Phantom for Microwave Device Testing

Tian Zhou (Team Leader), Molly Krohn (Communicator),
Andrew Hanske (BSAC), Kimberly Maciolek (BWIG)

University of Wisconsin - Biomedical Engineering Department
Client: Dr. Chris Brace
Advisor: John Puccinelli PhD

December 8, 2010

Table of Contents

1. Abstract

Microwave ablation is a cutting-edge process by which microwaves are emitted through thin antennas at 2.45 GHz to kill cancer cells through rapid heating. Our client, Dr. Chris Brace, tests new devices in bovine liver tissue; due to the opaque nature of the liver, it is very difficult to study the size of the ablation zone. In addition, the liver is only viable for a short period of time and is associated with a high cost. Therefore, a consistent, homogeneous, transparent liver phantom with a clear ablation zone indicator is needed. Different combinations of base gels – egg white, sodium polyacrylamide, silicone, sodium alginate, and poly(vinyl alcohol) – and indicators – thermo chromic dye, egg white albumin, and bovine serum albumin(BSA) – were tested. The dielectric properties, temperature of ablation, and size of the ablation zone were tested and compared to values obtained from similar tests on bovine livers. A liver phantom was created out of egg white and egg white albumin. For every egg white, 2.7grams of egg white albumin were added, and the combination was stirred gently until the protein dissolves. The phantom has a permittivity of 52.21Farads per meter (F/m) conductivity 2.25 Siemens per meter (S/m) at 2.45 GHz, an ablation temperature of 53.8^{o}C, and an ablation zone that measures 4.3 by 3.0 cm after five minutes of ablation. Further testing is still needed to verify the absolute consistency of these values; other materials may also be considered to better match the properties of the liver.

2. Introduction

2.1. 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

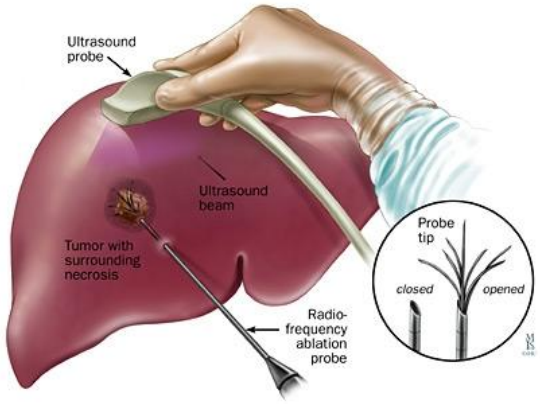

Figure 1: Microwave Ablation Diagram[1]

devices and ablation techniques are in demand. The current phantom models are heterogeneous and inconsistent. 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.

2.2. Current methods

The current testing methods are not able to show the ablation zone being formed over time. One method currently used is to test microwave ablation on excised tissues from porcine, canine, bovine, and even human livers[2]. 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, have been successfully created for other types of ablation. A polyacrylamide gel phantom has been used with bovine serum albumin (BSA) for ultrasound studies[3] and for radiofrequency ablation[4]. Figure 2 shows the ablation zone over time in a polyacrylamide gel phantom for radiofrequency ablation. These materials, however, do not 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[5]. By learning from these previous models and performing extensive research, a liver phantom was successfully constructed for microwave ablation.

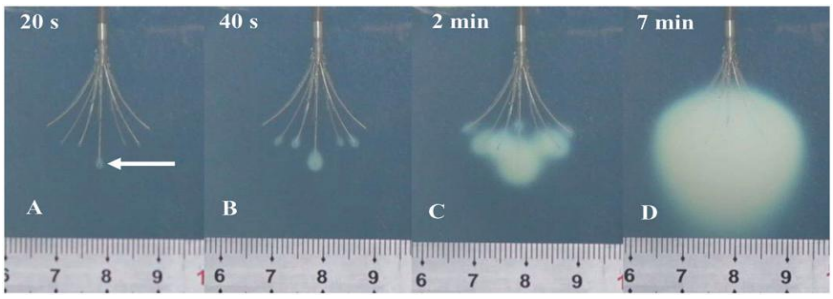

Figure 2: Photos of ablation zones over time in polyacrylamide gel phantom and radiofrequency ablation[4].

2.3. Liver properties

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[6], displays all of the properties the microwave phantom should portray. Even with careful consideration it may be very difficult to mimic all of the desired properties of the liver.

	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^3	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[6]

3. Design Specification

Our client, Dr. Brace, seeks to find a phantom liver that can be used 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 ± 5 Farads per meter (F/m) and conductivity 1.7 ± 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°C. The liver phantom must mimic the qualities of the liver and be able to withstand high temperatures from 160 to 180 °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 also 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.

4. Procedures

4.1 Materials

4.1.1 Base gels

The base gels selected for testing were dielectric silicone gel, poly(vinyl alcohol), sodium alginate, and polyacrylamide gel. The selection was primarily based on the transparency, and high melting point.

Silicone gels were found to have high melting points with desirable densities and dielectric properties. The Dow Corning® 3-4170 Dielectric Silicone Gel Kit was selected. 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[8].

Valued for its elasticity and high tensile strength, poly(vinyl alcohol) (PVA) is used to produce breast, blood vessel, and brain phantoms[8,9]. Stock PVA applied in this experiment exists in a white crystalline powder form. The PVA was prepared as in Hyon et al[10]. The solid PVA was mixed with 80% DMSO and 20% deionized water solvent solution and froze under -20^{o}C to condition to allow crystallization. The final product was a hydrogel with high optical transparencies and melting points[10,11].

The sodium alginate gel used in this experiment exists in a powder form. The 1.5% sodium alginate power was mixed with aqueous calcium carbonate solution and then aqueous glucono delta-lactone (GDL) solution. The molar ratio of sodium alginate to both calcium carbonate and GDL was 1 to 1.5. The solution was cured for 24 hours before testing. This gel was prepared as described in Kuo et al[12].

Polyacrylamide gels are commonly used in gel electrophoresis and thus possess the desirable transparency and electrical conductivity characteristics. The polyacrylamide gels were prepared from a white powder, commonly known as "Water Lock". The polyacrylamide powder dissolves in water instantly forming a gel. The density and transparency of the gel depends upon the concentration of polyacrylamide powder. The prototyping product of the polyacrylamide gel possessed high transparency with low viscosity.

