Controllable Radiofrequency Ablation for Liver Tumors
Radiology Team Final Report

Submitted by

Caitlin Cobb Gari Eberly Lydia Kappelmeier Anurag Vaidya

17th May 2021

Faculty Advisor
Karlo Malaga, PhD
Assistant Professor, Biomedical Engineering, Bucknell University

External Advisor
Aalpen Patel, MD
Chair, Geisinger System Radiology

BMEG 402 Senior Design
Department of Biomedical Engineering
Bucknell University
Lewisburg, PA

Table of Contents

Abstract

Radiofrequency ablation (RFA) is a procedure used to treat solid tumors, such as hepatocellular carcinoma. RFA is used to heat and kill small liver tumors in patients that do not qualify for surgical intervention. However, current RFA probes are only capable of generating spherical ablation zones. This lack of spatial control over ablation zones leads to increased risk of treatment complications, including incomplete tumor ablation and healthy tissue necrosis, and limits the patients that qualify for this minimally-invasive procedure to those with centrally-located, spherical tumors. Moreover, if the RFA probe is inserted into the tumor off-center, the probe must be removed from the tumor and reinserted, thereby risking bleeding, to avoid off-target and incomplete tumor ablation.

The design of a RFA probe that is capable of generating differently shaped and sized ablation zones that match the unique geometries of each tumor is presented (Figure 1). This updated probe includes four plungers that can be deployed separately to create different tine arrays and ablation zones that more accurately match the geometries of target tissues. To evaluate the probe's ability to generate differently-shaped ablation zones, different tine array ablation zones were computationally modeled in COMSOL and experimentally validated in beef liver tests. Probe deployment was tested in agar liver phantoms.

The **differential probe** will be marketed as a probe with the ability to match ablation zone shape with the geometries of individual tumors, i.e. it will be customizable to individual patients. As a radiofrequency lesion probe, the device will follow the regulatory pathway of a Class II medical device.

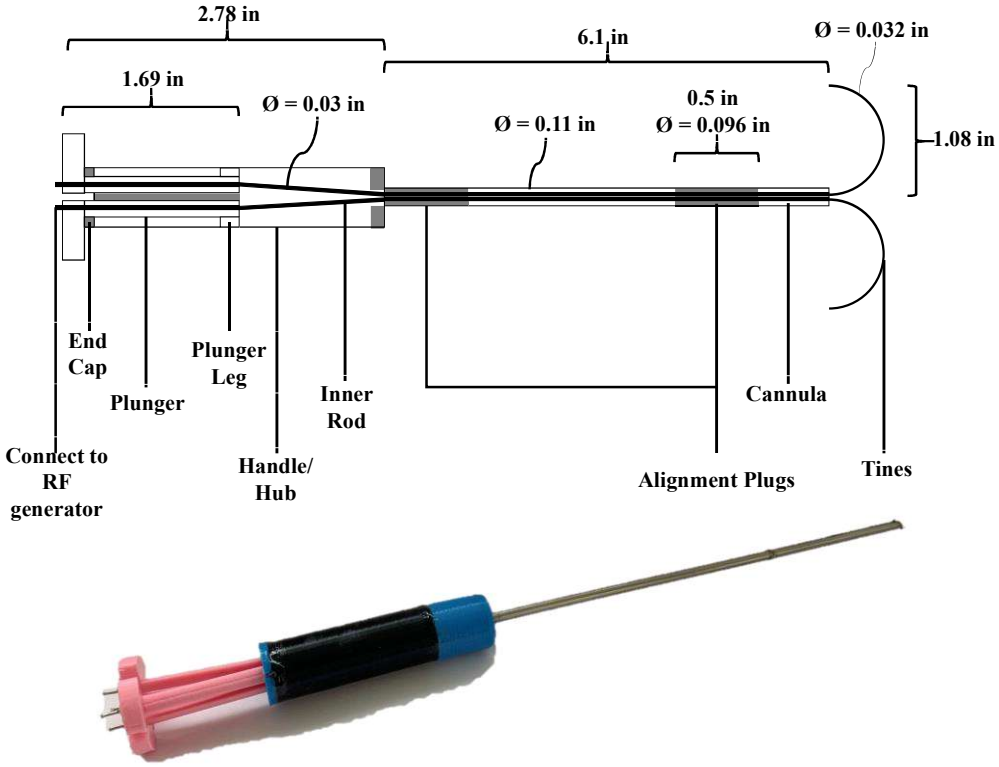


Figure 1: Prototype schematic and real-life prototype

Project Release Forms

Bucknell UNIVERSITY

STUDENT PROJECT RELEASE

By accepting student project results you agree with the following:

