

# PHANTOM FOR MICROWAVE ABLATION DEVICE TESTING

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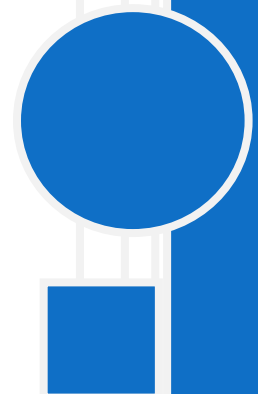
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Client: Dr. Chris Brace

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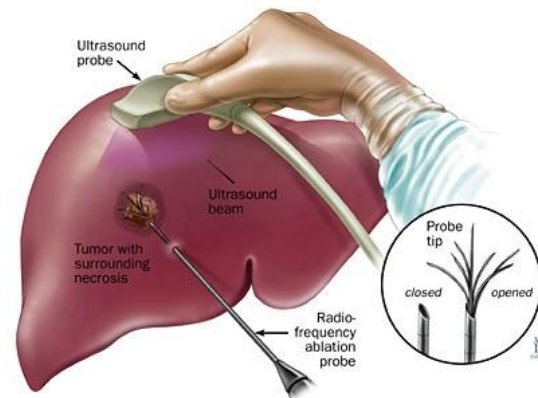
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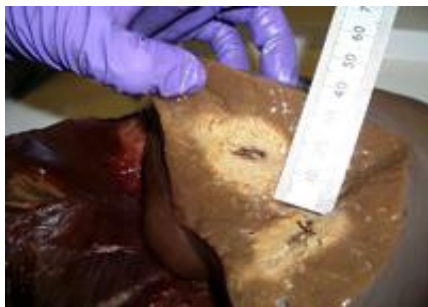
## PROBLEM STATEMENT

Microwave ablation is a medical treatment for many abdominal cancers in vivo. Thin antennas positioned in the tumor cells deliver microwave energy to destroy the tumor cells as seen in Figure 1. This method has achieved some clinical success; however, improved devices and ablation techniques are in demand. The current tissue models are heterogeneous and inconsistent and impede device development. Dr. Brace is currently developing new ablation devices and desires a reliable medium to test his innovations. Our collective goal is to create a phantom for microwave ablation that is nearly transparent, mirrors the dielectric and thermal properties of a liver, and provides visual identification of ablation zones.



**Figure 1: Microwave Ablation Diagram<sup>1</sup>**

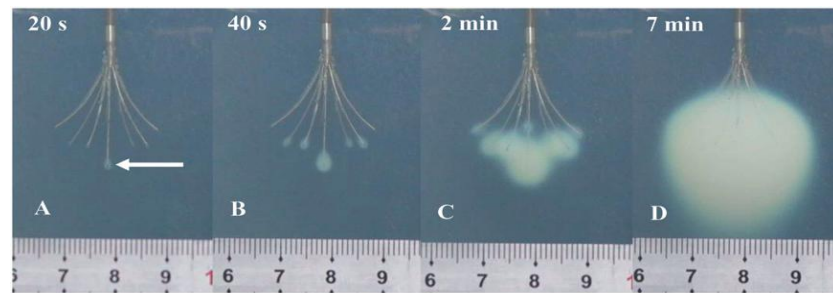
## BACKGROUND INFORMATION



**Figure 2: Ablated Liver Tissue<sup>3</sup>** The current methods for testing microwave ablation are insufficient to advance the use of microwave ablation. One method currently used is to test microwave ablation on excised tissues from porcine, canine, bovine, and even human livers<sup>2</sup>. Although these tissues possess ideal properties, they are not always readily accessible and are not reusable. According to the client, the liver tissues have a very short shelf life and the

properties substantially change over time. In addition, these livers must be cut open to observe and measure the ablation zone.