4.1.2 Indicators

Clear indication of an ablation zone is an essential aspect of the phantom. Four indicators were tested: Hallcrest@ Thermo chromic pigment, bovine serum albumin, egg white albumin, and egg white.

The Hallcrest@ brand water-based thermo chromic pigment concentrate was chosen as a possible indicator. The critical temperature of this dye was between 53-59^{o}C. The color changed from cream to dark grey when subjected to its critical temperature. The color change appeared to be gradual and irreversible. In addition, the thermo chromic pigment has low viscosity and is extremely sensitive to external chemical environment. Mixing the dye with potential base gels caused unwanted complications, such as a changed critical temperature and variations in the type of color it assumed after the critical temperature.

Most importantly the dye is opaque, and therefore could not be used in any transparent phantom. For these reasons the thermo chromic dye failed as a potential indicator.

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 egg albumin (ovalbumin).

Bovine serum albumin is a protein that was used in a phantom created by Zhang et al[4] for radiofrequency ablation testing. This protein is initially a translucent crystalline solid that completely dissolves in the transparent phantom solution but when sufficiently heated, 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°C, which is higher than the desired temperature of 50 to 60°C[4]. This coagulation temperature, however, 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[4].

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[5]. 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[14]. If we use 20g per sample, as suggested by Zhang et al[5], 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 egg albumin, 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 albumin, much like the coagulation of BSA mentioned earlier. The coagulation temperature for egg albumin is 80°C at a pH of 7.522[15]. This temperature is substantially greater than the desired ablation zone temperature; however, during testing in this design process, egg albumin was found to denature around the desired range of 50°C while in egg white. Another advantage of egg albumin is its relatively low cost. Sigma Aldrich sells 250g of 62-88% pure egg albumin powder for $31.70[17].

The final indicator that was tested was egg whites. The main advantage of this option is its simplicity. Egg whites fulfill the functions of both an indicator and a bas gel. Eggs can easily be purchased from a local grocery for less than $2 per dozen, which is a very affordable price for onetime use ablations. Also, the only preparation required for making an egg white phantom is separating the egg white from the yoke.

4.2 Experimental

The Agilent Technologies® E50701C ENA Series Network Analyzer was used to test the dielectric properties of the various materials in Dr. Brace's Lab. Proper setup of the analyzer was necessary to ensure accurate data was collected. Calibration of the system required the antennae to be exposed to open (air), short (foil), and load (deionized water) circuits. The software provided 3 columns of information consisting of frequency, dielectric constant and conductivity of the material tested.

Ablation of materials utilized the Cober Muegge microwave source. A power adjust of 24.7 watts, an actual power of 50 watts, and a frequency of 2.45 GHz was used in all

experiments. Temperature readings of the material tested were observed simultaneously with the ablation. A Neoptix® Fiber Optic Temperature Sensor was attached to the antennae of the microwave source and provided digital temperature readings of the material on the computer. Accurate readings of initial, final, and ablation temperatures were obtained from digital display on the computer as well as a spreadsheet of temperatures recorded by the device. Upon visual observation of the start of ablation, the corresponding time was identified with a stopwatch and the temperature with the sensor. Ablation of all materials lasted five minutes. Dimensions of the final ablated area was analyzed with a ruler and recorded.

5. Results

5.1 Final Design

The final design of the microwave liver phantom project is a mixture of egg white and added egg albumin. The egg albumin and other proteins in the egg white act as the indicators; the remaining portion of egg white (mainly water) is the base gel. The experimental data in Table 2 summarizes an ablation of egg white. The dimension information of ablation experiments are summarized below.

	Egg White	*Bovine Liver	Egg White Plus Egg Albumin
Quantity	4 eggs	225ml	4 eggs plus 0.8g albumin
Ablation Time	5 min	5 min	5 min
Initial Temp	15.3°C	22.6°C	16.6°C
Ablation Temp	56.8C	Not observed	53.8°C
Final Temp	111.7°C	139.3°C	108.8°C
Width (cm)	2.8	3.2	3.0
Height (cm)	4	5.5	4.3

Table 2: The size, ablation time, temperatures and sizes of the ablation zones were studied for egg white, bovine liver, and phantom ablations. The bovine liver ablation data was from Dr. Brace's post-doctor, Zhen's experiment.

The pure egg white has a smaller ablation zone comparing to the bovine liver. After adding egg white albumin to the egg white, the ablation zone was closer to the shape and dimension of a bovine liver specimen. The liver ablation was performed by a post-doctor in Dr. Brace's lab, Zhen Ji. See Appendix for of this ablation. The exact ablation settings are uncertain; this might contribute to the large difference in ablation height in Table 2. It is still reasonable to conclude that the addition of albumin caused enlargement of the ablation zone.

The addition of egg white albumin not only contributes to the enlargement of the ablation zone, but also adjusts the dielectric properties of the egg white to the baseline level. Figure 3 shows the effect of egg white albumin addition to lower both the permittivity and conductivity of an egg white sample when measured at 2.45 GHz. The blue line is the baseline of a liver specimen. The red line demonstrates the descending trend with increasing albumin addition.

