TECHNIQUES ON ANALYSIS OF PHOTO PHASE SHIFT IMAGING

A Senior Scholars Thesis

by

ROBIN TERRY

Submitted to Honors and Undergraduate Research
Texas A&M University
in partial fulfillment of the requirements for the designation as

UNDERGRADUATE RESEARCH SCHOLAR

May 2012

Major: Biomedical Engineering

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Approved by:

Research Advisor: Mark Lenox
Associate Director, Honors and Undergraduate Research: Duncan MacKenzie

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ABSTRACT

Techniques on Analysis of Photo Phase Shift Imaging. (May 2012)

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In order to locate and destroy cancerous tumors, piglets with naturally occurring melanoma were injected with gold nanoparticles and exposed to laser irradiation. This causes necrosis of the tumor cell while sparing the surrounding, healthy tissues. Real-time MRI temperature mapping was evaluated using the magnitude and phase difference DICOM images. To reduce noise on the temperature maps, a mask was created using the magnitude images and eliminating pixel values greater than a set threshold. The mask was overlaid onto the phase difference images, and the proton resonance frequency was applied. A temperature analysis was recorded displaying the gradual heating then cooling of the tumor. It was proven graphically that the tumor was subjected to heat, while the surrounding tissue remained unharmed and at the same temperature.

DEDICATION

This thesis is dedicated to my parents, without them I wouldn't be where I am today.

ACKNOWLEDGMENTS

This work would not have been possible without the support of Dr. Mark Lenox. From the start, he has believed in my ability to succeed and has offered the best words of wisdom and guidance. As my teacher and mentor, he has taught me more than I ever could give him credit for here; and by his example, I have learned what it takes to be a good scientist and engineer.

I would especially like to thank Dr. David Purdy for his detailed mathematical explanations about temperature mapping. Dr. Mary Preston McDougall helped me get my foot in the door with MATLAB and offered unending support. I also want to thank my co-worker, Jonathon Madsen, for showing me a few programming techniques that were greatly needed.

Nobody has been more important to me during this time than the members of my family. I would like to thank my parents for their continuous love and support, which has guided me through many stressful days. I am so blessed to have parents like them in my life. For everything they have done, including financial support, I am eternally grateful. My oldest sister, Kristen, has been an excellent role model, and I hope to attend graduate school like she has. And Alyson, my youngest sister, has been a light in dark places, and I can only hope to become a great role model for her.

NOMENCLATURE

DICOM	Digital Imaging and Communications in Medicine
MRI	Magnetic Resonance Imaging
PRF	Proton Resonance Frequency
TIPS	Texas A&M Institute of Preclinical Studies

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CHAPTER I

INTRODUCTION

Targeting specific tumorous cells using thermal energy is proving to be very promising in eliminating cancer. The method of thermo-ablation therapy subjects the tumor to elevated temperatures, which causes the tumor to undergo necrosis. Currently, this is accomplished in a non-invasive way by using a high-intensity focused ultrasound [1] or in a minimally invasive way using the laser or radiofrequency techniques [2].

This study explores the removal of melanoma cells in piglets using a laser to perform photothermal therapy. Laser photothermal therapy was chosen because it destroys cancer cells directly without harming the surrounding healthy tissue. Also, this method is not affected by target motion and can heat up slowly, thus producing no image artifacts [3].

Many Sinclair swine newborns are predisposed to melanoma. Typically, once the piglets hit puberty (around 6 months of age) the tumors regress. A remarkably small number of piglets die from the melanoma [4]. In humans, melanoma is the deadliest type of skin cancer and can spread rapidly. The disease is prevalent in all ages, but the risk of developing the melanoma increases in people with a greater exposure to sunlight or

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This thesis follows the style of *IEEE Transactions on Biomedical Engineering*.

ultraviolent radiation. Chemotherapy, radiation, and surgery are the common forms of treatment today. We want to eliminate these harsh treatments by finding a more effective and less invasive solution.

Temperature mapping

In order to evaluate the effectiveness of photothermal therapy, it is necessary to accurately measure the rising temperature of the tumor, as well as the temperature of surrounding tissues. The best modality for observing this progress is magnetic resonance imaging (MRI).   MRI has multiplanar capabilities that allow the visualization of temperature in hard to see areas, while providing excellent soft tissue contrast [3]. Most importantly, this imaging modality allows for continuous real time temperature mapping and target definition [5]. Clinicians will then be able to fully assess the tumor size and shape during the ablation process.

