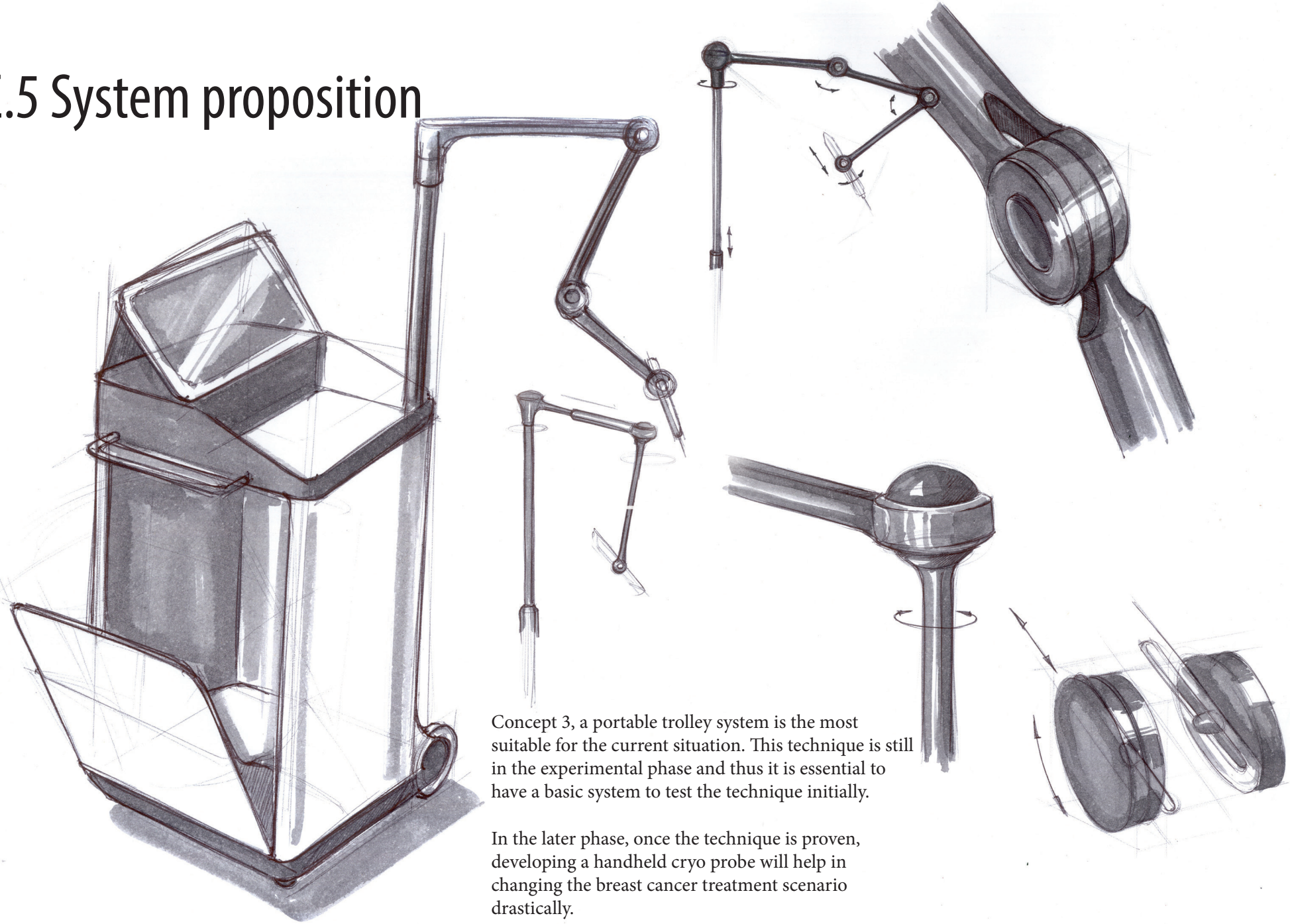
The system will have an inbuilt infrastructure in the Operation theatre. The main container will be kept in another room and the LN2 will be supplied through pipes.

The structure will also be inbuilt to hold the probe.

