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CONQUERING TISSUE-SENSOR CONTACT -- *for* A Breast Cancer Detector

NSF Summer Undergraduate Fellowship in Sensor Technologies
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ABSTRACT

Current imaging diagnostic techniques demand better detection methodology to non-invasively monitor the angiogenesis of breast cancer. One of the emerging imaging techniques is to use near infrared (NIR) light to image the biophysical signs of cancerous tumor cells using optical spectroscopy. Two of the problems that arise from implementing such a method are optode-tissue coupling while fitting the contours of the breast and pressure equalization. The purpose of this project is to build upon the previous work in fabricating a device to counteract the two problems. Over the 10-week span of the SUNFEST program, an improved breast cancer detection probe has been designed, built, and validated.

This new prototype introduces two new components: Poron Quick Recovery Polyurethane Foam and a rigid delrin backing plate. The foam allows localized articulation at specific sites to fit the contours of the breast while the rigid plate aids in equalizing the pressures. Another vital advance of this device is implementation of an improved photodiode with 9.7mm * 9.7mm active area, which permits a high signal-to-noise ratio. Experiments have been conducted to validate this prototype and they have shown promising results. The next stage will involve clinical trials in monitoring angiogenesis *in-vivo*.

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1. INTRODUCTION

Breast cancer is the most malignant tumor and the leading cause of cancer death in the western world [1]. Early detection of breast cancer, which helps reduce the need for therapeutic treatment and minimizes pain and suffering, plays an essential role in reducing the mortality rate[2]. Current screening techniques for cancer detection include X-ray mammography, magnetic resonance imaging (MRI), and ultrasound [3] [4] [6]. However, due to morphologic similarity between benign and malignant lesions, these imaging modalities become less useful [7]. Consequently, most technicians resort to biopsies for definitive diagnosis. However, up to 80% of patients who undergo breast biopsies were discovered negative for malignancy [5]. Therefore, a better diagnostic technique is needed to prevent unnecessary biopsies, which cause patients to suffer from both physical and emotional trauma.

One of the emerging imaging modalities that show promising results of illuminating the biochemical processes of tissue is using near infrared (NIR) light as a source to non-invasively monitor angiogenesis with diffuse spectroscopic techniques. When practicing this technique, several problems arise; two of them are addressed by this project: optode-tissue coupling and pressure equalization throughout the surface of the breast.

2. BACKGROUND

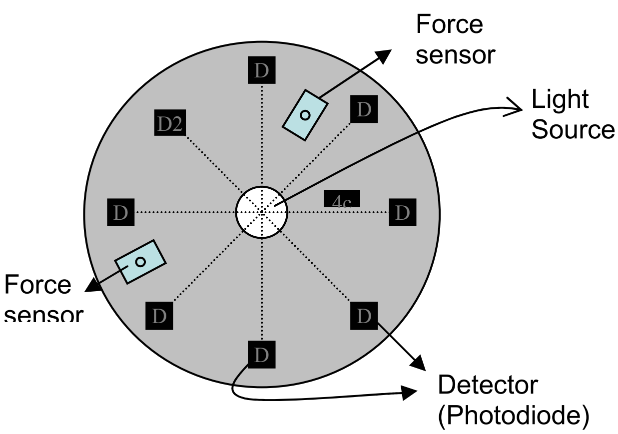

Figure 1 - The bottom view of the earlier breast cancer detection probe with an LED in the middle, which is flanked by 8 detectors to pick up the light information.

Earlier probe uses eight detectors, which are arranged in a circle, as illustrated in Figure 1. An LED is embedded in the middle of the probe to emit lights with three different wavelengths: 730nm, 805nm, and 850nm. This probe incorporates two force sensors to measure the pressures experienced in the vicinity of the detectors. Experimental trials show that it’s almost impossible to equalize pressure using only two sensors in such a probe. The fact that this device is hand-held increases the complexity of equalizing the forces, due to human hand trembling, difficulty in coordinating the forces exerted by each finger, and the high sensitivity of the force sensors.

Since the bottom of the probe makes direct contact with the breast skin, the placement and orientation of the force sensors causes a problem. The force sensor has a small metal ball protruding that pushes against the breast tissue, thereby imposing a point contact with the breast; this point contact induces pain on the breast under a relatively high pressure, even within the desire range of examination. In addition, this probe does not have any necessary components to avoid the air bubbles in-between the detectors and the skin.

The goal of this project is to build on the existing probe and improve it by eliminating the voids and the point contact with the breast tissue. In addition to addressing the two problems, affordability is also a goal of this project.