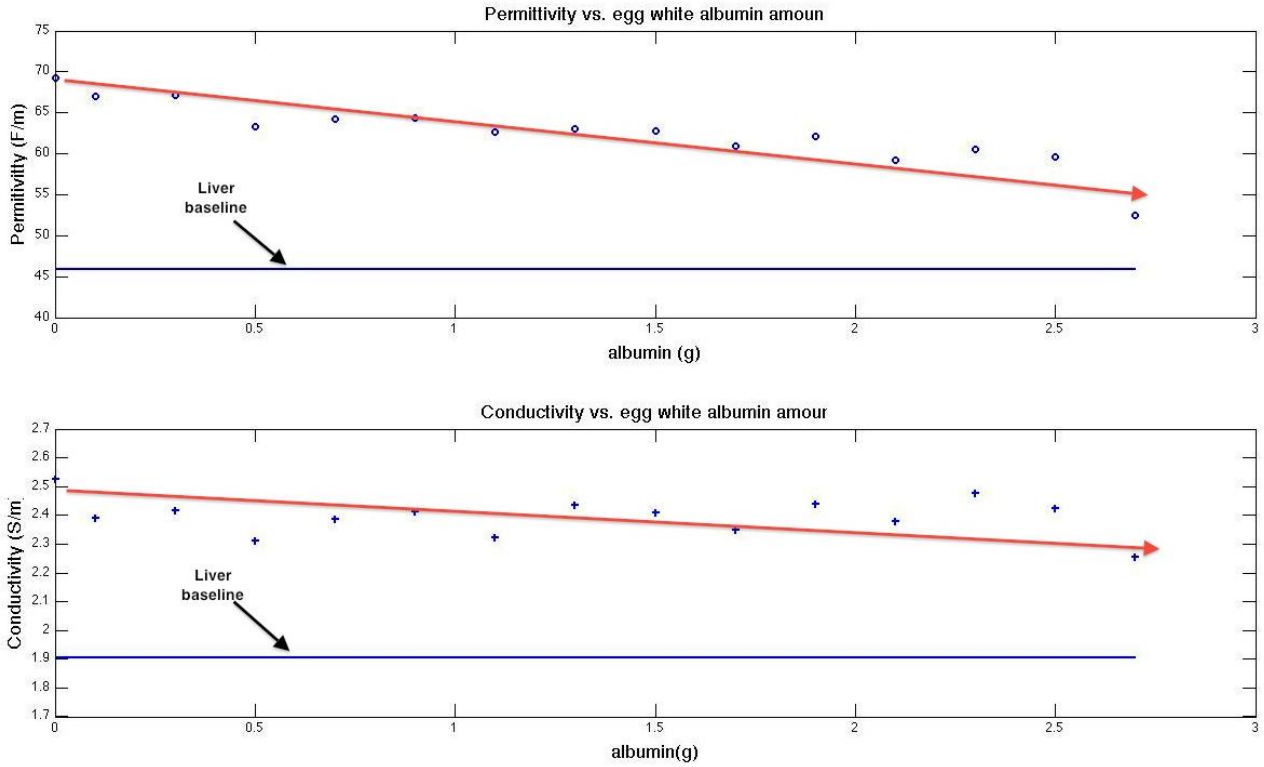

Figure 3: Adding egg white albumin lowers dielectric properties at microwave frequency (2.45 GHz)

5.2 Egg white vs. Liver ablation and dielectric properties

Egg white is composed of about 11 percent protein[16] and has higher permittivity and conductivity than a liver specimen. Figure 4 summarizes the dielectric properties of a bovine liver specimen, egg albumin with water, egg white, and the egg white plus albumin phantom. The dielectric property of the liver specimen was measured at 14.8°C. Several measurements were made and the average of these measurements was used to minimize errors. The egg white was measured at 13.3°C. 0.5g of egg white albumin was dissolved in 200mL deionized water for the measurement of the protein albumin. The dielectric measurements for the proteins in water are presumed to be high due to the low concentration of protein and the relatively high conductivity and permittivity of water.

It is worth-noting that the addition of egg white albumin does not equally affect the permittivity and conductivity. According to figure 4, the addition of albumin has a stronger effect on permittivity than conductivity.

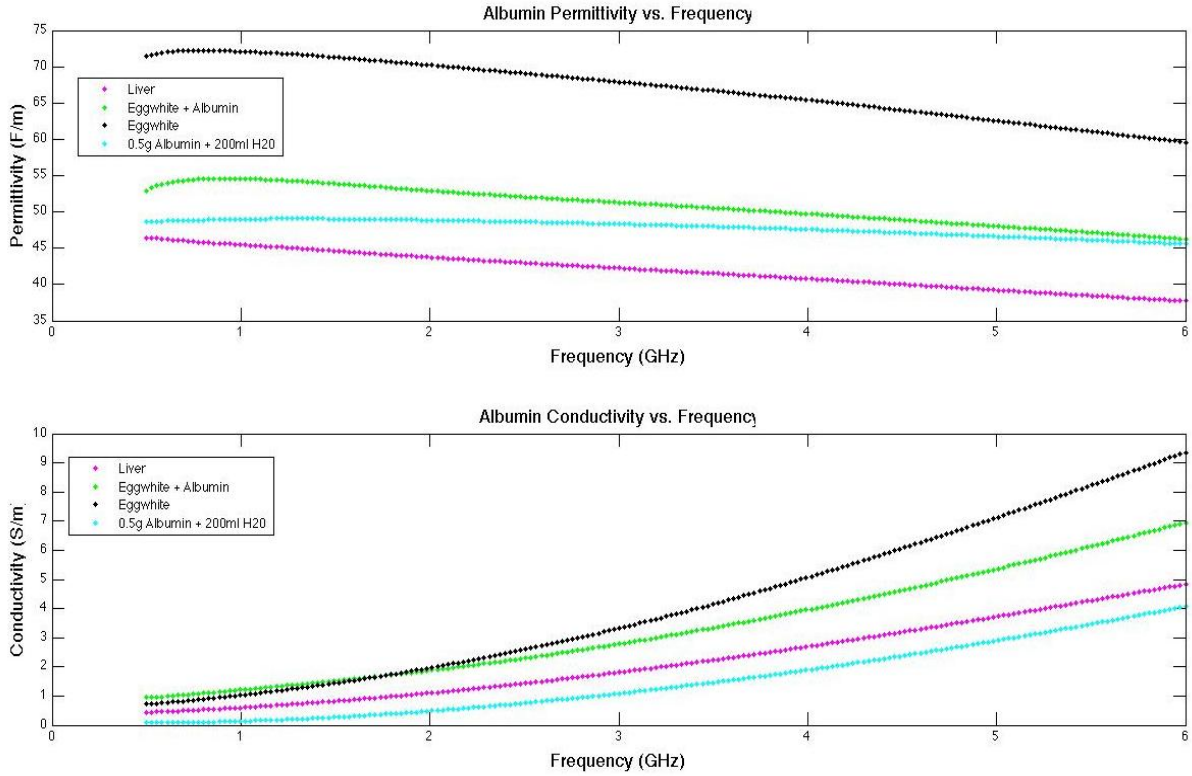

Figure 4: Comparison of dielectric properties of liver, egg white, albumin, and phantom

5.3 Different materials at microwave frequency

The dielectric properties of several kinds of base gels and indicators were measured. The base gels tested in the experiment include: sodium polyacrylamide (water lock), poly(vinyl alcohol), sodium alginate, dielectric silicon, and egg white. The indicators tested in laboratory include: bovine serum albumin, egg albumin and thermo chromic pigment. The liver specimen was measured to establish an experimental baseline. Figure 5 summarizes the dielectric properties of each material.