Other methods of testing, including gel phantoms, are used for other types of ablation. A polyacrylamide gel phantom has been used with bovine serum albumin (BSA) for ultrasound studies<sup>4</sup> and for radiofrequency ablation<sup>5</sup>. Figure 3 shows the ablation zone over time in a polyacrylamide gel phantom for radiofrequency ablation. These materials, however, do not



**Figure 3: RF ablation zones in polyacrylamide gel<sup>4</sup>**

mimic liver properties at the high frequency associated with microwaves. Also, a biomaterial consisting of TX-150, polyethylene powder, water, and sodium chloride exists, but would melt during microwave ablation<sup>6</sup>. By learning from these previous models and performing extensive research, a liver phantom will be constructed that will work for microwave ablation.

	Units	Liver
Relative permittivity	F/m	43.3
Effective conductivity	S/m	1.68
Wavelength	Cm	1.8
Thermal conductivity	W/m K	0.564
Density	kg/m <sup>3</sup>	1050
Specific heat capacity	J/kg K	3600
Perfusion rate	ml/min kg	1000

**Table 1: Tissue Properties of the Liver at 37°C, 2.45 GHz<sup>7</sup>**

To accurately portray the microwave ablation of the liver, the microwave phantom must mimic the properties of the liver. Table 1, adapted from Brace et al<sup>7</sup>, displays all of the properties the microwave phantom should portray. However, even with careful consideration it may be very difficult to mimic all of the desired properties of the liver. According to our client, the most vital properties of the liver include the dielectric constant of 43.3 and conductivity of  $1.7 \pm 0.2$  Siemens per meter.

## CLIENT SPECIFICATIONS

Our client, Dr. Brace, seeks to find a phantom liver that he can use for microwave ablation device testing. It is important to note that it does not need to model the appearance of the liver, but just the properties. The important qualities Dr. Brace requests is that the permittivity of the phantom should be  $45 \pm 5$  Farads per meter (F/m) and conductivity  $1.7 \pm 0.2$  Siemens per meter (S/m). Ideally, the phantom liver would be transparent until subjected to a 2.45 GHz microwave frequency ablation and then clearly indicate the ablation zones when the temperature exceeds the threshold of  $50^{\circ}\text{C}$ . The liver phantom must mimic the qualities of the liver and be able to withstand high temperatures from 160 to  $180^{\circ}\text{C}$  without melting or deforming. Ideally, the phantom would be reusable, but if it is not, it must be easy to assemble for quick use. The phantom must be cost effective. The total cost must be within \$20 to \$30 for a onetime use phantom. Overall, the client requests the phantom to be reproducible, cost effective, homogenous, ideally transparent, have similar conductivity and permittivity to that of the liver, and clearly marks the ablation area. A detailed PDS is attached in Appendix C.

## BRAINSTORM DESIGN

### Base Gels

When discussing the design with our client, a large emphasis was placed on the ability to observe the formation of the ablation zone; thus when researching base gels, only transparent gels were considered. In addition, for operational safety, the gel must have a high melting point as to not deform or melt when subjected to microwave ablation. Based upon these main specifications and a throughout literature search, the following four compounds were chosen: dielectric silicone gel, poly(vinyl alcohol), sodium alginate, and polyacrylamide gel.

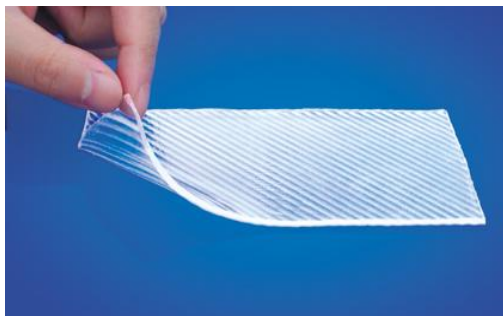


Figure 4: Silicone gel<sup>9</sup>.

Due to its known transparency and widespread use in biomedical applications, silicone was considered as a potential base gel. After further research, silicone gels were found to have high melting points with desirable densities and even dielectric properties. Due to availability of information and

price, the Dow Corning® 3-4170 Dielectric Silicone Gel Kit was selected; a sample was ordered (See Appendix A). According to the company's website, the product is a two part kit; when both components are mixed together the resulting gel is thermosetting and stable at high temperatures<sup>8</sup>.