I agree that the results reported are for information purposes only, and are not guaranteed by Bucknell University, including the faculty and students involved with the Project.

I will not use the name of Bucknell University, nor of any faculty, staff or student involved with the Project, in any publicity, advertising, applications, or news releases without prior written approval of an authorized representative of Bucknell.

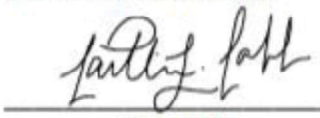
I understand that this was a student project only, and that Bucknell University gives no assurances, promises, or representations with respect to the applicability of the study data or conclusions for any particularized use. Bucknell disclaims and does not warrant in any way that the information contained in this project or its results are merchantable or fit for any particular use of any prospective use.

I also understand that the results of student projects should be reviewed and approved by a professional engineer, at Geisinger Health System's expense, before these results may be used for the (describe the project outcome – e.g. for clinical use, for validated results for patient training, etc.). No test results or certifications from Bucknell shall be in any way associated with the (project outcome).

I Caitlin L. Cobb, Bucknell 2020-2021 BME Radiology Senior Design Team Member

Name Title

am the authorized representative for Geisinger Medical Center and understand and I agree to the above statements.



Signature

5/16/2021

Date

Bucknell
UNIVERSITY

STUDENT PROJECT RELEASE

By accepting student project results you agree with the following:

I agree that the results reported are for information purposes only, and are not guaranteed by Bucknell University, including the faculty and students involved with the Project.

I will not use the name of Bucknell University, nor of any faculty, staff or student involved with the Project, in any publicity, advertising, applications, or news releases without prior written approval of an authorized representative of Bucknell.

I understand that this was a student project only, and that Bucknell University gives no assurances, promises, or representations with respect to the applicability of the study data or conclusions for any particularized use. Bucknell disclaims and does not warrant in any way that the information contained in this project or its results are merchantable or fit for any particular use of any prospective use.

I also understand that the results of student projects should be reviewed and approved by a professional engineer, at Geisinger Health System's expense, before these results may be used for the (describe the project outcome – e.g. for clinical use, for validated results for patient training, etc.). No test results or certifications from Bucknell shall be in any way associated with the (project outcome).

I Gari Eberly student
Name Title

am the authorized representative for Geisinger Medical Center and understand and I agree to the above statements.

Gari Eberly
Signature

May 16 2021
Date

Bucknell
UNIVERSITY

STUDENT PROJECT RELEASE

By accepting student project results you agree with the following:

I agree that the results reported are for information purposes only, and are not guaranteed by Bucknell University, including the faculty and students involved with the Project.

I will not use the name of Bucknell University, nor of any faculty, staff or student involved with the Project, in any publicity, advertising, applications, or news releases without prior written approval of an authorized representative of Bucknell.

I understand that this was a student project only, and that Bucknell University gives no assurances, promises, or representations with respect to the applicability of the study data or conclusions for any particularized use. Bucknell disclaims and does not warrant in any way that the information contained in this project or its results are merchantable or fit for any particular use of any prospective use.

I also understand that the results of student projects should be reviewed and approved by a professional engineer, at Geisinger Health System's expense, before these results may be used for the (describe the project outcome – e.g. for clinical use, for validated results for patient training, etc.). No test results or certifications from Bucknell shall be in any way associated with the (project outcome).

I Lydia J Kappelmeier, Student
Name Title

am the authorized representative for Geisinger Medical Center and understand and I agree to the above statements.