Phase difference

Siemens granted TIPS the right to use their work-in-progress software for spatially resolved real-time temperature mapping. This data is calculated using standard evaluation procedures and displayed with the online monitor by the scanner [6]. The software lets the user acquire the images in three different modes: reference image mode, phase difference image mode, and reference less mode. Reference image mode stores phase images to be used at a later time; phase difference image mode subtracts phase images from reference images and displays a color-coded temperature map; and

the reference less mode reconstructs background phase from the border and heated zone, where no reference image is needed. However, Siemens current software has some flaws. It does not eliminate the noise surrounding the phase difference image; thus, it displays the temperature change outside the region of interest. In addition, the thermal display only shows a few preselected temperature bands, making evaluation post-scan nearly impossible. Siemens designed this software such that the user can export the phase difference and magnitude images to an outside source and then evaluate the readings on an external platform. The magnitude raw data images are used to ultimately eliminate the noise in the phase difference images. To accomplish this, a pixel value is chosen as the noise threshold and the pixel values greater than that threshold are removed. This new mask is then overlaid on the phase difference image where temperature differentials are calculated to produce the temperature mapping.

All images, such as the phase difference and magnitude images are in the Digital Imaging and Communications in Medicine (DICOM) format. Created by the National Electrical Manufacturers Association (NEMA) and the American College of Radiology (ACR), DICOM enables users to communicate digitally between diagnostic and therapeutic systems using a standardized method [7]. A DICOM image is similar to a JPEG, except that the DICOM image has unique identifiers that contain information, or metadata, (series number, echo time, slice location, etc) specifically to the individual image. The identifiers are tagged with the image and allow for easy data sharing. Because MATLAB has the ability to easily view DICOM images and extract the

identifiers, this program was used to alter the DICOM images to create the temperature mappings.

Proton resonance frequency shift

The Proton Resonance Frequency (PRF) shift, along with other techniques such as the T_1 relaxation, the diffusion coefficient, and the magnetic transfer, has been proven to be sensitive to temperature, thus proving its importance to MRI thermotherapy. PRF is a useful MRI parameter for temperature mapping due to its real time quantitative nature [8] and its tissue independence, as well as its simplicity and speed, making this method the most promising available. It commonly works best on MRIs with field strength greater than 1T (TIPS MRI machine is a 3T). This technique relies on the fact that water proton resonance frequency changes as temperature changes [9]. In order to acquire the phase difference images needed for the study, the gradient-recalled echo (GRE) sequence is used. During heating, GRE phase shift images are created by water's frequency shift, which can then be subtracted from a baseline phase image and further processed to produce the estimated temperature maps. Additionally, this sequence is ideal because it helps reduce acquisition time to allow for real-time monitoring [10].

CHAPTER II

METHODS

The mathematics behind this design of temperature mapping using MRI's involves the proton resonance frequency. This known PRF equation, along with MATLAB coding and image manipulation, is the basis behind obtaining the desired results. For my purposes, I am working with MATLAB Version 7.7.0 (R2008b).

Mathematics of PRF

The PRF method is based on temperature dependent changes of the proton chemical shift relative to a baseline value. The equation below represents the calculation of the phase difference ($\Delta\varphi$) from the reference phase (non-heated tissue) and the present phase (during heating):

$$\Delta\varphi = \alpha \bullet \gamma \bullet B_o \bullet TE \bullet \Delta T \tag{1}$$

where α is the thermal coefficient, γ is the gyromagnetic ratio, B_o is the amplitude of static magnetic field, TE is the echo time, ΔT is the temperature difference.

The phase difference images (as well as the magnitude images) are obtained through the Siemens software and are portrayed in MATLAB in pixel values ranging from 0 to 4095 (unsigned integers). Therefore, in order to use the PRF equation in (1), this value must be converted into degrees ranging from -180 degrees to 180 degrees. A pixel value of

2048 represents zero degrees and a pixel value of zero represents -180 degrees. The conversion equation is obtained using:

$$\Delta\varphi = 180 \bullet \frac{GrayLevel - 2048}{2048} \qquad (2)$$

This phase difference equation in (2) will be substituted into equation (1). Additionally in (1), the α is assumed to be -0.01 ppm/°C, the γ is a given value of 42.577 MHz/T, B_o is 3 T for the Siemens Verio. TE is in seconds and depends on the particular image. The echo time applicable to my set of images is 10 ms, or 0.01 seconds. One "unit" is considered to be equal to one million ppm, for a simpler unit cancellation. This can be shown in the equation below:

$$\Delta\varphi = \frac{-0.01 \text{ ppm}}{1°C} \bullet \frac{unit}{10^6 ppm} \bullet \frac{42.577 \text{ MHz}}{T} \bullet \frac{10^6 Hz}{MHz} \bullet B_o \text{ (in T)} \bullet TE \text{ (in sec)} \bullet 360 \qquad (3)$$

It can be seen that ppm, degrees Celsius, MHz, and tesla are the units that cancel out. The unit of seconds can also be cancelled out by changing Hz to cycles/sec. The additional multiplication of 360 represents the conversion of the cycle into rotational degrees.

In order to yield the equation necessary for temperature mapping, the equation given in (1), along with the unit adjustments in (3), can be rearranged to obtain ΔT:

$$\Delta T = \frac{\Delta\varphi}{\alpha * \gamma * Bo * TE * 360} \qquad (4)$$

This final PRF equation in (4) and the conversion from pixels to degrees (2) are the two main equations later applied in the MATLAB code.