Valued for its elasticity and high tensile strength, poly(vinyl alcohol) (PVA) is used to produce breast, blood vessel, and brain phantoms<sup>10,11</sup>. Stock PVA exists in a white crystalline powder form. The solid PVA is mixed with water and a miscible organic solvent (commonly ethanol, methanol, or dimethyl sulfoxide) and froze which allows the PVA to crystallize. The final product is a hydrogel (a gel made from water but not soluble in water due to crosslinking) with high optical transparencies and melting points<sup>10,11,12,13</sup>.



**Figure 5: Poly(vinyl alcohol) hydrogel<sup>14</sup>.**



**Figure 6: Sodium alginate hydrogel<sup>17</sup>.**

Extracted from brown algae, sodium alginate is an organic thickening and emulsifying agent that is commonly used in textile production, food processing, and dental impressions. An aqueous solution of sodium alginate forms a hydrogel when mixed with an aqueous solution of calcium ions via crosslinking; however, the gelation kinetics is difficult to control and can result in heterogeneous gels<sup>15</sup>.

Polyacrylamide gels are commonly used in gel electrophoresis and thus possess the desirable transparency and electrical conductivity characteristics. Many phantoms, including liver phantoms, are made from polyacrylamide gel. These gels, however, have low melting points and melt when subjected to the high temperatures associated with microwave



**Figure 7: Polyacrylamide gel<sup>18</sup>.**

ablation. According to Zhang et al<sup>5</sup>, a mixture of polyacrylamide and BSA mimics the properties of the liver for radiofrequency ablation; considering this potential, the recipe could be modified to mimic the liver under conditions of microwave ablation<sup>5</sup>. Our client, Dr. Brace, was unhappy with the low melting point but suggested this manipulation as the basis of our research.

## Indicators

Clear indication of the ablation zone is one of the client's specifications. When brainstorming, two different materials, proteins and thermochromic dyes, were pursued as the ablation indicator.

### Thermochromic Dyes

The word "thermochromic" means changing color in response to temperature. The prefix "thermo-" means temperature, and the root "chrom-" means color. During the brainstorming process, thermochromic dye, or pigment, was considered as an option for potential indicator. When the ablation temperature reaches the critical point of the color pigment, it transfers from a lighter color to a darker color, and thus provides a visual cue of the ablation zone in the liver phantom.



**Figure 8: Commercial application reversible thermochromic dye<sup>19</sup>.**

There are two types of commercial thermochromic dyes. One kind is a permanent thermochromic pigment, which changes color permanently once the critical temperature is reached. The other kind is a reversible thermochromic pigment, which changes back to its original color as the temperature cools down below the critical point. Most of the thermochromic products available in the market

use the permanent pigment, because it is significantly cheaper than the reversible type<sup>20</sup>.

The thermochromic pigment is widely used in scientific research, industrial manufacturing, petroleum monitoring, and even military equipment. The application of these products is highly specialized. The pigment usually can be customized to have a desired color and specific critical point. The range of the temperature change, according to HallCrest LCR, can

vary between  $-40$  to  $2000^{\circ}\text{C}$ . The color could be customized from colorless to black, depending on the application<sup>18</sup>. Therefore, it is a rather convenient technique to monitor temperature. The price of the permanent thermochromic dye, according to the company METLAST, varies from \$26 to \$60 per pound, depending on the level of specialization. The reversible type costs a lot more and it is currently not available in the United States due to the Environmental Act. Therefore, it is entirely limited on the supplier import. The overall price of one kilogram customized reversible dye can cost up to \$12,500.

The advantages of applying the permanent thermochromic dye in our application are to lower the cost of using expensive proteins and to create a distinct ablation zone. The dye, however, is very sensitive to its environment; thus, its properties may change when mixed with other substances in the phantom. Also, these dyes are metallic based and may have an adverse affect on the dielectric properties of our phantom as a whole. The reversible thermochromic dye would allow us to produce a reusable phantom for long-term usage. However, the extremely high cost of the reversible dye prevents us from pursuing this idea.

## Proteins

In our search for visual indicators, proteins were discovered that would denature and aggregate to highlight the ablation zone. Our research focused on two specific proteins: bovine serum albumin (BSA) and ovalbumin.