Lydia J Kappelmeier 5-16-21
Signature Date

Bucknell
UNIVERSITY

STUDENT PROJECT RELEASE

By accepting student project results you agree with the following:

I agree that the results reported are for information purposes only, and are not guaranteed by Bucknell University, including the faculty and students involved with the Project.

I will not use the name of Bucknell University, nor of any faculty, staff or student involved with the Project, in any publicity, advertising, applications, or news releases without prior written approval of an authorized representative of Bucknell.

I understand that this was a student project only, and that Bucknell University gives no assurances, promises, or representations with respect to the applicability of the study data or conclusions for any particularized use. Bucknell disclaims and does not warrant in any way that the information contained in this project or its results are merchantable or fit for any particular use of any prospective use.

I also understand that the results of student projects should be reviewed and approved by a professional engineer, at Geisinger Health System's expense, before these results may be used for the (describe the project outcome – e.g. for clinical use, for validated results for patient training, etc.). No test results or certifications from Bucknell shall be in any way associated with the (project outcome).

I Anurag Vaidya, Student
Name Title

am the authorized representative for Geisinger Medical Center and understand and I agree to the above statements.

anurag vaidya
Signature

May 16th 2021
Date

Acknowledgements

This work was supported by the Joseph A. Ciffolillo Healthcare Technology Inventors Program, the generosity of Robert (`62) and Florence Chertkoff, and the Department of Biomedical Engineering at Bucknell University.

The Design Team also recognizes and appreciates the continual support provided by Dr. Aalpen Patel (Geisinger Medical Center, Danville, PA) and Dr. Karlo Malaga (Bucknell University, Lewisburg, PA). The team appreciates the additional guidance provided by Bucknell University's Biomedical Engineering faculty members, namely Dr. Eric Kennedy, Dr. Donna Ebenstein, and Dr. Daniel Cavanagh. For initial solution development, the Design Team received significant help from Thomas Thul (Director of Biomedical Engineering Laboratories). Finally, the team would like to thank the Project Development Lab (PDL) at Bucknell University for their continued support in manufacturing various iterations of the prototype. The Design Team appreciates their time and effort.

Background

Each year, approximately 43,000 people are diagnosed with liver cancer in the United States. Hepatocellular carcinoma (HCC) is the most common form of liver cancer, and tumor resection is often the first avenue of treatment for HCC [1]. However, less than 29% of patients with HCC qualify and have the physical condition to withstand resection, an invasive surgical procedure [2]. As an alternative, radiofrequency ablation (RFA) is a minimally-invasive procedure that uses high-frequency current to heat and kill small tumors (< 5 cm in diameter). Because RFA is minimally-invasive, necessary post-operative care and hospital stay is reduced. Due to these advantages, nearly 44.9% of liver cancer patients are treated with radiofrequency ablation [3].

However, due to the technical limitations of current RFA probes, not all liver tumors can be treated with RFA. Current probes can only generate spherical ablation zones. Shape mismatch between spherical ablation zones and non-spherical tumor geometries may lead to excessive healthy tissue necrosis as well as incomplete tumor ablation. Moreover, if the probe is inserted off-center into the tumor, the probe must be removed from the tumor and reinserted, risking bleeding, to avoid off-target and incomplete tumor ablation. Tumors near critical tissues such as portal veins and organs cannot be treated with RFA due to the risk of over-ablation caused by spherical ablation zones. As a result, these probes do not properly ablate non-spherical tumors, and treatment is limited to centrally-located liver tumors less than or equal to 5 cm in diameter. To increase the efficacy and acceptance of RFA as a treatment option for patients with small liver tumors, a novel radiofrequency ablation probe was designed and fabricated to **give interventional radiologists more control over the size and shape of ablation zones.** This technology reduces the risk of complications associated with RFA and increases the number of patients that can benefit from this minimally-invasive procedure.