2.1 Identify the Scale of Force and Equipment Dimensions

Although the relationship between the importance of the exerted force on the breast surface and the accuracy of the cancerous cell detection has not yet been discovered, a study has been conducted to test the relationship between patient comfort level and blood pressure. It found that pressures of 60 mmHg and above result in insufficient blood supply to the tumor cells, which in turn result in inaccuracy of tumor detection as well as patient discomfort. A blood pressure of 10mmHg gives an optimal outcome for cancer detection under normal blood supply. Figure 2 illustrates the relationship between the size of the breast and the amount of weight applied to the breast at 10mmHg. The graph shows that the typical amount of weight to apply to the breast at 10mmHg falls between 50g to 350g, regardless of breast size. Therefore, for the scope of this project, the desired force applied to the breast surface should roughly be 0.49N to 3.5N, assuming gravitational acceleration.

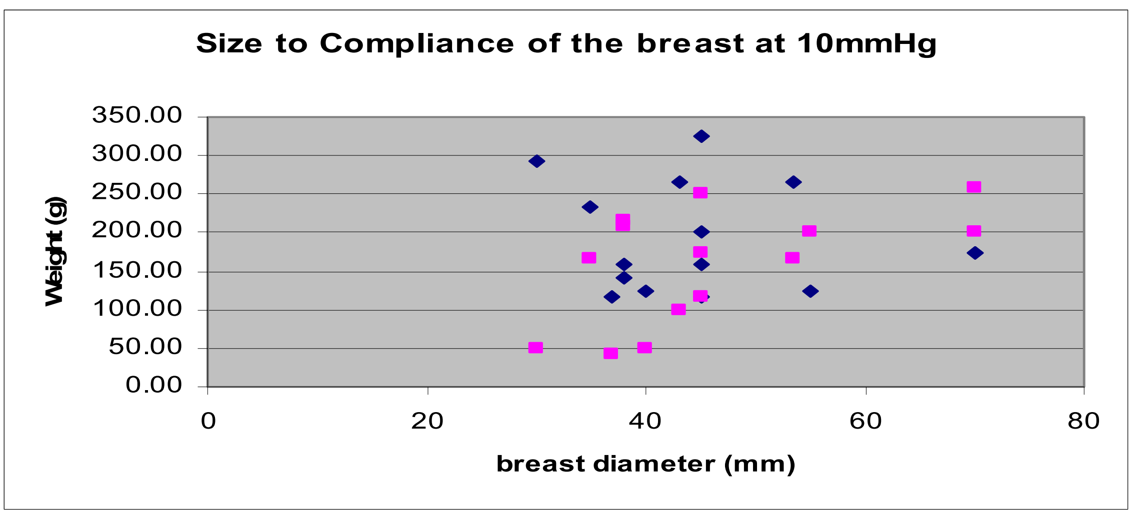

Figure 2 – A plot illustrating the relationship between the size of the breast and its compliance at 10mmHg pressure. This graph shows that the amount of mass applied to the breast is within 50g to 350g regardless of the size and firmness of the breast.

The photodiode and force sensor are approximately 10mm x 10mm x 1mm and 5.78mm*9.28mm*3.30mm, respectively. Knowing the scale of force and dimensions of the necessary equipment crystallizes the problems of this project, making them easier to attack.

3. POSSIBLE SOLUTIONS

Solutions to the problems must meet the following conditions: the probe must be an appropriate size to be hand-held; each sensors should detect similar, if not identical, force per unit area; and the probe must fit the contours of the breast.

3.1 A Preliminary Design

To equalize the pressures, programming may be the most convenient solution. A system incorporating a force sensor, an actuator and a microcontroller can be designed such that a threshold force is quantified prior to programming. The microcontroller can be programmed to communicate with the actuator and command it to exert a force on the force sensor, which pushes on the detector. Feedback is provided by the force sensor, which feeds the force information to the microcontroller. A basic sketch of this design system and the schematic of its working loop are shown in Figure 3. The actuator pushes the force sensor forward until the threshold has been reached. If the microcontroller detects that the force has not reached the specified threshold, it asks the actuator to stop pushing and maintain this amount of force.

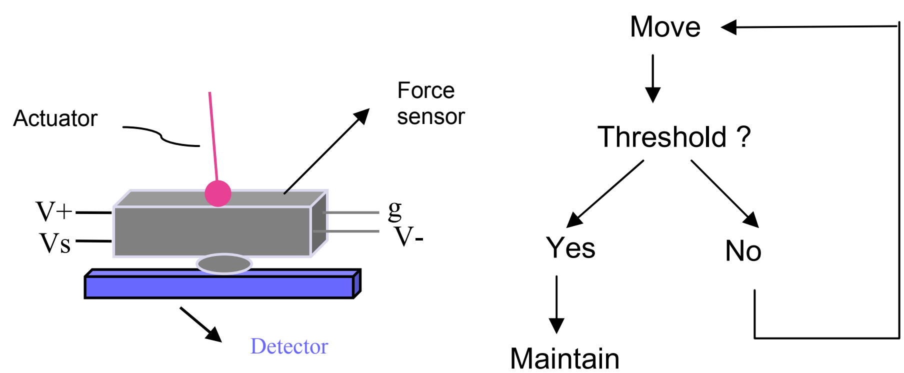

Figure 3 – A rough drawing of the preliminary design and an illustration of how this system works.