Bovine serum albumin is a protein that was used in a phantom for radiofrequency ablation testing, created by Zhang et al<sup>9</sup>, detailed earlier in the background section. This protein is initially transparent in the phantom solution but when sufficiently heated, it coagulates into a white opaque color. This allows the ablation zone to be easily observed and measured without dissecting the phantom. BSA denatures at a temperature slightly above  $70^{\circ}\text{C}$ , which is higher than the desired temperature of  $50$  to  $60^{\circ}\text{C}$  to best mimic the ablation of liver tissue<sup>5</sup>. This coagulation temperature, however,

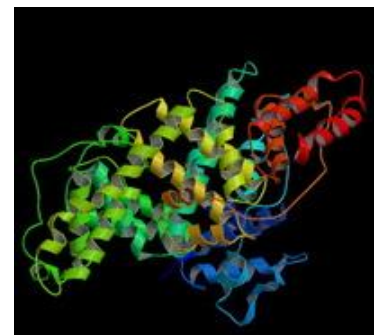


Figure 9: Quaternary structure of BSA <sup>25</sup>



was reduced to the desired temperature range by decreasing the pH of the phantom to around 4.3. This decreased pH can be achieved by adding a citrate acid buffer to the phantom solution<sup>5</sup>.

In addition to effectively highlighting the ablation zone, a protein like BSA may help the dielectric properties of the phantom mimic that of an actual liver. BSA has some physical properties, such as specific heat capacity, that are similar to the human liver<sup>5</sup>. This could improve the usefulness of the liver phantom as an accurate substitute for human tissue during testing. One negative aspect of using BSA is that it is relatively expensive. The company, BIOTANG is selling 250g of lyophilized BSA powder for \$216.00<sup>21</sup>. If we use 20g per sample, as suggested by Zhang et al<sup>5</sup>, the BSA alone would cost \$17.28 per phantom. This price is high for onetime use phantoms. However, besides its cost, BSA is a tested method that could prove to be an effective indicator for the liver phantom.

Another protein we research is ovalbumin, which is the major protein found in egg whites. It is common knowledge that egg whites go from a transparent state at room temperature to an opaque white color as heated. This is due to the coagulation of denatured ovalbumin, much like the coagulation of BSA mentioned earlier. The coagulation temperature for ovalbumin is 80°C at a pH of 7.5<sup>22</sup>. This temperature is substantially greater than the desired ablation zone temperature; however, lowering the pH should lower the coagulation temperature substantially. This assumption was made assuming that ovalbumin would behave similar to BSA when the pH is changed. This will have to be investigated later during our prototype development.

An advantage of ovalbumin is the relatively low cost of egg whites. Concentrated ovalbumin can be quite expensive; however, egg whites can be extracted from eggs purchased at the local grocery for a couple dollars per dozen. For our purposes, egg whites have the same desired properties as concentrated ovalbumin and they are much more readily available. Egg whites are an organic material largely composed of proteins, and therefore should have dielectric properties that are relatively similar to that of a liver, much like the properties of BSA mentioned earlier.

## DESIGN MATRIX

### Base Gel

Weight	Design Aspects	Dielectric Silicon Gel	Polyvinyl Alcohol	Sodium Alginate	Polyacrylamide Gel
0.2	Melting Point	8	10	9	3
0.2	Transparency	10	9	9	8
0.2	Dielectric Properties	8	6	5	8
0.15	Cost	5	9	7	7
0.05	Safety	9	6	8	3
0.05	Shelf Life	9	4	4	6
0.15	Assembly Simplicity	8	5	7	4
1	–	8.05	7.6	7.3	5.9

**Table 2: Base Gel Design Matrix**

As seen from Table 2, the four choices for base gels – dielectric silicone gel, poly(vinyl alcohol), sodium alginate, and polyacrylamide gel – were evaluated based upon their melting point, transparency, dielectric properties, cost, safety, shelf life, and assembly simplicity. Of these categories, melting point, transparency, and dielectric properties were weighted highly because these criteria are critical to the function and usefulness of the base gel. Of note, no literature was found to verify the dielectric properties of these gels at the desired frequency; thus gels were ranked upon its perceived ease of dielectric manipulation. Cost and assembly simplicity were also ranked relatively high because these were important to our client.

