Failure Detection in Embedded Biomaterials

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Abstract

Recent advances in the field of biomaterials open doors for various medical applications such as organ replacement, tissues repair, and drug delivery system. Currently, there exists no perfect method to detect failure in embedded biomaterials. The goal of our project is to determine a method that exploits a change in the intrinsic property of the biomaterial as it reaches failure. The method should be able to detect failure regardless of the tissue's response to the biomaterial. After analyzing three proposed solution s – impedance spectroscopy, microwave tomography, and elastography – we concluded that elastography is the most feasible method. Due to several limitations, we took advantage of mechanical testing to simulate elastography testing. We observed the viscoelastic response of the biomaterial of interest. In the future, we will perform ultrasonic based testing to confirm our hypothesis of using elastography to detect changes in stiffness of biomaterials as it reaches failure.

Background

Biomaterial is any material which is designed and built for the purpose of medical applications and interaction with biological systems. Currently materials such as metal, polymers, ceramics and biologically derived are widely used, alone and in combination, to build biocompatible devices. Advances in the field of biomaterials have led to numerous applications such as replacement of nonfunctional organs, repair of damaged tissues, and delivery of medications. Examples of current clinical uses of biomaterial are artificial arteries, pacemakers, hip replacement, prosthetic skin and the latest development in anti-cancer drug delivery system.

Exposure of biomaterials to living tissues can cause changes to the intrinsic properties of the biomaterials as well as initiate various host responses. Typical changes to an embedded biomaterial involve physical, chemical, and structural components. Similar to any other man-

made devices, biomaterials posses a finite life-time and thus failure is unavoidable. At the point of failure, embedded biomaterials will require immediate removal or repair. A fast and accurate diagnosis of failure within embedded biomaterials is pertinent to avoid adverse host response such as inflammation and auto-immune diseases which can be harmful to patient's health.

Problem Statement

Various biomaterials are being installed and embedded within biological system. The wear and tear of these biomaterials will cause changes to its intrinsic properties. Currently, a device that can measure a parameter with high specificity and selectivity in detecting failure within embedded biomaterials is unavailable. The goal of this project is to determine a specific property of a biomaterial that changes as it reaches failure. We will determine a method to detect and quantify this change in property non-invasively. In the long term, our goal is to design a device that will reliably measure property changes so as to determine biomaterial failure.

Competition

The current FDA approved technique for failure detection of some types of biomaterial is the magnetic resonance imaging (MRI). MRI shows inflammation within the biological tissue in response to biomaterial defects rather than the specific property change within the biomaterial itself. Advances in biomaterials however have minimized the chance of inflammation thus decreasing the efficacy of an MRI scan. MRI can image structural changes within a biomaterial although with limited contrast. Moreover, the use of MRI is limited to non-metal based biomaterials. The biggest downfall of MRI as a failure detection method is the expensive cost that typically is several thousand dollars per scan.

Another method of failure detection of biomaterials is x-ray tomography. X-ray scanning detects density differences between tissues and biomaterials. Unfortunately, biomaterials failure

does not always correspond to drastic density changes. X-ray does however give images with high contrast and can be used to detect obvious structural changes in embedded biomaterials. In addition, X-ray scanning is relatively low cost compared to an MRI scan, ranging in the hundreds of dollars.

Design Requirements

As mentioned in our problem statement, we are looking for a non-invasive method to detect failure within embedded biomaterials. The method of detection should be based on changes in the intrinsic property of the biomaterials itself, regardless of variations occurring in the surrounding biological tissues due to host response. Due to the time constraint of the semester, we will focus on a specific property change to be detected and a well tested method to effectively detect these changes. In the future, we are hoping to design a hand-held device based on the knowledge gained this semester that will be appropriate for the clinical setting. The integration of our future prototype into clinical use is intended to reduce the cost per testing to be less than $500. In addition, our goal is to produce an output that can be directly interpreted by the primary physician.