3.1.1 Pros and Cons of the Preliminary Design

Although the idea of programming simplifies equalization and eliminates the need to exert a force from human hands, its consequent problems seem to outweigh the benefits. One problem is overshooting the necessary force; this system cannot cope if the actuator exerts a force greater than the threshold. However, an immediate difficulty is to find an actuator that is small enough – preferably the size of the detectors - yet has the ability to produce a 1mm to 3 mm stroke and to block an approximated 3N of force, which was discussed in detail in section 2.1. A displacement of approximately 1mm to 3mm is assumed to be enough to deform the breast tissue for a reliable result from the photodiodes.

Another problem associated with this system might be keeping the probe in place. According to Newton's Law, when the probe is exerting a force on the breast, the breast is pushing the same amount of force back to the probe. The only counteracting force to the force exerted by the actuators comes from the weight of the probe itself, which might not be enough to prevent it from sliding off the breast. It's possible that the probe will slide far off to the sides of the breast, due to the actuated forces, causing the detectors to totally lose contact with the breast tissue. Since this design solves the problem by bringing out more problems, it is not ideal.

3.2 The Ultimate Design

A more practical and economical solution to the challenges faced by this project is to use foam, which is readily available to replace actuators, which are expensive and also hard to locate. The elastic property of foam allows compression and decompression, which is lacking in the preliminary design. A rigid backing plate is employed to accomplish the goal of pressure equalization. Although the forces might not be exactly the same at each of the eight sites, they should be close to each other with the aid of a rigid plate.

Figure 4 shows the basic layout of this design. The force sensor is on top of the photodiode such that the force experienced by the photodiode can be directly passed on to the force sensor for a more accurate analysis. The foam cushions between the force sensor and photodiode allow the diode to maneuver around and fit the contours of the breast.

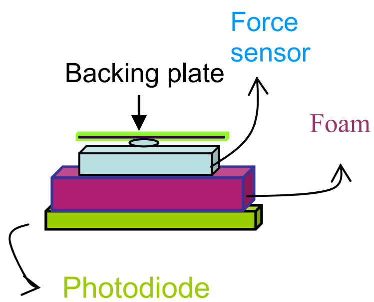

Figure 4 – A representative unit of the eight sites in the final design. The major components to this unit are labeled.

3.2.1 Materials Chosen

A vital and innovative component for this system is the foam and the backing plate, which work in combination to meet the design constraint. The Poron Quick Recovery Polyurethane Foam chosen allows instant recovery when compressed. This foam is made of an ether and ester blend that permits high-cycle compression loads. It has a firmness of 1-5 psi, which is relatively soft. To confirm that the Poron Polyurethane Foam has the characteristics needed for the probe, a simple experiment was conducted to examine the compliance of the foam. The experiment was performed by adding forces to the foam incrementally and observing the relationship between the grams of mass applied and the displacements. A plot demonstrating their linear relationship is shown in Figure 5. Since the data shows that the foam does not undergo plasticity within the desired range of force (100g = .98N, assuming gravitational acceleration), it is appropriate for this system.

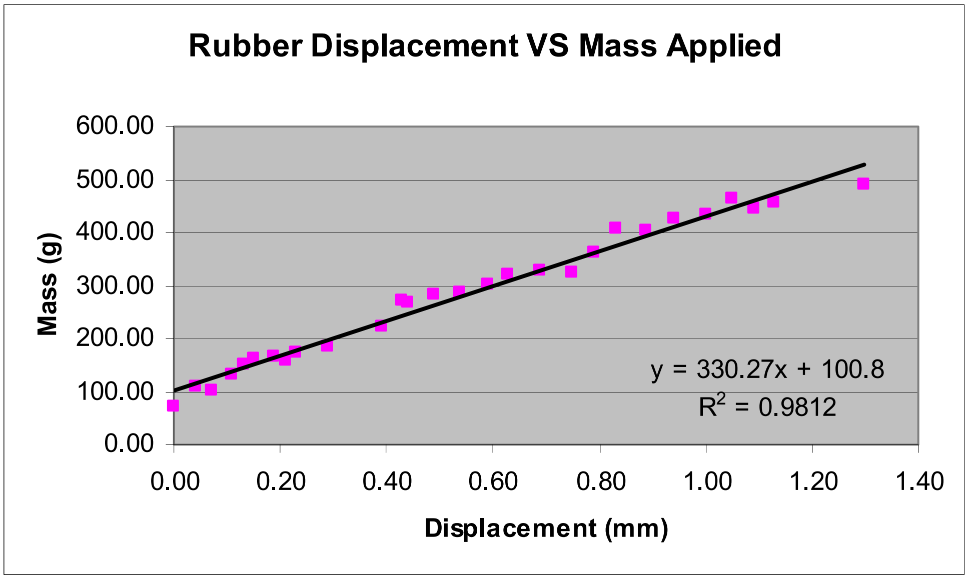

Figure 5 – Plotting of the foam's displacements versus the corresponding masses applied. This graph shows that this foam is appropriate to be used in the probe.