Project Objective Statement

A differential tine deployment mechanism for RFA probes was developed to grant physicians the ability to modify ablation zone shape after probe insertion into the patient. Current probes can only deploy tines uniformly, resulting in spherical ablation zones. In differential deployment, tine groups can be deployed to different lengths, enabling the generation of customized and non-spherical ablation zones. Via differential deployment, ablation zones can be matched to the unique shape of each tumor. This innovation personalizes treatment based on the tumor shape and reduces the risks of complications associated with shape mis-match between ablation zones and tumors. Overall, the differential probe will confine damage to targeted tissue and decrease the rate of partial tumor ablation. An RFA probe with a plunger that supports differential tine deployment was designed and fabricated. Unlike current probes, which only have 1 plunger, the differential probe contains 4 plungers, each which controls the deployment of 3 tines. These plungers can be pushed separately from one another to create different tine arrays. Compared to current RFA probes, like Boston Scientific's LeVeen Needle Electrode, the differential probe supports both spherical and non-spherical tine arrays while maintaining the device's small size and weight (Table 1).

Table 1: Specifications of the prototype Differential Probe and the LeVeen Needle Electrode.

	Differential Probe	LeVeen Needle Electrode
Number of Tines	12	12
Cannula Gauge	11.5	12.5
Weight (g)	15.3	14.9
Maximum ablation radius (cm)	5	5
Customize Ablation Size	YES	NO
Customize Ablation Shape	YES	NO

Design Documentation

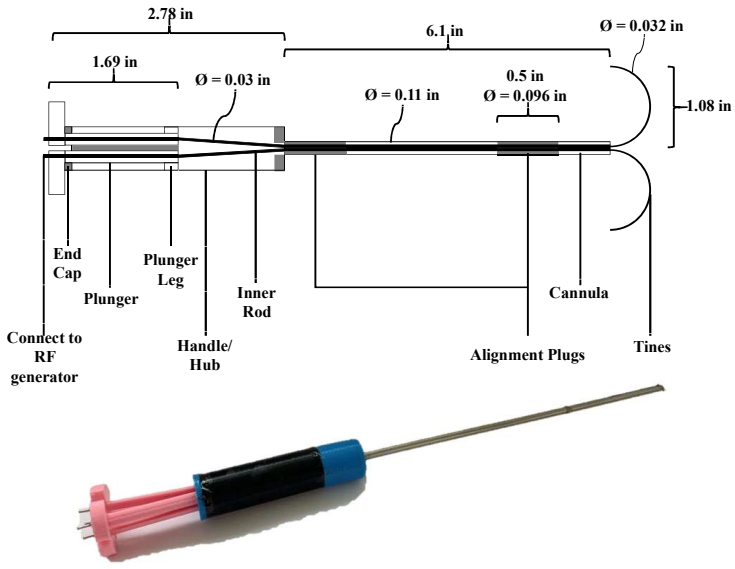


Figure 1: Prototype schematic (top) and real-life prototype (bottom)

The differential probe consists of seven components: the plungers, handle, end cap, cannula, alignment plugs, inner rods, and tines. (Figure 1, 2D). For rapid prototyping, the plunger and handle are currently composed of 3D-printed polylactide, although polyethylene, a common medical plastic, may be used to fabricate these parts in the future. The cannula consists of stainless steel, a common non-cytotoxic metal used in medical devices. These components are now presented.

The plungers control tine group deployment: 4 plungers each control a set of 3 tines (Figure 2A). Each plunger consists of a cap that the user pushes on to set deployment length, a through hole that holds an inner rod, and a "leg" that prevents the plunger from being pulled out of the handle by hitting the end cap which is attached to the handle. There are also spacers that clip onto the plungers and hold the plungers in place during the procedure (Figure 2C).

During the procedure, the user holds onto the device handle. The handle consists of 4 compartments, each of which hold 1 plunger. Separate compartments ensure that each plunger moves independently from the other plungers. To hold the 4 plungers, the handle is marginally longer (by 2%) and wider (by 15%) than the dimensions of the LeVeen Needle Electrode. In future iterations of the differential probe, a rubber grip will be added to the outside of the handle to make it easier for the user to hold. The handle is also connected to the cannula. The end cap is attached to the end of the handle by epoxy.