Structure of code

The magnitude and phase difference DICOM images are obtained from the Leonardo

workstation computers at TIPS. The two different folders for the magnitude and phase

difference data each contain 105 DICOM images. Due to the long filenames associated

with each image, the images' location and names are placed into two text files, one for

the magnitude and the other for the phase difference (Fig. 1).

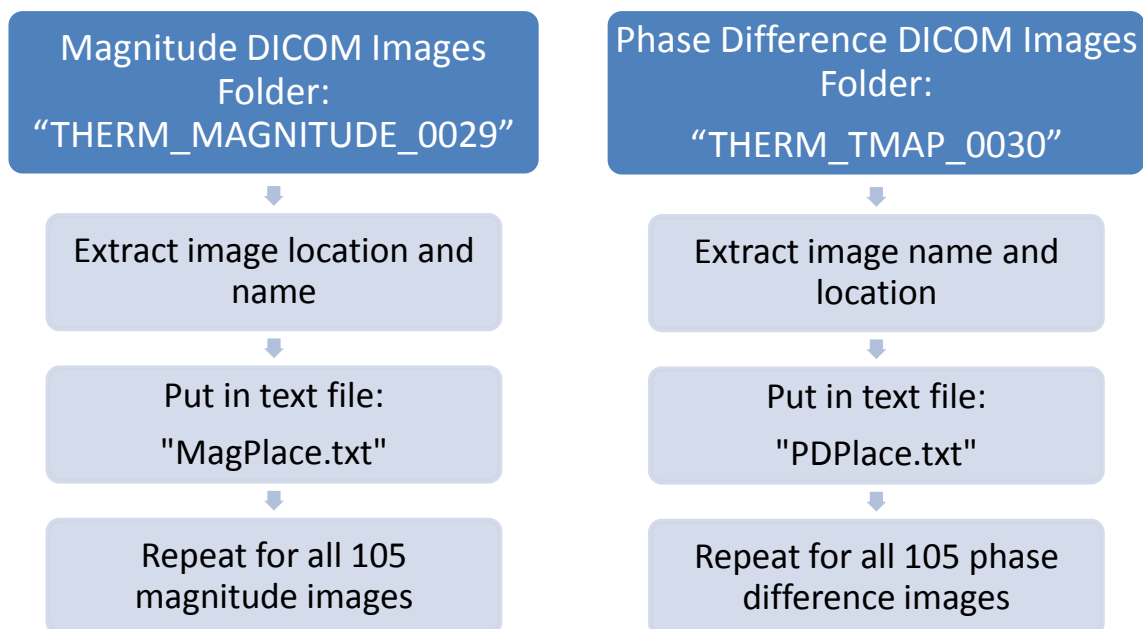| Magnitude DICOM Images Folder: "THERM_MAGNITUDE_0029"	Phase Difference DICOM Images Folder: "THERM_TMAP_0030"
⬇	⬇
Extract image location and name	Extract image name and location
⬇	⬇
Put in text file: "MagPlace.txt"	Put in text file: "PDPlace.txt"
⬇	⬇
Repeat for all 105 magnitude images	Repeat for all 105 phase difference images

Fig. 1.   Text file method

This method is used to import the images in MATLAB in an easy and quick manner

with less coding necessary. The text files are stored in the same folder as the MATLAB

code which allows MATLAB to find, open, and read the file. Once open, the file

identifier, fid, is passed to the other functions to process the data, conduct manipulations, and close the data.

A loop, starting before the while loop and ending inside the while loop, reads the images one after another in the text file continuously until the last line. The approach used in the magnitude while loop involves importing the DICOM image then applying a magnitude mask (Fig. 2).
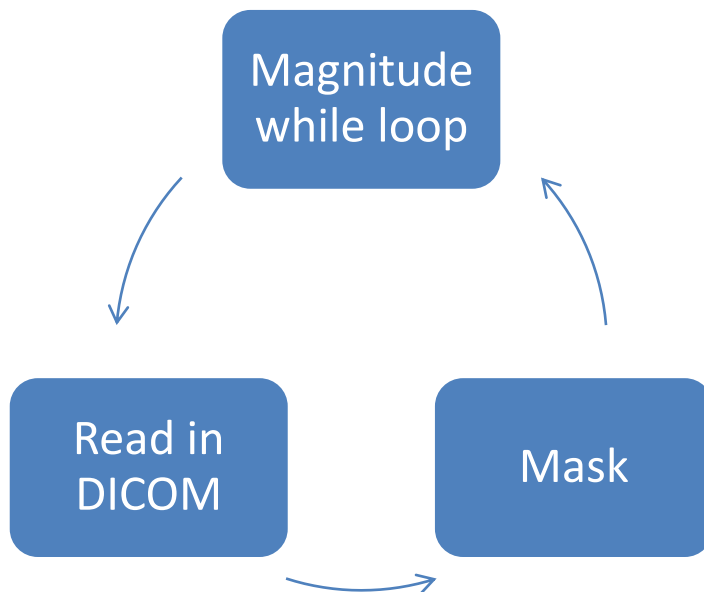
Fig. 2.   Magnitude while loop.