The material for the backing plate is delrin, which is rigid enough to spread the concentrated forces evenly to the eight sites. The force sensors used are the same as the ones in the older probe except that the point contact has been changed from skin to the backing plate. The photodiode chosen is FDS1010 supplied by Thorlabs; it has an active area of 9.7mm * 9.7mm which permits a higher signal to noise ratio than the OPT101 photodiode used previously, thereby allowing for a more accurate signal output.

4. FABRICATION OF THE PROBE

A completed prototype requires eight force sensors and eight photodiodes. For simplicity and testing purposes, only two of each are included in this prototype. The original design model drills two holes on the backing plate for the cable wires to go out through the plate allowing circuitry for the force sensors and the photodiodes to be connected outside the probe. This model was built at the machine shop, based on the design specifications, so that multiple probes can easily be fabricated if desired. The probe itself was molded using silicone rubber, because it is widely used for medical applications [8]. Figure 6 shows a cross-section of the probe to help in visualizing each of the eight units. The foam protrudes approximately 2mm from the bottom surface of the probe to free itself from encasing inside the probe, enabling the photodiodes to tilt. This length of the protrusion can be adjusted by stacking the foam of different sizes to different thicknesses. The foam avoids the spaces between the photodiodes and the skin by allowing for pressure changes without losing contact between the two.

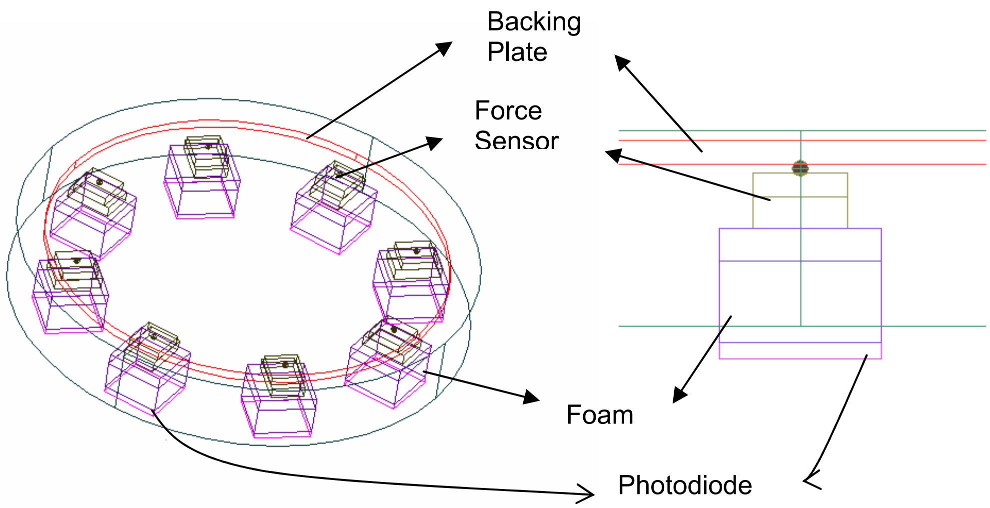

Figure 6 – Three dimensional view of the probe from a 45 degree angle from the x-y plane and a side view of one of the eight sites in the probe.

A differential circuit was built on a chip to amplify the output signal from the force sensors. This circuitry was designed with a gain up to the order of 20. The built-in Wheatstone bridge circuit in the force sensor transduces a potential difference across the outputs of the sensor whenever the metal ball is depressed and a force is detected. The circuit amplifies this voltage difference 20 times to eliminate the noise from the internal impedances of the force sensor and displays the reading on a digital voltmeter.

The circuitry for the photodiodes, which was built previously for a senior design course, serves as a converter to transform the current to voltage and amplifies the output. An RC low-pass filter using 8pF and 1MΩ resisters was also included in the circuit after the output voltage amplification to eliminate high-frequency noise.