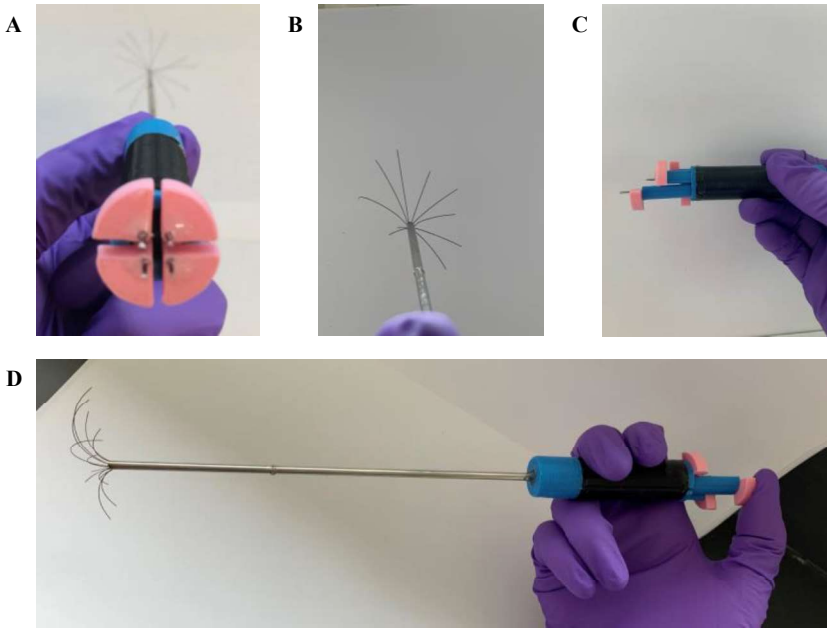


Figure 2: (A) Four plungers, with each one controlling three tines (B) Differentially deployed tines (C) Spacers holding plungers at different levels (D) Full probe

The other end of the cannula is cut at a 45° angle, increasing the ability of the cannula to pierce tissue. The cannula is inserted into the patient to deliver the inner rods and tines to the target location. To reduce tissue damage during insertion, the cannula's outer diameter was selected as 11.5 gauge, or 0.29 cm. This diameter is 10% larger than the LeVeen Needle Electrode's cannula (12.5 gauges), an increase in size

that is required to hold the probe's alignment plug. The resin-based alignment plug aligns the plungers and inner rods, ensuring that the inner rods do not twist in the cannula. It is 1.27 cm in length, 0.23 cm in diameter, and has 4 through holes, each of which holds 1 inner rod. In the future, computer numerical control machining may be used to manufacture a smaller plug, reducing the size of the probe's cannula.

Passing through the entire length of the probe, the inner rods link the radiofrequency generator to the tines. Each rod consists of stainless steel hypodermic tubing with an inner diameter of 0.05 cm. From the plungers, the inner rods connect to the generator. At the other end, 3 tines are inserted and fixed in place. The tines are separated by a 30° angle. The tines propagate radiofrequency current into the tumor to heat and kill tissue. The tines consist of a nickel-titanium alloy, or nitinol, which can be shape-set via heat treatments. For the device, 0.25 mm diameter nitinol wire was shaped into semi-circles with a diameter of 2.5 cm.

These components work in tandem during ablation procedures (Figure 2). Before surgery begins, the probe is connected to the radiofrequency generator via the inner rods. Images guide cannula insertion through the patient's body and to the tumor. The interventional radiologist determines how to deploy the tine groups. The appropriate plungers are pressed, deploying the tines. Once the tines are in place, the generator is turned on, and current flows through the inner rods and tines to heat and kill the tumor. Once ablation is complete (proportional to size of the tumor, but on average 15-20 minutes), the plungers and tines are retracted. The probe is removed and discarded.