The MATLAB command 'dicomread' reads the image data and allows the user to view the DICOM image or do any calculations regarding the image. Because the phase difference data has random noise outside the body of interest, a "mask" needs to be applied to cancel out this unwanted background. This will allow for a more precise

temperature mapping. The mask is calculated using the magnitude image which will then be overlaid on top of the phase difference image. Any pixel value in the magnitude image with intensity below 20 is considered noise and is eliminated. The MATLAB command takes the data from the DICOM magnitude images (represented by P) and then gives an index value of one if the data is above 20 pixels or gives an index value of zero if the pixel values are below 20.

The methodology used for the phase difference while loop is more complex than that of the magnitude while loop (Fig. 3).
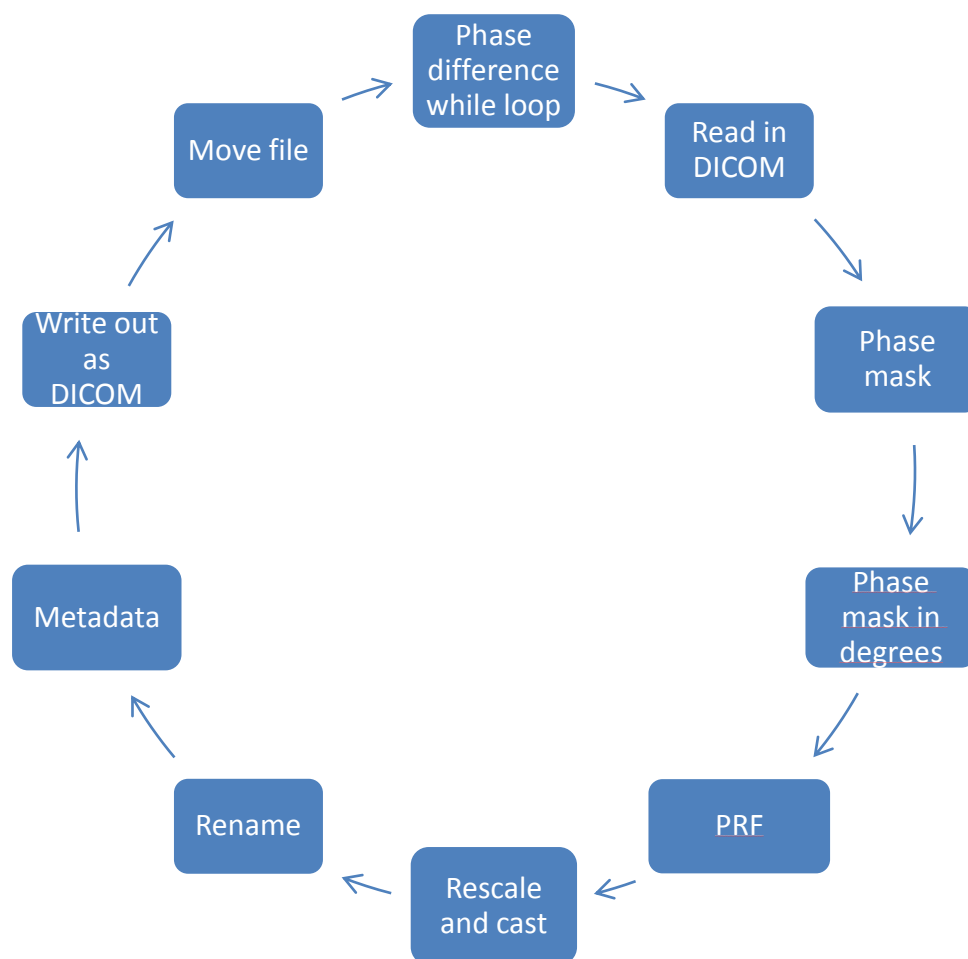

Fig. 3. Phase difference while loop

Inside the phase difference while loop, the images are read using 'dicomread' as before and a "phase mask" is applied by multiplying the magnitude mask by the phase difference image. In order for the arrays to be multiplied successfully together, they must be of the same length. Therefore, the magnitude mask and the phase difference image must be converted to the class 'double'. The new phase mask image must be converted into degrees by using equation (2), which was stated previously as:

$$\text{PDdegrees} = 180 \cdot \frac{\text{PhaseMask} - 2048}{2048} \tag{2}$$

so that it may be mathematically inputted into the PRF equation. By assigning the values to the variables in the PRF equation, the final equation is:

$$\Delta\text{T} = \frac{PDdegrees}{0.01 * 42.577 * 3 * 0.01 * 360} \tag{5}$$

Because ΔT is automatically accepts the class 'double', yet the original DICOM magnitude and phase difference images is each a 16-bit unsigned integer (uint16) class, it is necessary to cast ΔT as a uint16, as well. However, it must be rescaled before its class can change. This was accomplished by multiplying ΔT by 10 and adding 100. It was then converted to a unit16 class by using the "cast" command in MATLAB.