Shelf life was given a low weight because after initial research it was unlikely that a reversible phantom would be made (see explanation of indicators to follow) and thus a single-use phantom needs to be stable over a much shorter time than that of a reusable phantom. Similarly, safety was given a low ranking because the phantom was defined to be non-

hazardous thus extremely dangerous reagents were not considered. Although the actual properties of the gel are based upon all components, the gels were ranked based upon data from the manufacturer or from literature.

The dielectric silicone gel (Dow Corning® 3-4170 Dielectric Silicone Gel Kit) ranked the highest of the four base gel options<sup>8</sup>. According to the manufacturer, the transparent green silicone gel is stable up to 150 °C with a working time of 12,960 minutes and a shelf life of 365 days; thus, the transparency, melting point, and shelf life categories were ranked very high. Although the dielectric properties were not provided for the desired frequency, the gel ranked high in the dielectric category because it has satisfactory dielectric character at 100 kilohertz. The gel ranked high in the safety and assembly simplicity categories because it is a product of mixing two non-hazardous compounds. The gel, however, has a relatively high cost of \$199.75 for 7.2 kilograms<sup>8</sup>.

Due to its high melting point, high transparency, and low cost (as it is a relatively standard lab reagent), poly(vinyl alcohol) ranked second. Its porous nature, however, is very susceptible to molding and, even when stored in water, has a shelf life of only a week. In addition, preparation takes place over a 24-hour period, and gel must be subjected to temperatures as low as 20 °C and as high as 60 °C. Furthermore, transparent gels must be submerged in water to remove all excess organic solvent; it may cause a biohazard if the organic solvent is not removed completely<sup>10,12</sup>. This process is not only tedious, but also may alter the properties of an indicator dye and influence the dielectric properties. Therefore, low ranks were given for safety and shelf life.

The sodium alginate gel is an alternative to the poly(vinyl alcohol). It has a similar melting point, transparency, dielectric properties, cost, and shelf life<sup>16</sup>. The gels, however, vary in their safety and assembly simplicity. The sodium alginate is an organic substance that gels at room temperature in the presence of calcium ions; therefore, it is a relatively safe and easy to produce compound. The poly(vinyl alcohol), as discussed earlier, requires extreme cold to form a gel and therefore is less safe and more difficult to produce.

The polyacrylamide gel scored the lowest out of the four gel choices. Although transparent, it has many unfavorable characteristics including: low melting point, less

transparency, high cost (due to multiple ingredients), hazardous starting materials, low shelf life, and poor assembly simplicity<sup>5</sup>.

## Indicator

Weight	Design Aspects	Albumin (Bovine Protein)	Ovalbumin (Egg White)	One Time Use Dye	Reversible Thermochromic Dye
-	Reversible	No	No	No	Yes
.20	Accuracy	10	6	8	8
.20	Cost	3	9	7	1
.10	Preparation	9	7	9	9
.25	Effectiveness	10	10	7	7
.15	Dielectric Properties	8	8	3	3
.05	Safety	10	10	6	6
.05	Shelf Life	7	7	10	10
1	-	8.05	8.25	6.9	5.3

**Table 3: Indicator Design Matrix**

As seen in Table 3, the preliminary indicator options were compared on a scale of 1-10 based off of a variety of weighted design criteria. Effectiveness was weighted the highest because the number one priority of the indicator is to clearly identify the ablation zone. The two proteins scored well in this area because BSA was effectively used in the phantom made by Zhang et al<sup>5</sup>, and ovalbumin was assumed to have similar qualities. The two dyes scored slightly lower because we were told by the manufacturer that these dyes are fairly sensitive to their environments and their thermochromic properties may change depending on the substance they are mixed with.

Accuracy was also weighted highly in the matrix because the indicators need to highlight the ablation zone at the desired temperature range (50 to 60 °C). BSA again received a high score because it was shown to denature at a temperature of 50°C in a previous phantom<sup>5</sup>.