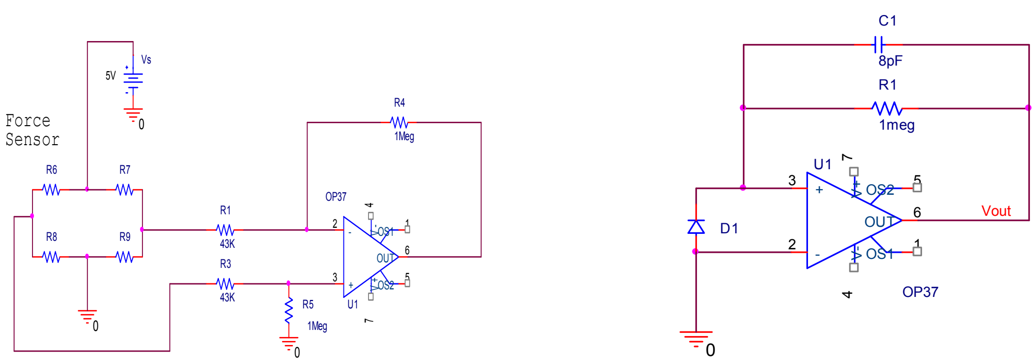

Figure 7 – Circuits used for the probe. The differential circuit on the left is for the voltage output of force sensors and the circuit on the right acts as an RC low-pass filter for the output of photodiodes.

Soldering also plays a major role in fabricating the probe. The four leads of the force sensors need to be bent upwards to fit the rectangular cases of the probe before soldering the wires. Epoxy was applied to all the soldering sites of the wires to prevent detachment of wires. All the circuits were tested on a breadboard and later transformed onto a chip by soldering.

5. EXPERIMENTAL SETUP

Three experiments were conducted to examine the operational behavior of the probe. The major components for the experimental setup were labeled in Figure 8. These components include: a power supply for the force sensor circuit, a control box to convert the output signal from the photodiodes to a computer program, and a laptop for display. The output from the force sensors was displayed on the digital voltmeters on a circuit board, whereas the voltage output from the two photodiodes was displayed on a laptop screen via a control box. Three filters with different absorbance were used for the first preliminary test; objects with known masses and five sand bags of about 100 grams each were prepared for the second and third tests as sources of force.

The first experiment was performed specifically to examine the photodiodes' sensitivity to absorbance of the filter paper. The second experiment measured the behavior of the force in response to added weight. The third experiment involved a human subject to test how well the photodiode could respond to incremental weights when testing the probe on the human skin. During the third experiment, the subject was on a supine position with the probe on her abdomen area, which resembles the breast in its fatty characteristic.

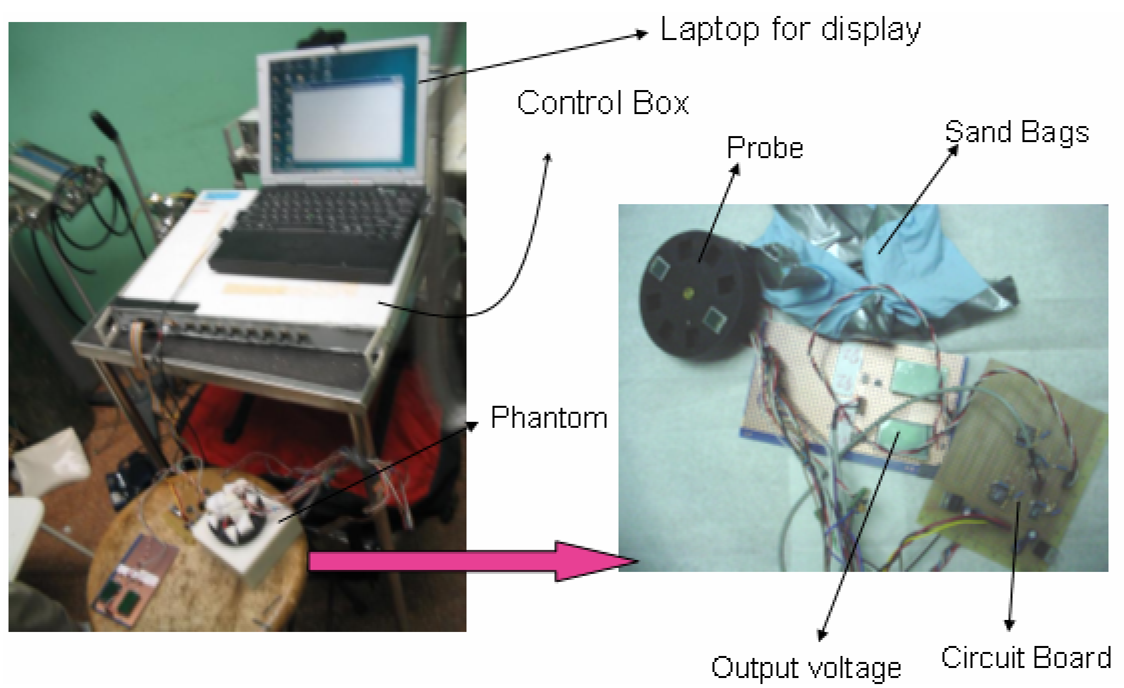

Figure 8 – Components for the experimental setup are labeled above on the figure. The picture on the right is an enlarged view of the probe and the sensor circuit.