In order for the new temperature mapping images to have metadata, like other DICOM images, it is assigned the same metadata as the phase difference metadata, while altering some information. All of the metadata for the temperature maps are the same as the phase difference metadata except the series number, series description, and image comments. This aids in differentiating the two series of images.

Concatenation is used to preserve the information in the filename for the new images. It will have the same filename as the phase difference name except an additional "_temp" will be added to the end to help distinguish the difference between the two images. This will also help to identify which temperature map is paired with which phase difference image. This method used deletes the last four digits in the original filename (which represents '.IMA') and gives the temperature mapping the new name with "_temp.IMA" on the end.

In order to view and manipulate the new temperature map images on the Leonardo workstation computer at TIPS, the images must be written out as DICOM images. These 105 new DICOM images are then placed in their own folder called "OutputDicomImages" for organization and easy access. In the 'dicomwrite' command line, 'CreateMode' and 'copy' allow all the metadata to be copied from the input and do not generate missing values for certain sections. Because all of the images are automatically placed in the same folder where the MATLAB code is saved, the command 'movefile' must be used in order to move the new DICOM images to a separate folder.

This new folder with the output DICOM temperature mapping images can be opened from the workstation computers at TIPS where a region of interest analysis can be applied to represent the temperature change graphically. To do this, a small region where the heated tumor lies is selected and dynamic analysis is taken. A graphical

representation of the heating for every image that has a slice location of zero is

displayed.

CHAPTER III

RESULTS

Displaying the magnitude and phase difference images are necessary in order to prove the commands 'dicominfo' and 'dicomread' are correctly working with no error in syntax. Additionally by using the Data Cursor in the MATLAB figure toolbar, the pixel threshold of 20 was chosen. The phase difference DICOM image (Fig. 4) shows the body of interest surrounded by noise. This image is number 53 out of 105 (InstanceNumber = 53), and the slice location is zero.
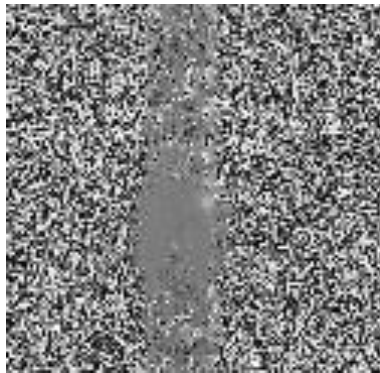

Fig. 4.   Phase difference DICOM image.

The goal of the magnitude mask is to ultimately eliminate this noise. The pixel value threshold of 20 is a nice medium between the black outside region and the body of interest. The Data Cursor shows the differing index values for both areas (Fig. 5).
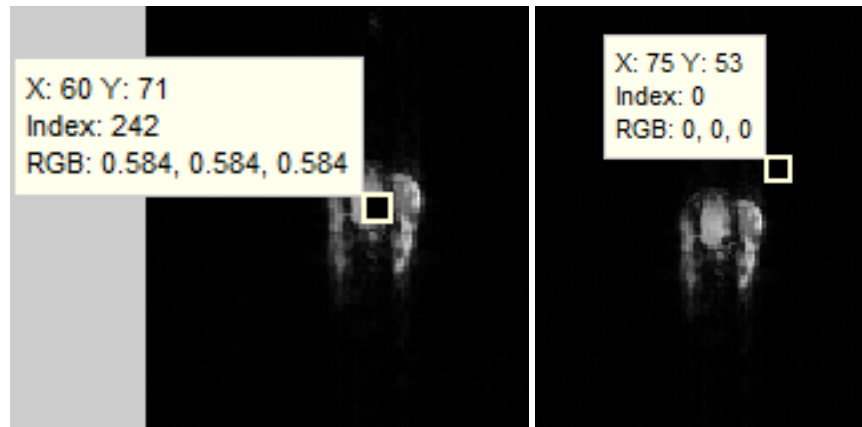
Fig. 5.   Magnitude image with index values.