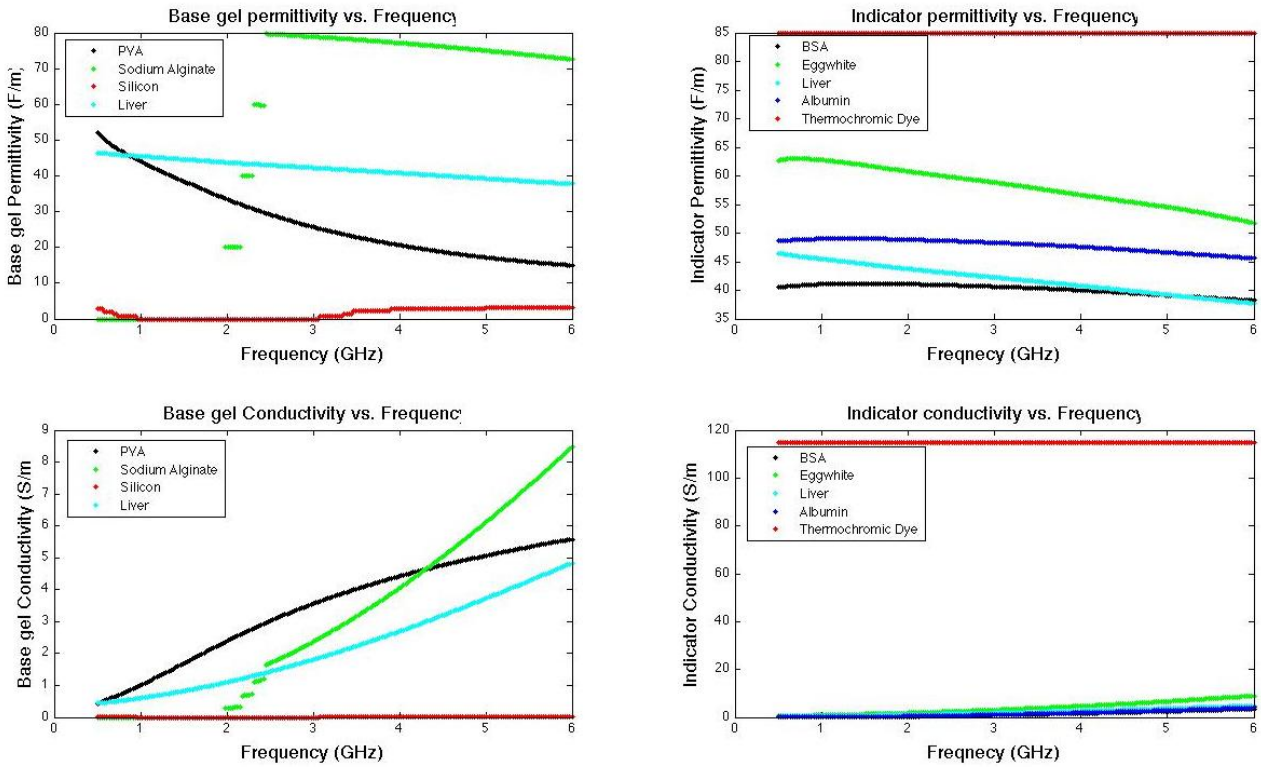

Figure 5: Summary of dielectric properties of each base gel and indicator samples

Water lock gel was not included in the above data because it was ruled out as a potential base gel before dielectric testing began. It boiled at a temperature of 90-100°C. The gel movement due to boiling makes the formation of an appropriate ablation zone impossible.

5.4 Mixed vs. Unmixed egg white

In an attempt to improve the homogeneity of the egg white, an egg white sample was stirred constantly and intensively for 5 minutes. The resultant mixture formed foam on the surface of the egg white sample. The dielectric properties of the mixed egg white did not vary significant from an unmixed egg white sample. However, the ablation zone of the mixed egg white sample has a dumbbell shape, instead of an oval shape. A synchronized temperature measurement during ablation shows that the mixed egg white sample exhibits thermal instability during the microwave ablation. On the other hand, the unmixed egg white sample demonstrates a stable, ascending curve at the initial stage of microwave ablation. Figure 6 shows a comparison of ablation temperature between mixed and unmixed egg white samples. The arrow indicates the starting point of protein coagulation.