E.4 Concept merits and demerits

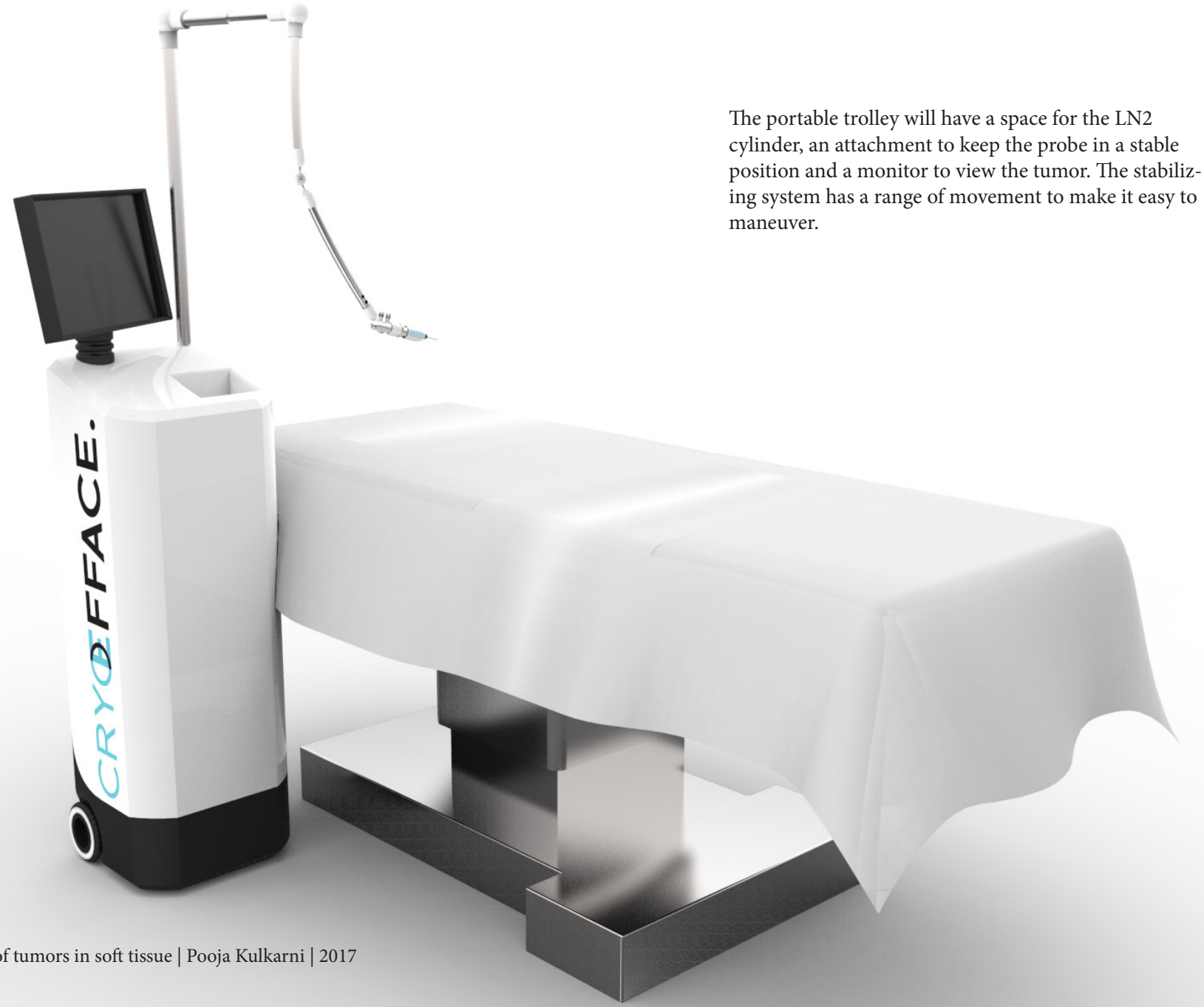
	Concept 1: Hand held device	Concept 2: Table top device	Concept 3: Mobile compact setup	Concept 4: Inbuilt setup for OT
Advantages	Small Compact device Portable Less wastage Easy to adapt	Probe support Smaller initial investment costs	Mobile setup Integrated design Probe support	Cheaper in the long run Specialized Operation theatres No dependency on external agency
Disadvantages	Higher component costs Complicated setup Amount of LN2 required for surgery	Not an integrated system Amount of LN2 required for surgery Complicated setup Higher component cost	Larger size	Higher initial investment costs Time required to modify OT

E.5 System proposition



Concept 3, a portable trolley system is the most suitable for the current situation. This technique is still in the experimental phase and thus it is essential to have a basic system to test the technique initially.