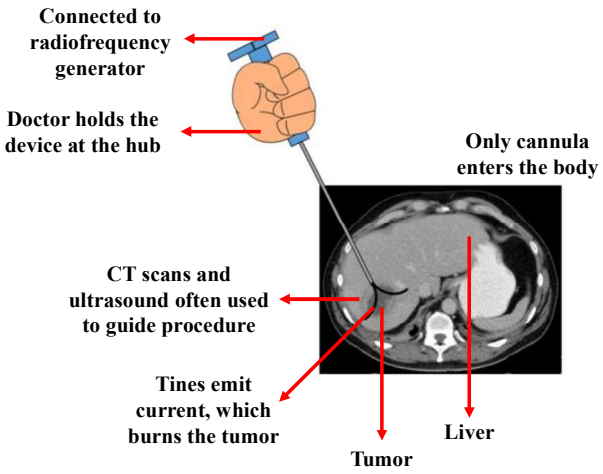


Figure 3: How different parts of the clinically ready device are used

Verification Testing

To evaluate the performance of differential deployment probes, three tests were developed: a finite element (FE) model of tumor ablation, an experimental model of beef liver ablation, and an experimental agar-based liver phantom to test probe deployment.

FE models of liver and tumor tissue ablation were developed to demonstrate that differential deployment could create non-spherical ablation zones. An existing COMSOL FE ablation model [4] was modified to match the proposed dimensions of the differential deployment probe. Three cases were modeled: centered ablation in a spherical tumor, off-centered ablation in a spherical tumor, and ablation in a non-spherical tumor. Ablation zones of both conventional and differential probes were modeled. In the case of centered ablation in a spherical tumor, the differential probe functions like the conventional probe by deploying all tines uniformly. In the cases of off-centered ablation in a spherical tumor and ablation in a non-spherical tumor, the tine array of the differential probe can be changed to restrict damage to the tumor, while the conventional probe would cause excessive damage to healthy tissue (Figure 3).

These models show how the differential probe's tine array can be adapted to the unique characteristics of each procedure. To validate the computational models of non-spherical ablation zones arising from differential deployment, a soldering-iron ablation probe was built and used to generate symmetric and asymmetric ablation zones in beef liver (Figure 5). This mechanism was used instead of the inaccessible radiofrequency generator. All tines were 2.49 cm in diameter. In the symmetric deployment

condition, both tines were 3.05 cm long. In the asymmetric deployment condition, one tine was 1.53 cm long while the other was 3.05 cm long. Forward Looking Infra-Red (FLIR) thermal imaging guns were used to visualize the ablation zones' temperature gradients. These heat maps as well as visual inspection of the beef livers after ablation show that ablation zone shape is dependent on tine array shape. (Figure 4). Additionally, the ablation zone diameter in the x and y directions was measured in ImageJ. For the symmetric deployment condition, the average x-diameter was 3.81 ± 2.29 cm, and the y-diameter was 3.05 ± 1.27 cm, showing that the ablation zones were approximately circular in shape. For the asymmetric deployment condition, the diameter of the ablation zone arising from the fully deployed tine measured to be 2.29 ± 1.02 cm and the ablation zone of the half-deployed tine was 1.04 ± 0.70 cm, indicating an aspherical ablation zone. Thus, these tests validated the computational models and showed that ablation zone shape is dependent on tine array shape.