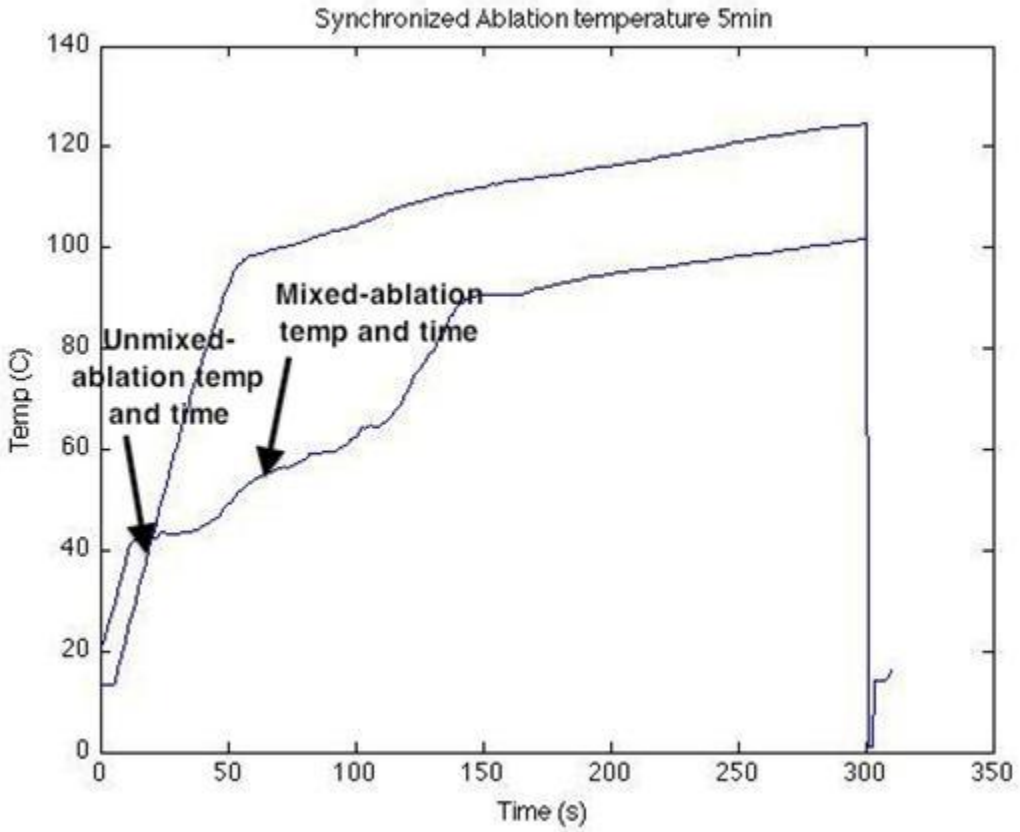

Figure 6: Synchronized temperature during ablation of mixed and unmixed egg white samples.

6. Discussion

6.1 The advantages and disadvantages of the final design

As mentioned earlier the final design is a mixture of egg white with added albumin from eggs. This design creates an ablation zone indicated by a clump of coagulated protein that can easily be measured after the ablation by pulling out the aggregate of protein. Also the transparent nature of the egg white allows a viewer to observe the formation of the ablation zone. Using this phantom, a viewer is able to observe and record the initial formation of the ablation zone and document it's progression throughout the ablation. The size and dimensions of the ablation zone from this phantom come very close to matching the ablation zone of a liver as show in Table 2. This occurs due to the coagulation temperature of the egg proteins and the dielectric properties of the phantom. The proteins in the phantom denature at a temperature of approximately 54^{o}C which is very close to the desired liver ablation temperature of approximately 50^{o}C. Also, as shown in Figure 3, by adding extra egg white albumin both the permittivity and conductivity approaches the values of a liver. This allows the heat to propagate through the phantom in a manner similar to the liver. All of these characteristics cause the phantom to be a successful model of the human liver.

Another benefit of this design is the relatively low cost. A phantom with four eggs of egg white (approximately 225mL) with an additional 2.7g of egg albumin costs less than $2.00. This is a very inexpensive price that allows for many repetitions with minimal costs. In addition the

preparation of the phantom is relatively easy and time efficient. Unlike other gels that may take days to cure, this phantom can easily be prepared in 5 minutes. The hardest part about the preparation is the mixing of the albumin into the egg white, which only dissolves after considerable stirring.

A negative to the design is that adding extra albumin reduces the transparency of the phantom. However, despite this reduced transparency the ablation zone is still easily visible throughout the ablation. Also the phantom appears to not be completely homogeneous. Some parts are thicker than others and the dispersion of the added albumin is not completely uniform. The liver, however, is not homogenous, and therefore our model in fact imitates the heterogeneous nature of the liver. This model is relatively successful in mimicking the properties of a liver and its ablation zone during microwave ablation.

6.2 The advantages and disadvantages of alternative designs

The best alternative design is plain egg white. It has an ablation temperature of about 50-55^{o}C which is in the desired range. It also forms an oval ablation zone that is close to that of a liver. Plain egg white is not only cheaper but easier to prepare than our final design. The cost for a 4 egg phantom is about $0.50, and cracking the egg and separating the egg white is the only preparation necessary; however, these improvements are fairly insignificant. The major advantage of this design, when compared to the final design, is its transparency. Despite this greater transparency, our final design is still superior because it has dielectric properties closer to that of a liver. Egg whites alone have a permittivity and conductivity that is noticeable higher than the liver as seen in Figure 4.

During the testing process combinations of base gels and indicators were created; however, most of these phantoms did not meet the client's requirements. The thermo chromic dye was completely opaque which ruined the transparency of any base gels it was mixed with, and its critical temperature and color was very sensitive to the chemical environment of the base gel. Therefore, any phantom containing thermo chromic dye was not a viable option.

Every base gel besides sodium polyacrylamide (Water Lock) required long curing times, which were all at least 24 hours (see Appendix – 10.3). Silicone had very low dielectric properties as seen in Figure 5. In addition, every indicator sank to the bottom of the container during the curing process, leaving trace amounts in the bulk of the phantom. When the silicon gels were ablated there was no observable ablation zone which eliminated it as a potential solution. PVA gels were transparent, but they melted early in the ablation process. All of the sodium alginate gels only partially gelled, most likely due to the high water content in the gel. The resulting samples were not fit to be ablated. The Water Lock gel was very easy to prepare: mixing the desired amounts of sodium polyacrylamide and water was the only step in the preparation. However, due to the large concentration of water present, the gel boils at a temperature of 90-100^{o}C; this moves the contents of the gel around and prevents the formation of an ablation zone, as seen in a liver ablation. When a mixture of egg white and Water Lock was ablated, the whole phantom had minimal transparency and there was no observed ablation zone.

6.3 Dielectric properties contribute to the size of ablation zone

It was observed that the dielectric properties contribute to the size of the ablation zone. When adding powdered albumin from eggs to the egg white, the dielectric properties

were affected and were closer to that of the liver. Ablation of the egg white and albumin also had a larger ablation zone than that of pure egg white. Possible reasoning includes that with the addition of more albumin makes more protein available to be denatured. Since, egg white is only 11 percent protein[16], a greater amount of protein allows a greater ablation zone. Or, according to Dr. Brace, when mixing in the powdered egg albumin, it may allow more air into the egg white. Consequently, this air could affect the permittivity and conductivity.

6.4 Temperature affects dielectric properties

The temperature of the specimen affects the dielectric properties. It was observed that the specimen had a slight difference in dielectric properties when measured at different temperatures. Figure 7 illustrates an example of the effect of temperature on the liver specimen taken at 13.5°C and 14.8°C. The data measured at a higher temperature has lower permittivity and conductivity.