6. EXPERIMENTAL RESULTS

The result from the standardized filter test is graphed in Figure 9, which plots the output signal from the photodiodes in mVs against the number of points recorded. Data collection started with a baseline without any light filtration and proceeded by testing the probe on three filter papers with absorbance $0.1mm^{-1}$, $0.2mm^{-1}$, and $0.3mm^{-1}$.

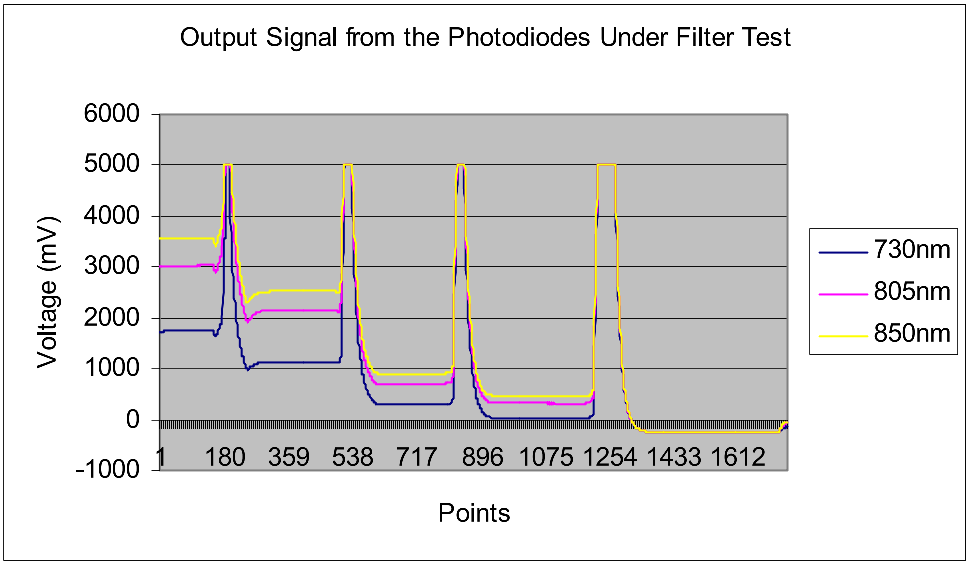

Figure 9 – Plot from the filter test for photodiodes at wavelengths 730nm, 805nm, and 850nm. This graph shows that the detectors were sensitive to different absorbance.

Experiment two specifically examined the output of the force sensors. Its result is shown in Figure 10, which displays a linear plot of the mass added to the probe against the voltage output from the two force sensors.

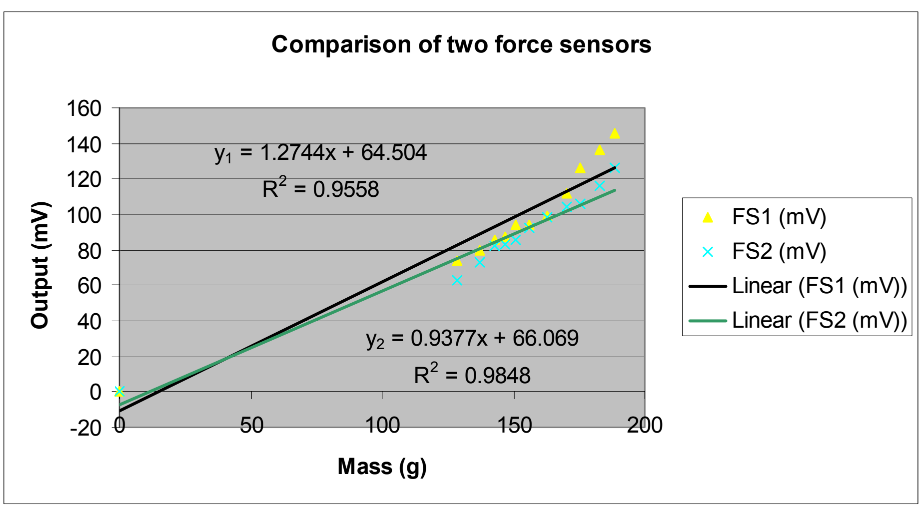

Figure 10 – Graph of output signals from the force sensors versus grams of mass added.

Figure 11 and figure 12 are both graphed from the abdominal test. Figure 11 combines the voltage output from both the force sensors and the photodiode together by extracting the points at each increase of 100 grams. By comparison, figure 12 is an enlarged view of the signals from the photodiode alone to closely analyze the voltage output from the diode. Note that each arrow indicates an increase of 100g mass.