Ovalbumin scored relatively poorly because it has a coagulation temperature of 80°C. However, decreasing the pH value could potentially reduce this temperature. Another criterion that was weighted highly was the cost of the indicator. BSA scored low in this category but the reversible dye scored by far the lowest due to the substantial overseas shipping cost. After calculating the scores for each indicator, egg white received the highest score and was chosen as the indicator for our prototype.

## FINAL DESIGN

For our final design we decided to combine the base gel and indicator that scored the highest in the design matrixes. Therefore, moving forward we will work to fabricate and test a phantom made of silicone gel and egg whites.

## ALTERNATIVE DESIGN

### IR Camera

An alternative design is to use a thermal camera to serve as a temperature monitor during the microwave ablation process. A thermal camera detects temperature changes of an object without contact. The most common type is the Infrared (IR) camera, which captures infrared radiation to form an image of the object<sup>23</sup>. Applying an IR camera in our design can avoid the complication of mixing different components without interrupting properties of each other. In addition, an IR camera can allow the use of opaque phantoms with material properties that better mimic the liver. It is reusable and convenient. Also, it is readily available in the university physics lab; therefore, an IR camera would not need to be purchased for initial testing.

The drawback of using the IR camera is the limited detection depth, as it usually only detects the temperature on the surface of an object<sup>23</sup>. The overall size and shape will need to be modified in order to fit the detection depth criteria of the thermal camera. Since microwave ablation traditionally occurs deep within the liver tissue, testing the devices at the surface of the phantom introduces many variables including but not limited to the effects of the thermal



Figure 10: Nikon Thermal Camera

conductivity of the large surface area and the hindered analysis of the true size of ablation zones over time.

## Alternative Material Combinations

In addition to the final design, sample materials have been ordered for design alternatives to allow for further testing and to provide a fall back design, should the current design fail to meet the client's standards. See Appendix A and C for images of the sample base gel and thermochromic dye.

Besides ovalbumin, the following indicators could also be tested:

1. Whey protein.

It is a cheap, but not homogeneous protein mixture. The temperature at which whey protein denatures is closer to that of the liver (55 °C). Also, a recipe exists to make transparent liquid form from opaque whey protein<sup>24</sup>. This whey protein, however, requires long preparation time.

2. Albumin (BSA).

The albumin proved to be suitable indicator when tested in a phantom for radiofrequency ablation<sup>5</sup>. Therefore, if the cost can be mediated, BSA could prove to be an excellent indicator.

3. Permanent Thermochromic dye

The permanent thermochromic dye ordered from Hallcrest LCR<sup>®</sup> has a critical temperature of 55°C, which is close to the desired denaturation temperature of liver proteins. Also, it provides a drastic color change once the critical temperature is reached.

Besides the silicon-based gel, the following base gels can also be tested:

1. Poly(vinyl alcohol) base gel

It is readily available in the lab and is used in other phantom designs. It also has a relatively high melting point. Therefore, it serves as an alternative choice for a base gel.

## **FUTURE WORK**

First, the current final design must be tested for its effectiveness and accuracy. Ideally, data will be collected to quantify and describe the following characteristics: 1) how temperature change and visual feedback correlates; 2) duration of the ablation and indicator behavior; 3) shape and size of the ablations zone. Another important aspect of this biomaterial design project is to develop a liver phantom that mimics a human liver. Therefore, liver properties, especially the dielectric properties, are crucial to our design. The recipe will be edited at will to match the dielectric properties of the phantom to a human liver when subjected to microwaves. During our experiment, the shelf life and degradation over time will be observed as the testing proceeds.

Secondly, the alternative materials will be tested as needed. The alternative indicators and base gels may yield better combinations. Therefore, it is important to investigate all possible combinations. In addition to testing, research on base gels and indicators will continue. Our communicator will arrange meetings with other department faculty members to seek professional opinions and suggestions. This research will not only aid in the creation of the most realistic phantom but also deepen our understanding of biomaterials.

## **SAFETY AND ETHICS**

This project involves biomaterial testing, which can possibly produce hazardous products. The materials for testing, such as the permanent thermochromic dye, may cause irritation to the skin. Therefore, safety is a high priority for all group members. Datasheets for each biomaterial component will be read carefully, and hazards and proper handling technique will be noted.