The mask, with the pixel values below 20 eliminated, is applied to the magnitude mask (Fig. 6). The color bar on the right side shows the body of interest equals a value of one (in red), while the outside area is given a value of zero.
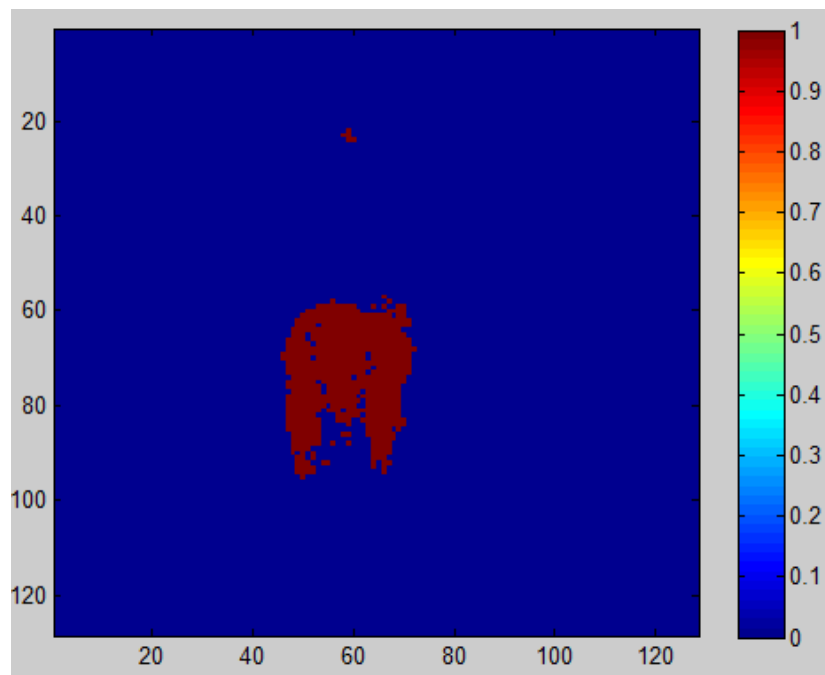

Fig. 6.   Magnitude mask.

The magnitude mask is then overlaid on the original phase difference image and the results are shown in Fig. 7. The data cursor from the MATLAB toolbar is applied again to see show the index value differences.
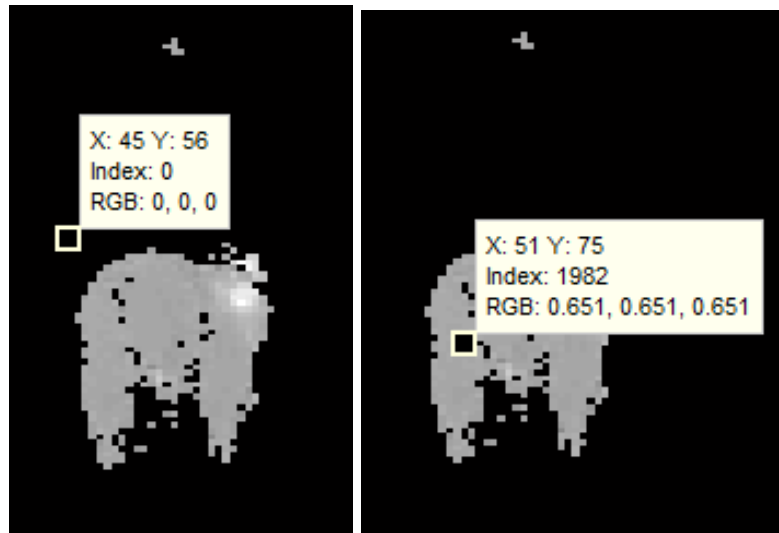

Fig. 7.   Phase mask image with index values.

The phase difference is calculated in degrees and then plugged into the proton resonance frequency (PRF) equation. The resulting temperature map for instance number 53 is shown below (Fig. 8).
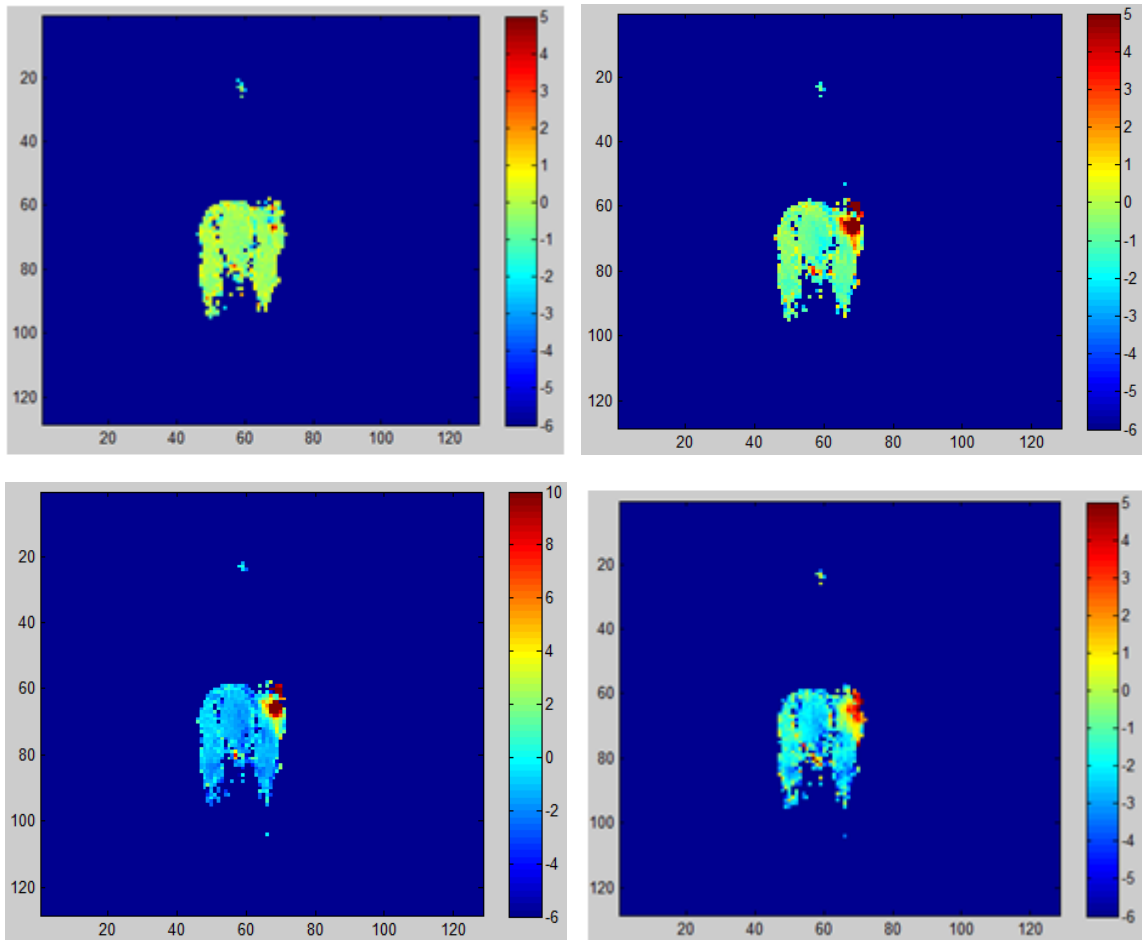
Fig. 8.   Temperature map progression. Slice location is zero for all subfigures and instance numbers are 4, 32, 60, and 102 (from top-left to bottom-right).