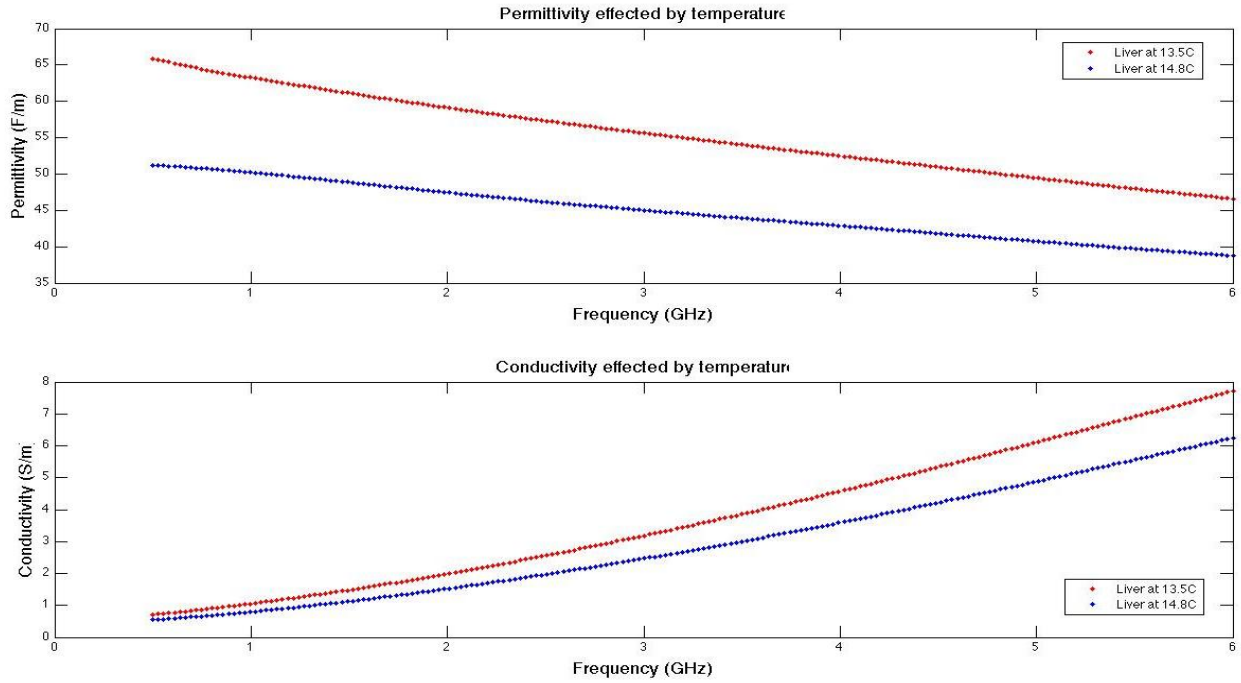

Figure 7: The dielectric properties of a liver specimen decreases with increasing temperature.

6.5 Future work

The sodium alginate was prepared as indicated in the article by Kuo et al[12], and the polyvinyl alcohol gel was prepared as indicated in the article by the Hyon et al[10]. The sodium alginate gel did not significantly gel. The polyvinyl alcohol gel, however, was very dense, which was not suitable for this specific application. Therefore, it may be beneficial to prepare PVA and sodium alginate gel using another preparation method (see Appendix-Figure 15). The physical and dielectric properties might be different compared to the current gels prepared.

Addition of albumin to the egg white lowers the dielectric properties, and the amount of albumin was adjusted in the final design to come close to matching the liver. Egg white albumin was added into the egg white due to its biocompatibility, and dielectric properties. However, egg white is consists of multiple kinds of proteins, and it may be possible to substitute egg white albumin for another protein compatible to the egg white in the future. Other proteins may better match the properties of the liver. The exact concentration of egg white proteins in the phantom is desired in order to produce a prototype which best mimics the liver properties. In addition, different mixing techniques could be tested to improve the homogeneity of the phantom. It was observed that the dielectric property parameters fluctuated significantly when taking the measurements. This may have been due to added egg albumin not being thoroughly mixed into the egg white.

General trends in properties associated with the addition of albumin were discovered. The egg white albumin did not reduce the dielectric properties equally: the permittivity decreased more significantly than conductivity. Therefore, some high conductivity substances could be added to the sample to adjust these two dielectric parameters closer to those of the live. Firm numerical data to determine the exact percentage of egg white albumin in the phantom is yet to be determined. Further testing should emphasize on more accurate data collection, finalization of the amount of add egg albumin, and improved precision of measurements. To achieve this goal, the team should repeat one experiment multiple times, use accurate measurement devices, and make estimations based on various observations.

6.6 Safety and Ethics

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

Some biomaterials require individual bio-hazard disposal and may cause pollution if used in large amounts, such as the thermo chromic dye. In light of the Environmental Act, the minimum amount of material was used during testing, and the materials were properly stored under desirable conditions (i.e. refrigeration of protein indicators). 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.

7. Conclusion

A liver phantom for microwave ablation was created using egg white and added albumin protein. Other base gels – sodium polyacrylamide (i.e. Water Lock), silicone, sodium alginate, and poly(vinyl alcohol) – and other indicators – thermo chromic dye and bovine serum albumin – were tested; these, however, did not meet the client's specifications for a homogeneous, transparent, and reproducible phantom that mimics the properties of the liver. The egg white and albumin phantom not only meets the client's demands but also is easy to prepare, cost effective, and provides a means to observe and measure the ablation zone over time. Only general trends were observed during testing; therefore, more testing is necessary to confirm the phantom's properties and to best match

these to that of the liver. Further testing should emphasize on more accurate data collection, finalization of the amount of usages, and improve precisions of experiments.

8. Acknowledgements

We would like to extend a special thanks to Dr. Chris Brace, our client, and Dr. John Puccinelli, our advisor. Additional thanks are due to Zhen Ji and Lisa Sampson for their help with testing and ordering supplies.