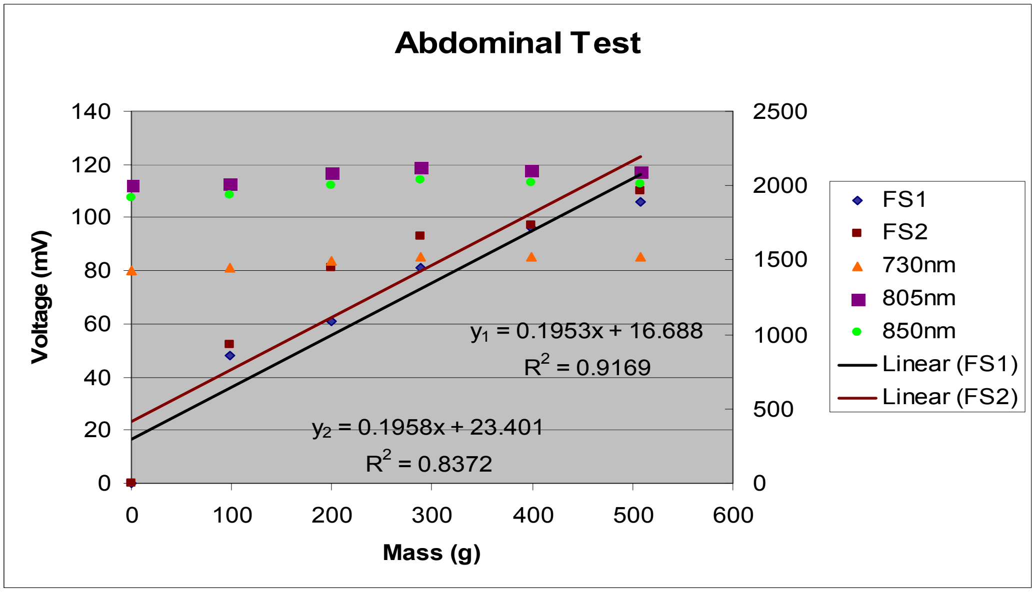

Figure 11 – Experimental results from the abdominal test, which examines the function of the probe on human skin.

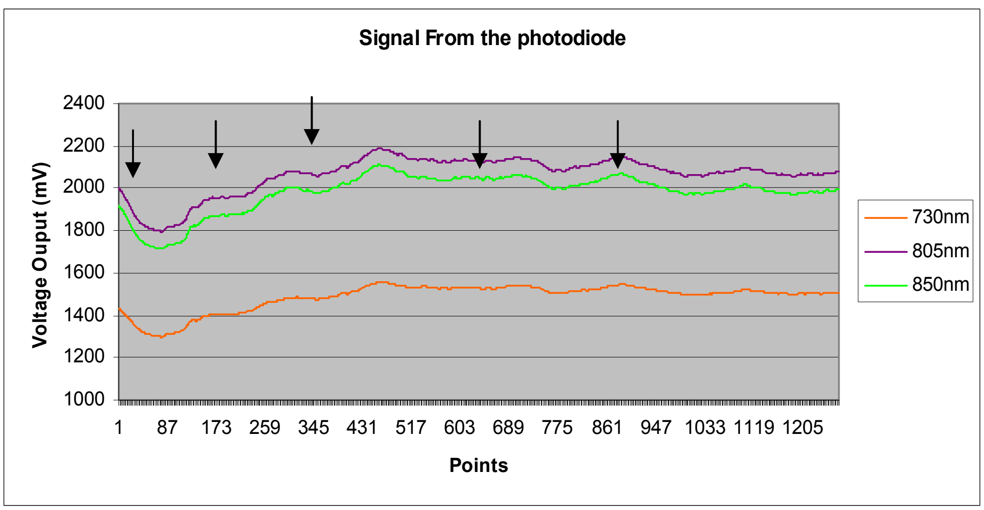

Figure 12 – An enlarged view of the signal output from the photodiodes under abdominal test.

7. DISCUSSION

The result from the filter test demonstrates that the photodiode has a higher output when the light absorbance is small. There are four spikes on the graph; when switching the filter paper, the diodes detect dim room lights in the media. Under normal condition without any light filtration, the signal output is the highest. As the filter papers with increasing absorbance are used, the output gets smaller and smaller. Such a result is reasonable because high absorbance lessens the light transmission, leaving a smaller voltage output signal.