Some biomaterials require individual bio-hazard disposal and may cause pollution if used in large amounts, such as the thermochromic dye. In light of the Environmental Act, the minimum amount of material will be used during testing, and the materials will be properly stored under desirable conditions (ie refrigeration of protein indicators). A record of the waste and degradation products during the experiment will be kept. The collective goal of this project is not only to engineer a prototype to satisfy the client but also to create an environmental friendly and efficient product.

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## APPENDIX A – C

### A. Picture of a base gel sample



Figure 10 – Silicon base gel sample order from Dow Corning Inn@.

### B. Permanent thermochromic concentrate sample



Figure 11 – Permanent thermochromic concentrate sample from Hallcrest LCR@.

C. Project Design Specification

**Project Design Specifications—Phantom for Microwave Ablation Testing**

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**Problem Statement:**

Microwave ablation is a medical treatment for many abdominal cancers *in vivo*. Thin antennas positioned in the tumor cells deliver microwave energy to destroy the tumor cells. This method has achieved some clinical success; however, improvements for devices and ablation techniques are in demand. The current tissue models are heterogeneous and inconsistent and impede device development. Dr. Brace is currently developing new ablation devices and desires a reliable medium to test his innovations. Our collective goal is to create a phantom for microwave ablation that is nearly transparent, mirrors the dielectric and thermal properties of a liver, and provides visual identification of ablation zones.

**Client Requirements:**

- Reproducible
- Homogenous
- Ideally transparent
- Cost effective
- Similar conductivity and permittivity to the liver
- Clearly marks ablation area

## Design Requirements:

- 1) Physical and Operational Characteristics
  - a) *Performance requirements:* The phantom must be able to withstand high temperatures without melting or deforming (160-180 degrees Celsius). It must mimic the liver when subjected to a 2.45 GHz microwave frequency. Ideal permittivity of the phantom should be  $45 \pm 5$  F/m and conductivity  $1.7 \pm 0.2$  S/m. It must distinguish ablation areas when the temperature exceeds the threshold of 50° C.
  - b) *Safety:* The phantom must not produce harmful gases or liquids when heated. No hazardous materials can be used.
  - c) *Accuracy and Reliability:* The phantom must perform consistently for repeated tests. The results need to be within a range specified by the client.
  - d) *Life in Service:* The phantom may be utilized for one time use only if readily producible. If reusable, it must remain stable and accurate while providing desired amounts of testing for cost.
  - e) *Shelf Life:* For one time use, the phantom must be able to sit refrigerated or at room temperature for one week.
  - f) *Operating Environment:* The phantom must be able to perform in standard laboratory conditions. During ablation, it must withstand very high temperatures exceeding 160° C.
  - g) *Ergonomics:* The phantom solution must be easily produced and portable.
  - h) *Size:* The phantom must be approximately the size of a human liver.
  - i) *Weight:* Weight restrictions are not specified but should be easily handled by one person.
  - j) *Materials:* The base gel will consist of the Dow Corning Dielectric Silicon Gel and the indicator will be made of ovalbumin (egg white).
  - k) *Aesthetics, Appearance, and Finish:* The phantom does not need to model after the appearance of the liver.
  
- 2) Product Characteristics
  - a) *Quantity:* Enough phantoms must be produced for tests and demonstrations.
  - b) *Target Product Cost:* Total cost must be within \$20-\$30 for several ablations.
  
- 3) Miscellaneous
  - a) *Standards and Specifications:* The phantom must mimic the properties of the liver. Thus, it must have a dielectric constant of 43.3, electrical conductivity

of 1.68 S/m, thermal conductivity of 0.564 W/mK, wavelength of 1.8 cm, density of 1,050 kg/m<sup>3</sup>, and perfusion rate of 1,000 mL/min Kg.

- b) *Customer:* Dr. Brace would like a phantom he could use to reliably determine differences in microwave ablation devices.
- c) *Patient Related Concerns:* N/A
- d) *Competition:* Microwave ablation devices are currently tested on animal livers and excised human liver tissue. Other types of gel phantoms exist, but none for microwave ablation.