9. References

[1]Johns Hopkins Medicine. http://www.hopkinsmedicine.org/liver_tumor_center/treatments/ablative_techniques/radio_frequency _ablation.html

[2]Stauffer, P. R., Rossetto, F., Prakash, M., Neuman, D. G., & Lee, T. (2003). Phantom and animal tissues for modeling the electrical properties of human liver. International Journal of Hyperthermia,19(1), 89-101.

[3]Lafon, C., Zderic, V., Noble, M. L., Yuen, J. C., Kaczkowski, P. J., Sapozhnikov, O. A., et al. (2005). Gel phantom for use in high-intensity focused ultrasound dosimetry. Ultrasound in Medicine & Biology, 31(10), 1383-1389

[4]Zhang, B., Bing, H., Kuang, S., Ying, H. & Wu, Rong., et al. (2008). "A polyacrylamide gel phantom for radiofrequency ablation." International Journal of Hyperthermia 24:7, 568-476.

[5]Lazebnik, M., Madsen, E. L., Frank, G. R. & Hagness, S. C. (2005). "Tissue-mimicking phantom materials for narrowband and ultrawideband microwave applications." Med. Phys. 20 4245, DOI 146.151.19.194.

[6]Brace C. L. "Temperature-dependent dielectric properties of liver tissue measured during thermal ablation: toward an improved numerical model,". Conf. Proc. IEEE Eng. Med. Biol. Soc. 2008;2008:230–3

[7]Dow corning silicones. (2010). Retrieved on October 12th, 2010 at: http://www.dowcorning.com.

[8]Price, B. D., Gibson, A. P., Tan, L. T., & Royle, G. J. (2010). "An elastically compressable phantom material with mechanical and x-ray attenuation properties equivalent to breast tissue." Physics in Medicine and Biology, 55, 1177-1188.

[9]Surry, K. J. M, H. J. B. Austin, A. Fenster & T. M. Peters. (2004) "Poly(vinyl alcohol) cryogel phantoms for use in ultrasound and MR imaging." Physics in Medicine & Biology. 49. 5529-5546.

[10]Hyon, S. H., Cha, W.I., & Ikada, Y. (1989). Preparation of transparent polu(vinyl alcohol) hydrogel. Polymer Bulletin, 22, 119-122.

[11]Kharine, A., Manohar, S., Seeton, R, Kolkman, R. G. M., & Bolt, R. (2003). "Poly(vinyl alcohol) gels for use as tissue phantoms in photoacoustic mammography." Physics in Medicine and Biology, 48, 357-370.

[12]Kuo, C. K., & Ma, P. X. (2001). "Ionically crosslinked alginate hydrogels as scaffolds for tissue engineering: Part 1. structure, gelation rate and mechanical properties." Biomaterials, 22, 511-521.

[13]Miura, K., Kimura, N., Suzuki, H., Miyashita, Y., & Nishio, Y. (1999). "Thermal and viscoelastic properties of alginate/poly(vinyl alcohol) blends cross-linked with calcium tetraborate." Carbohydrate Polymers, 39, 139-144.

[14]BIOTANG. Bovine Serum Albumin, 250g (BSA). http://www.biotangusa.com/bt/bovine-serum-albumin-250g-bsa.html.
[15]Photchanachai S., Mehta A., Kitabatake N.. "Heating of an ovalbumin solution at neutral pH and high temperature." Biosci. Biotechnol. Biochem., 66 (8), 1635-1640, 2002.
[16] Divkovic, G.W., M. Liebler, K. Braun, T. Dreyer, P.E. Huber, J.W. Jenne. (2007). "Thermal properties and changes of acoustic parameters in an egg white phantom during and ablation by high intensity focused ultrasound." Ultrasound in Medicine & Biology, 33:6, 981-986.
[17] Sigma Aldrich. A5253 Albumin from chicken egg white-powder, 62-88% (agarose gel electrophoresis).http://www.sigmaaldrich.com/catalog/Lookup.do?N5=All&N3=mode+matchpartialmax&N4=a5253&D7=0&D10=a5253&N1=S_ID&ST=RS&N25=0&F=PR

10. Appendices

10.1 Project Design Specifications

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 ± 5 F/m and conductivity 1.7 ± 0.2 S/m. It must distinguish ablation areas when the temperature exceeds the threshold of 50^{o} 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^{o} 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^3, 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.

10.2 Budget

Material	Cost
Base Gel	
Dow Corning ® Dielectric silicone base gel	$0.00
Dow Corning ® Dielectric silicone base gel (firm)	$0.00
Sodium alginate gel	$0.00
Sodium polyacrylamide gel	$0.00
Dimethyl sulfoxide	$129.60
Poly(vinyl alcohol)	$75.80
Calcium chloride anhydrate	$27.80
Calcium Carbonate Bioxtra	$32.31
N,N'-Dicyclohexyl carbodiimide	$31.60
Ethylenediamine Bioxtra	$38.50
Sodium alginate	$40.00
D-Gulcono delta lactone	$31.60
Indicators	
Bovine serum albumin	$70.00
Albumin (egg white)	$0.00
Hallcrest® permanent thermochromic ink	$0.00
Eggs (10/24/2010)	$2.69
Eggs (10/27/2010)	$0.99
Eggs (11/17/2010)	$1.69
Others	
Lime (2)	$0.00
Total	**$482.58**

10.3 Preparation Procedures

Alginate Gels

Kuo Method[12]

1. Prepare 1.5% (0.03-0.05g in 100mL)alginate solution in DI H_2O
2. Prepare ($3CaCO_3$: 2GDL) $CaCO_3$
3. Prepare GDL solution
4. Add sodium alginate solution to $CaCO_3$ suspension
5. Mix and vortex for 1 minute to initiate gelation
6. Add GDL solution and vortex for 1 minute

Miura Method[13]

1. Prepare 2.0% (wt%) solution of sodium alginate (room temp) with continuous stirring
2. Prepare 6.0% (wt%) solution of PVA (approx 70^{o}C) with continuous stirring
3. Mix two solutions
4. Stir overnight
5. Clear "viscous solutions" can further be dried at 50^{o}C for approximately 12 hours in vacuo and stored in a desiccator

6. Treat with 0.8 wt% solution of CaB_4O_7

PVA Gels

Hyon Method[10]