Fig. 8 shows that the tumor is successfully heating up and cooling down over a period of time. The top-left image, where the instance number is 4, shows little to no heating of the tumor located in the top right of the body of interest. Throughout time, the tumor becomes brighter, showing the increase in heat. The bottom-left image (instance number 60) shows the maximum heat possible. Then the tumor gradually cools, as displayed in the bottom-right, or instance number 102, image.

To observe the overall change in temperature as time progresses, the DICOM temperature map images were analyzed by determining the mean intensity values over a small region of interest. Table I represents the mean temperature value associated with each instance number (every image where slice location is zero).

TABLE I
TEMPERATURE VALUES

Instance Number	Temperature (°C)
4	2.2090
11	5.4692
18	6.6980
25	8.0687
32	8.5486
39	10.2073
46	10.8702
53	11.4955
60	11.5474
67	11.1214
74	8.8715
81	7.5908
88	5.4665
95	4.1559
102	4.6555

The instance number versus the temperature values are then displayed graphically (Fig. 8) using Excel.
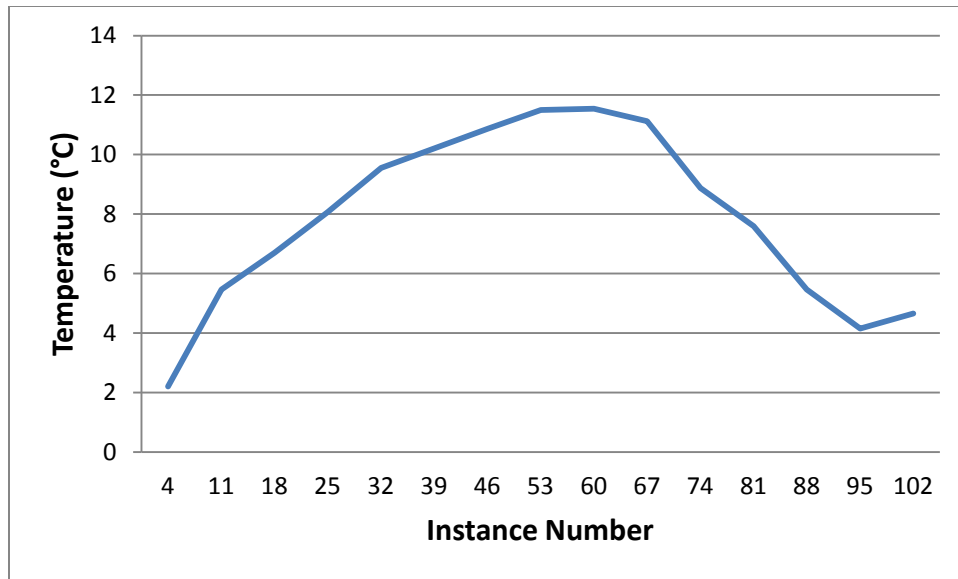
Fig. 9. Mean value curve displaying temperature change.

Fig. 9 shows that the tumor is progressively heating up then cooling back down. It reaches a maximum temperature rise of 11.5°C at instance number 60 and continues to cool afterwards.