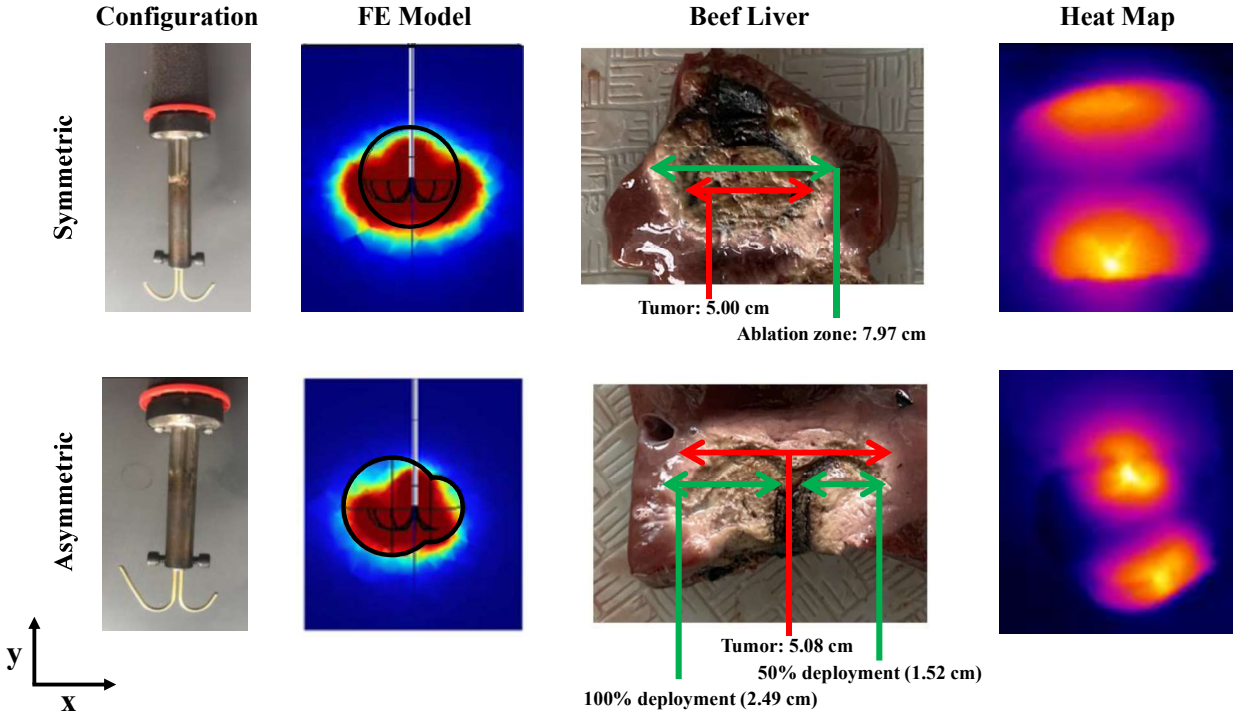


Figure 4: Symmetric and asymmetric configurations created to validate COMSOL FE models

Differential probe deployment in tissue was assessed and compared to LeVeen Needle Electrode deployment (for details refer to Appendix K). Agar-gel liver phantoms were prepared using recipes described in Dabbagh et. al. [5]. To increase the stiffness of the phantom tumor, the recipe was refined to contain 1.6% w/w agar and 3% w/w sucrose. Centered and off-centered deployment was assessed in spherical 5 cm and 3 cm diameter tumors as well as in a non-spherical 5 cm diameter tumor to test the ability of the probes to adjust to different tumor and insertion conditions (Figure 5, 6). The tine array of the differential probe could be modified to match different conditions, which would reduce the risk of partial tumor ablation and minimize damage to healthy tissue. For off-centered deployment in the 3 cm tumor, 2 tine groups were fully deployed, and 2 tine groups were quarter-deployed to cover the tumor region. For centered deployment in the 3 cm tumor, all tines were half-deployed to avoid unnecessary tissue penetration. During deployment in the non-spherical tumor, 1 tine group each was deployed 100%, 75%, 50%, and 25%. All tines were fully deployed in the 5 cm tumor. The tine array of the LeVeen Needle Electrode could not be modified, leading to increased risk of incomplete ablation and healthy tissue necrosis during off-center probe insertion and non-spherical tumor ablation.

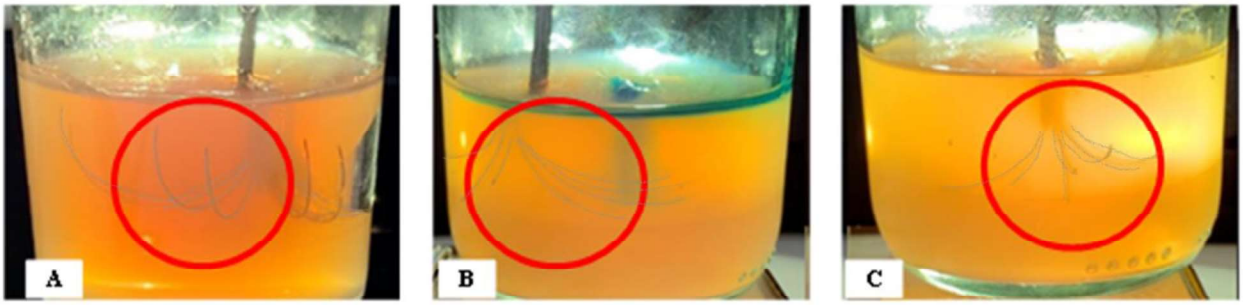


Figure 5: 3 cm tumor. **(A)** Off-centered deployment, LeVeen probe **(B)** Off-centered deployment, differential probe **(C)** Centered deployment, differential probe.