In the later phase, once the technique is proven, developing a handheld cryo probe will help in changing the breast cancer treatment scenario drastically.



The portable trolley will have a space for the LN2 cylinder, an attachment to keep the probe in a stable position and a monitor to view the tumor. The stabilizing system has a range of movement to make it easy to maneuver.

P3 | Cryoablation of tumors in soft tissue | Pooja Kulkarni | 2017


CRYOEFFACE.
FACE.

F | CONCLUSION

F.1 Conclusion

Cryogenics for cancer treatment is an upcoming field and a lot of research has been going in this domain. Designing and developing device that will reduce the side effects of the cancer treatment, will be highly accurate and will also aid in faster recovery and low relapse rate is the current need of the hour. The technology is still in the developmental phase and thus needs to be tested before it can be used as a definite cure. Thus the aim was to design a basic device that can be used for testing and then it can be developed further.

The device can have a sophisticated monitoring system that will enable the surgeon to get the accurate location of the tumor. Also the healthy tissue conservation can be maximised and the current proposed system can be made more accurate. Thirdly the entire system can be mechanised to reduce human dependancy and to also reduce the chance of error.

Reference

Number	Title	Author	Year of publication	Page
1	Taber's Cyclopedic Medical Dictionary		Edition 21st	395
2	Gray's Anatomy	Elsevier, Churchill and Livingstone	Edition 39th	6
3	Breast Cancer facts and Figures 2015-2016	https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2015-2016.pdf	2016	1
4	Cancer Research UK	http://www.cancerresearchuk.org/about-cancer/what-is-cancer	11.02.2017 11.34PM	
5	Breast Anatomy	http://www.webmd.com/women/picture-of-the-breasts#1	12.02.2017 4.11PM	
6	Minimally Invasive Treatment of maalignant Hepatic Tumors: At the Threshold of a Major Breakthrough	Gerald D. Dodd III, Michael C. Soulen, MD, Robert A. Kane, MD, Tito Livraghi, MD, William R. Lees, MB BS, FRCR, Yasuyuki Yamashita, MD, Alison R. Gillams, MBChB, MRCP, FRCR, Okkes I. Karahan, MD, Hyunchul Rhim, MD, PhD	2000	
7	Minimally invasive surgery:Laparoscopy	https://www.gleneagles.com.sg/specialties/advanced-procedures/minimally-invasive-cardiac-surgery	17.02.2017 9.37AM	
8	Minimally invasive surgery:Laparoscopy	http://wecareindia.com/spinal-fusion-surgery/	17.02.2017 9.40AM	
9	Magnetic Resonance Imaging	https://www.scienceabc.com/humans/why-must-you-remove-all-metal-objects-before-an-mri-scan.html	17.02.2017 9.45AM	
10	Ultrasound biopsy	http://blog.universalmedicalinc.com/why-ultrasound-guided-procedures-are-common-in-medical-settings/	17.02.2017 9.48AM	
11	Cryosurgery for breast cancer	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4115688/	17.02.2017 1.35PM	
12	Basics of Cryosurgery	Nikolai N. Korpan (ed.)		
13	Cryoablation	http://www.mdmag.com/medical-news/cryoablation-successful-for-atrial-fibrillation	18.02.2017 11.13AM	
14	National Cancer Institute	https://www.cancer.gov/about-cancer/treatment/clinical-trials/search	18.02.2017 11.53AM	
15	Next Generation Design Development and Evaluation of Cryoprobes for Minimally Invasive Surgery and Solid Cancer Therapeutics In Silico and Computational Studies	Abdul Mateen A. G. Shaikh, Atul Shrivastava and Milind Atrey	2015	
16	MSDS for Liquid Nitrogen	http://www.afrox.co.za/internet.global.corp.zaf/en/images/Liquid%20Nitrogen266_92254.pdf?v=.	25/03/2017 4.04 PM	
17	FDA website for device classification	https://www.fda.gov/default.htm	25/03/2017 4.06 PM	
18	CDSCO website for device classification	http://www.cdsco.nic.in/forms/Default.aspx	25/03/2017 4.08 PM	
19	Cryosurgery for renal fibroid	https://www.youtube.com/watch?v=YpDkQ30FHV4&oref=https%3A%2F%2Fwww.youtube.com%2Fwatch%3Fv%3DYpDkQ30FHV4&has_verified=1	30/01/2017 5.59 PM	
20	Lumpectomy	https://www.cedars-sinai.edu/Patients/Health-Conditions/Images/Breast/Lumpectomy-Surgery-Horizontal.jpg	01/04/2017 5.25 PM	
21	Practical demonstrations of Ergonomic Principles	Department of Health and Human services, Centers for Disease control and Prevention and National Institute of Occupational Safety and Health	July 2011	
22	Guidelines for Disinfection and Sterilization in healthcare facilities	Centers for Disease control and Prevention	2008	