CHAPTER IV

SUMMARY AND CONCLUSIONS

The task was to graphically display real-time temperature mappings while tumors were subjected to laser photothermal ablation. The benefit of this code is that the original noise of the phase difference data was eliminated, thus, resulting in more accurate and simplified temperature images. Siemens work-in-progress temperature mapping software does not remove this noise. This makes it very difficult to determine the precise region of interest. Therefore, it is ideal and necessary to use the magnitude data to solve this problem.

A constraint is that the program is user friendly in that the user only has to put forth minimal effort to achieve their outcome temperature mappings. The code is written in such a way that the user only has to do make a text file, which the program can then read and display the results.

To summarize, it has been proven that noise-eliminating and real-time temperature mapping can be achieved using the magnitude and phase difference DICOM images using the proton resonance frequency. Temperature mappings can be useful in cases where the doctor or researcher is trying to determine the exact temperature at which the tumor can be destroyed. It is also a way to graphically prove that the tumor, or area of interest, did reach a particular temperature, while the surrounding tissue remains intact.

Recommendations and future work

The focus of the code has been to create a fast, user-friendly MATLAB code which displays the temperature change of the desired region of interest. The most important issue has been to eliminate the outside noise of the phase difference image and correctly calculate the proton resonance frequency equation with the correct units. Like any software program, there is room for upgrade with this code.

It would have been desirable for the MATLAB code to access the file with the magnitude and phase difference images directly without having to create a text file as the median.

The next step for this project would be to imbed the program into the Leonardo Workstation computers at TIPS. The user could then image the tumor using an MRI and send the images to the Leonardo computers, where they could run the temperature mapping software in one easy step.

A later addition would be that the software could be accessible over the Internet to anyone. The user could upload their magnitude and phase difference DICOM images online and display their corresponding temperature maps.

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APPENDIX- MATLAB CODE

```
clear all;
close all;

% Begin to deal with the magnitude DICOM images:
m = 1;

% Open the magnitude text file:
fid = fopen('MagPlace.txt', 'rt');
tline = fgetl(fid)

% While loop to continuously scan the magnitude text file:
while ischar(tline)

% Read the magnitude DICOM image and assign it a variable called "P":
P(:, :, m) = dicomread(tline);

% Assigns a pixel threshold of 20. If pixel in the magnitude image is above 20 then give
% it a value of 1. If pixel in magnitude image is below 20 then give it a value of 0.
mask(:,:)=P(:,:,m)>20;

% Continue to scan the text file and repeat this process until it reaches the last filename.
% Once it reaches the last filename then close the loop and continue to the next line of
% code:
m = m + 1;
tline = fgetl(fid);
end
fclose(fid);

% Begin to deal with the phase difference DICOM images once the program has
% completed work with the magnitude DICOM images:
i = 1;

% Open the phase difference text file:
fid = fopen('PDPlace.txt', 'rt');
tline = fgetl(fid)

% While loop to continuously scan the magnitude text file:
while ischar(tline)
```

% Read the phase difference DICOM image and assign it a variable called "P":
P(:, :, i) = dicomread(tline);

% Obtain the metadata from the phase difference image and give it the name "metadata"
metadata = dicominfo(tline);

% Multiply the magnitude mask by the phase difference image and call it "phasemask":
phasemask=double(P(:,:,i)).*double(mask(:,:));

% Calculate the phase difference in degrees therefore it can be applied to the PRF
% equation:
PDdegrees = 180.*(phasemask-2048)./2048;

% Assigning values to the variables of the PRF equation. GR is the gyromagnetic ratio,
% Bo is the magnetic field used, TE is the echo time, and TC is the thermal coefficient:
% GR=42.577;
Bo=3.0;
TE=10/1000;
TC = 0.01;

% Write the PRF equation and call it "deltaT":
deltaT = PDdegrees./(TC.*GR.*Bo.*TE.*360);

% Rescale and cast deltaT as an unsigned 16-bit integer:
RescaleDT = deltaT*10 + 100;
CastDT=cast(RescaleDT,'uint16'

% Remove the last four digits (".IMA") of the phase difference filename and add in
% "_temp.IMA" to name the new temperature maps:
S = tline
S = S(1:end-4)
filename = sprintf('%s%s', S, '_temp.IMA')

% Write the new temperature mapping as a DICOM image:
dicomwrite(CastDT, filename, metadata, 'CreateMode', 'copy');

% Temperature mapping will have the same metadata as the phase difference images,
% except the series number, series description, and image comments will be different for
% easy identification:
metadata.SeriesNumber = 95;
metadata.SeriesDescription = 'Output_Temp_Maps';
metadata.ImageComments = 'Temperature_Mapping';

% Move the temperature mappings from their original location to a new folder called "OutputDicomImages":

```
movefile(filename,'F:/Undergraduate_Research_Scholar /OutputDicomImages/');
```

% Continue to scan the text file and repeat this process until it reaches the last filename.
% Once it reaches the last filename, the program will stop:

```
i = i + 1;
tline = fgetl(fid);
end
fclose(fid);
```

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