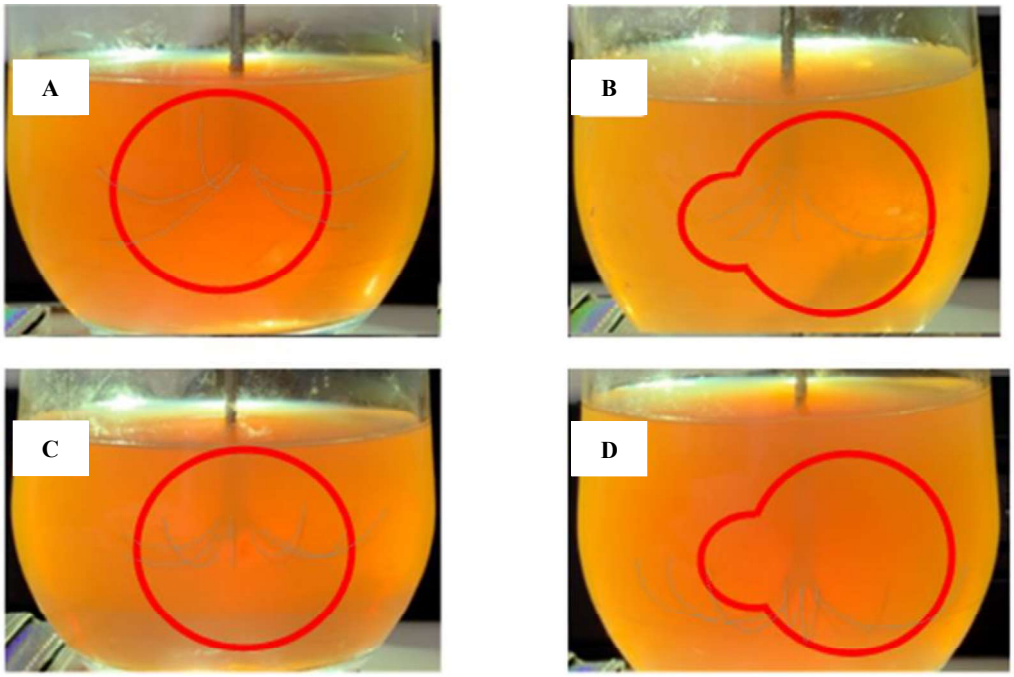


Figure 6: 5 cm tumor **(A, C).** Non-spherical tumor **(B, D). (A)** Spherical, differential probe. **(B)** Non-spherical, differential probe. **(C)** Spherical, LeVeen probe. **(D)** Non-spherical, LeVeen probe.

A major limitation of the *ex vivo* feasibility test is that no radiofrequency current was passed through the probe; instead, the probe itself was heated to create the ablation zones. In the future, laser welding will be used to connect the inner rods to the tines, creating a conducting path for the current. The tine attachment locations will be refined so that all tines completely retract into the cannula. Finally, the tines will be made stiffer and thicker so that tumor tissue can be penetrated without any tine buckling.

In all, to create non-spherical and customizable ablation zones, the Design Team developed a novel technology, the differential probe. While the probe is inspired from the LeVeen needle, significant changes were made in order to allow the user to individually control the tines, and thus acquire more spatial control over the ablation zones. The efficacy of the differential probe was shown through computational modelling, *ex vivo* testing, and agar gel deployment. The solution is a critical advancement as it can lead to better ablation results while maintaining the ease of use provided by the predicate LeVeen needle.