The results from the force sensors suggest that the two sensors have output readings close to each other. Both show a linear relationship between grams of mass and the voltage output. It seems as if the gain is bigger at higher forces for both force sensors. This may be because the force sensors might behave a little differently from each other. The output amplification may also augment this difference. In the abdominal experiment, the two force sensors have the same slope with a small offset. The reasons for their unexpected behaviors may be random, such as the nonzero voltage output under no force and the different slopes displayed by the two force sensors. First of all, the high sensitivity of the force sensors alters the results when the orientation of the wires is different. Second, the internal impedances of the transducers itself may differ from one another. After a number of trials, it has been ascertained that when the operator accidentally moves the cable wires, the reading on the digital voltmeters differs immediately without changing the force added to the probe. It is reasonable to believe that the torque produced by twitching the wires puts additional force on the force sensors and the photodiodes may not anticipate this unexpected force, resulting in experimental errors. In addition, there are frictional forces between the foam and the walls of the probe, which can also be a contributing factor to the slight output difference of the two force sensors.

The results from the photodiodes in the abdominal test seem reasonable. Output is minimal at no force. When 100g sand bags were added to the probe one after another, the signal increased linearly until the fourth one. After that, the output seems to level off. One possibility is that the blood vessels keep narrowing as they accept the first 300 grams of weight, and the output signals increases linearly as a result. The fat in the abdomen cushions the blood vessels after 300 grams, protecting them from narrowing further due to the force increase. So from that point on, the output signal fluctuates randomly. These three experiments give sufficient evidence that the probe works as expected although some experimental errors contaminated the force sensor outputs. Overall, the renovated prototype has operational improvements over the previous one.

8. RECOMMENDATIONS AND CONCLUSIONS

There are several things that can be done to improve on this prototype. The most important and challenging one is to minimize the friction between the walls of the probe and the foam to get a more accurate result from the force sensors. The difficulty encountered in doing so is as follows: friction is necessary to tightly encase the foam in the probe, however it might cause random force change. Reshaping the foam such that only four corners of the rectangular foam push against the walls to keep the pieces of each unit in place can greatly reduce the friction force while remaining the required tension to ensure that the foam does not fall out of the probe.

A second improvement to this prototype is to use an improved amplifier specifically designed for differential circuits. There is no null offset to the force sensor circuitry right now, making it hard to compare the outputs of the two force sensors. Starting all the force sensors at the same reference voltage, preferably 0 mV, will make it easier for the operator to compare the voltage outputs. A bigger improvement would be to display the voltage readings on a computer screen, graphing the results in lines, instead of point readings, and placing it adjacent to the photodiode output. This would eliminate the digital voltmeter on a circuit board and also enable automation.

At present, the weight of cable wires is believed to be an error factor for the force sensor output. An optimal output may be attainable by switching to thinner and lighter wires, thereby imposing less weight and less torque on the force sensors. Packaging of the probe also needs to be improved so that no wires can be seen by the patients. The appearance of the probe directly affects its potential to be involved in clinical trials for further validation. One possible solution to the complex wiring is to use telemetry. As an alternative to cable connections, Bluetooth should be considered for wireless communication. In the future, we hope to commercialize this device at an affordable price. The ultimate goal of this project is to be able to provide patients who suffer from breast cancer with better imaging and diagnostic techniques.

9. ACKNOWLEDGMENTS

I want to thank everyone in Chance's lab, especially Juan Du and Kiran Gangavarapu, for their kindness and encouragement in making my SUNFEST experience a memorable one. I would like to extend my gratitude to Dr. Britton Chance for his advice, patience, and dedication to this project. I also appreciate Michael, who works at the machine shop for his technical support. Thanks to the National Science Foundation for their support through an NSF-REU grant and Microsoft Corporation for their financial support. Without any of them, SUNFEST would never be possible.

10. REFERENCES

1. American Cancer Society, Available from http://www.cancer.org/docroot/CRI/CRI_2_1x.asp?dt=5, accessed 31 July 2004.

2. C.C. Boring, T.S. Squries, T. Tong, Cancer Statistics, *CA Cancer J. Clin.*, 44 (1994) 7-26.

3. G. Simonetti, E. Cossu, M. Montanaro, C. Caschili, V. Giuliani, What's new in mammography, *Eur J Radiol,* 27(1998)S234-S41.

4. J. Elmore, M. Barton, V. Moceri, S. Polk, P.J. Arena, S.W. Fletcher, Ten-year risk of false positive screening mammography and clinical breast examinations, *New Engl J Med,* 338(1998)1089-96.

5. R.P. Burns, Image guided breast biopsy, *Am J Surg,* 73(1997)9-11.

6. Silicone Rubber, Available from http://www.azom.com/details.asp?ArticleID=920, accessed 31 July, 2004.

7. S.L. Edell, M.D. Eisen, Current imaging modalities for the diagnosis of breast examinations. *Del Med J,* 71(1999)377-82.

8. Y. Zou, Z. Guo, A review of electrical impedance techniques for breast cancer detection, *Medical Engineering & Physics,* 25(2003)79-90.