Bibliography

Name	Link	Relevance	Date	Time
Cryopen Video	https://www.youtube.com/watch?v=TDZpkoM5Aas	Product	13/01/2017	4.10 PM
Cryosurgery	https://www.youtube.com/watch?v=TDZpkoM5Aas	Technique	13/01/2017	4.11 PM
Cryosurgery	https://www.youtube.com/watch?v=Riwzl1SNaRc&t=93s	Technique	13/01/2017	4.14 PM
Cryosurgery	https://www.youtube.com/watch?v=KDskkiMtAKE	Technique	13/01/2017	4.18 PM
Cryosurgery	https://www.youtube.com/watch?v=Bh4qPwPf-ug	Technique	13/01/2017	4.27 PM
Cryoprobe	https://www.youtube.com/watch?v=qY5tQmKzzD4	Product	13/01/2017	4.31 PM
Lumpectomy	https://www.youtube.com/watch?v=fNKcXBdJXpo	Parallel technique	30/01/2017	5.28 PM
Cryo for Cervix	https://www.youtube.com/watch?v=yJgRiHUwNl8&oref=https%3A%2F%2Fwww.youtube.com%2Fwatch%3Fv%3DyJgRiHUwNl8&has_verified=1	Technique	30/01/2017	5.32 PM
Radio frequency ablation	https://www.youtube.com/watch?v=95G0E7t-cnc	Technique	30/01/2017	5.36 PM
Radio frequency ablation	https://www.youtube.com/watch?v=PMpIb-7Fjo0	Technique	30/01/2017	5.39 PM
Radio frequency ablation	https://www.youtube.com/watch?v=eDEKSVGdRcE	Technique	30/01/2017	5.44 PM
Cryosurgery	https://www.youtube.com/watch?v=_sTAp6hqXeE	Technique	30/01/2017	5.48 PM
Cryosurgery for renal fibroid	https://www.youtube.com/watch?v=YpDkQ30FHV4&oref=https%3A%2F%2Fwww.youtube.com%2Fwatch%3Fv%3DYpDkQ30FHV4&has_verified=1	Technique	30/01/2017	5.59 PM
Cryosurgery for renal fibroid	https://www.youtube.com/watch?v=YrHePivoAkg	Technique	30/01/2017	6.02 PM
Ultrasound	https://www.youtube.com/watch?v=s23_d-qeEn4	Principle	09/02/2017	12.06 AM
Ultrasound	https://www.youtube.com/watch?v=JqVGgq5bE-Y	Principle	09/02/2017	12.14 AM
For Atrey sir, comparision about liq N2 and argon	https://www.ncbi.nlm.nih.gov/pubmed/9425653			
	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1472868/			
Cryosurgery	https://www.google.co.in/search?q=cryoablation&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjR9KnK95jSAhXGvI8KHZ30BagQ_AUICSgC&biw=1536&bih=710#imgrc=6VhrgvqKDtV3hM:	Image	18/02/2017	12.27 PM
Biocompatible materials	http://www.uni-sz.bg/tsj/vol8,Suppl.2,2010/D.Mihov.pdf	Materials	30/03/2017	4.11 PM