1. Prepare mixture of 80% DMSO, 20% DI H_2O
2. Prepare homogeneous 15% (wt%) by heating a mixture of PVA in DMSO/DI H_2O mixture at 140°C for 2 hours
3. Lower temperature to 60oC and pour to desired container
4. Store at -20°C for at least 10 hours
5. Allow formed gel to be in contact with flowing DI H_2O to remove DMSO for 4 days

Price Method[8]

DMSO Based-Gels

1. Prepare solvent (4 parts DMSO:1part DI H_2O)
2. Heat solvent on 200°C hot plate, heat to 75-85°C
3. Add 72 grams of PVA in 800 mL of solvent
4. Stir for 25-45 minutes or until PVA is dissolved
5. Cool for 1 hour at room temperature
6. Freeze gels at -13°C for 22 hours
7. Submerge gels in solvent to store

Ethanol Based Gels

1. Setup reflux condenser to prevent evaporation of ethanol
2. Prepare 50% ethanol, 50% DI H_2O solvent
3. Measure out 20% w/v portion of PVA
4. Add PVA to solvent and maintain solution temp of 83°C until PVA dissolves (approximately 70-130 minutes)
5. Cool for 1 hour
6. Place in freezer at -13°C for 22 hours
7. Submerge gels in solvent to store

10.4 Images

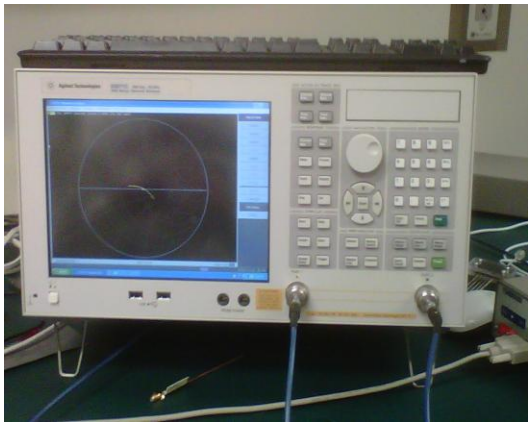

Figure 8: Agilent Technologies® E50701C ENA Series Network Analyzer was used to measure dielectric properties.

Figure 9: Ablation zone is clearly visible for ablated egg white. Measurements can easily be taken by lifting antenna.

Figure 9: Small sections of liver were ablated for 5 minutes to determine the size of the ablation zone. The temperature probes (yellow wire) as well as the copper antenna are inserted into the liver.

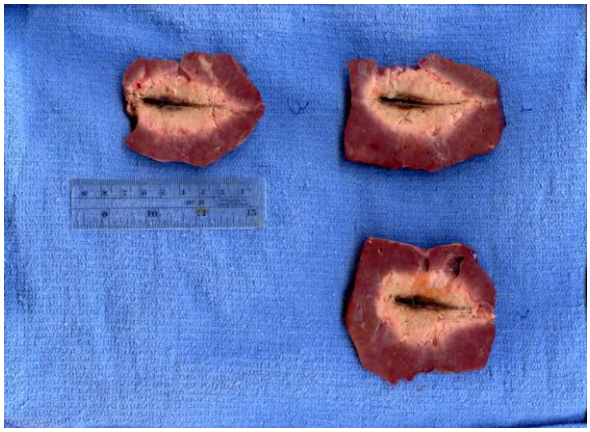

Figure 11: Cross section of liver after 5 minute ablation at 50 watts. Ablation zone appears as light tan. Photo courtesy of Ji Zhen.

Figure 12: Initial testing with sodium alginate was unsuccessful as seen by the opaque heterogeneous gel. Different sodium alginate was purchased for further testing.

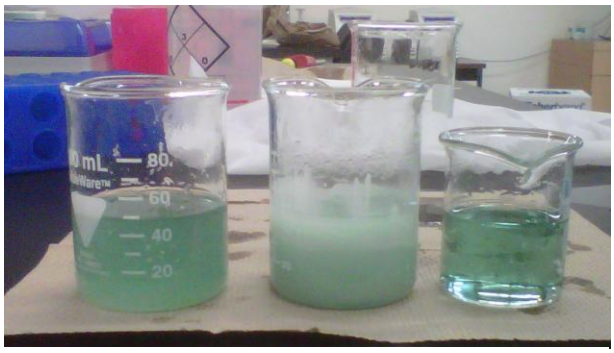

Figure 8: Silicone gels were also tested. From left to right, silicone gel with BSA, silicone gel with albumin, and just silicone gel

Figure 11: The poly(vinyl alcohol)gels were very clear but were very dense.

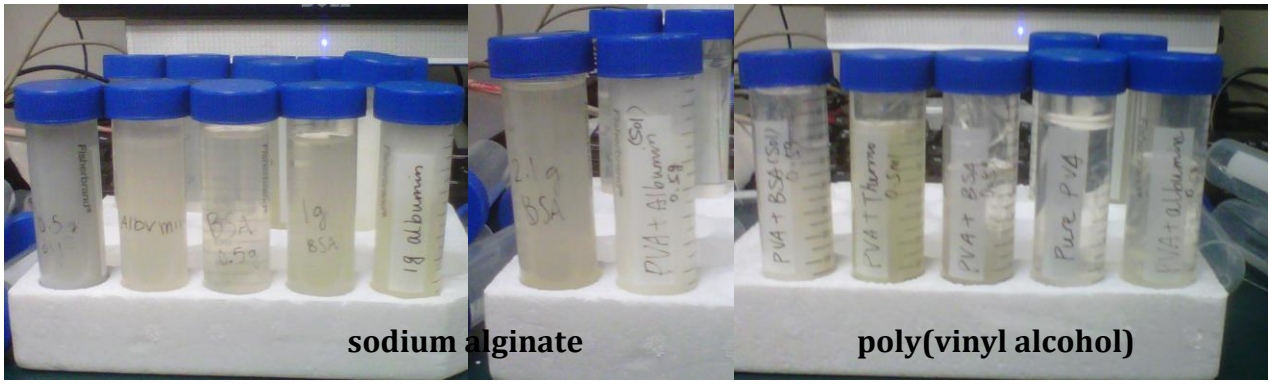

Figure 10:Poly(vinyl alcohol) and sodium alginate gels were also tested.