Design Proposals

I. Impedance Spectroscopy

The first idea of detecting failure in biomaterial by way of measuring changes in skin surface impedance was proposed by our client. Different materials possess different impedances which depend on their characteristic properties such as geometry and atomic structure, Impedance spectroscopy is a powerful method and has various applications in the field of bioinstrumentation due to its ability to investigate the activity of charges in the bulk or interfacial regions of any kind of material regardless of its state (Macdonald, 1987). Therefore, as an

embedded material undergoes any structural or electrical changes due to failure, the changes in impedance can theoretically be detected noninvasively by way of body surface electrodes. An example of impedance spectroscopy application is the impedance plethysmography. It is used to measure thoracic impedance that can be correlated to the air volume in the lungs. In order to apply this theory for our project; it is crucial to use a high frequency ac source, in the range of 100 kHz, to protect the heart from fibrillation, since human heart is very sensitive to low frequency currents (Webster, 2004).

The circuit design for measuring the impedance of a certain object is quite easy to build. All elements needed for the circuit are available in bioinstrumentation laboratory: resistors, op-amps, wires and an ac generator. This simple circuit gives a good outlook at the possibility of constructing a hand-held prototype, which is ideal for our client. However, biomaterials often have significantly higher impedance than our physiological body fluid, which has a pH of 7.4 and consists of mostly free flowing ions. Therefore, if current is applied by way of skin electrodes, it will take the path of least resistance, through the free flowing ions, rather than through the biomaterials, shown in figure 1. Due to this fact, it is unlikely that we will be able to detect the impedance of biomaterials surrounded by physiological fluid, intact or otherwise.

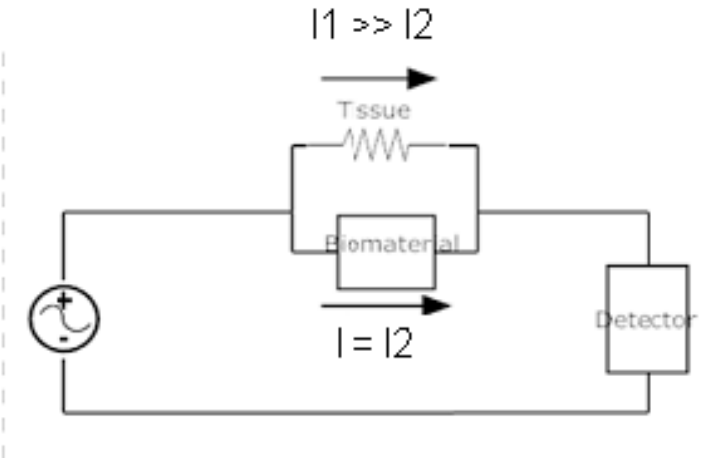

Figure 1. *Basic circuitry for impedance spectroscopy*. The figure demonstrates the basic idea behind impedance spectroscopy. Since the biomaterial and the surrounding tissue are effectively two resistors in parallel sequence, current will choose the branch with smaller resistance when the other branch's resistance is significantly higher.

II. Microwave Tomography

The principle behind microwave tomography is the detection of the difference of dielectric properties between biomaterials and biological tissues. Dielectric property is commonly used to describe how an electromagnetic field behaves inside a particular material. An important component of a material's dielectric property is the relative dielectric permittivity which measures how effectively an electromagnetic wave can move through the material of interest. Potential effectiveness of microwave tomography is dielectric properties of a material which are highly dependent on the surrounding physiological conditions. Examples of these physiological conditions are the material's molecular constituent, ion concentration and mobility, water concentration, and temperature (Smenov, *et al.*, 1996).

The detection of the difference in dielectric properties is done by exposure of the tissue to an electromagnetic field. As electromagnetic wave hits the interfaces of two materials with different dielectric properties, fraction of the wave will be transmitted while the rest will get

reflected. The reflected electromagnetic wave can be used to reconstruct an image of a particular tissue and biomaterial of interest and thus possibly detect failure on the biomaterials. Figure 3 shows a block diagram of a typical microwave tomographic system.

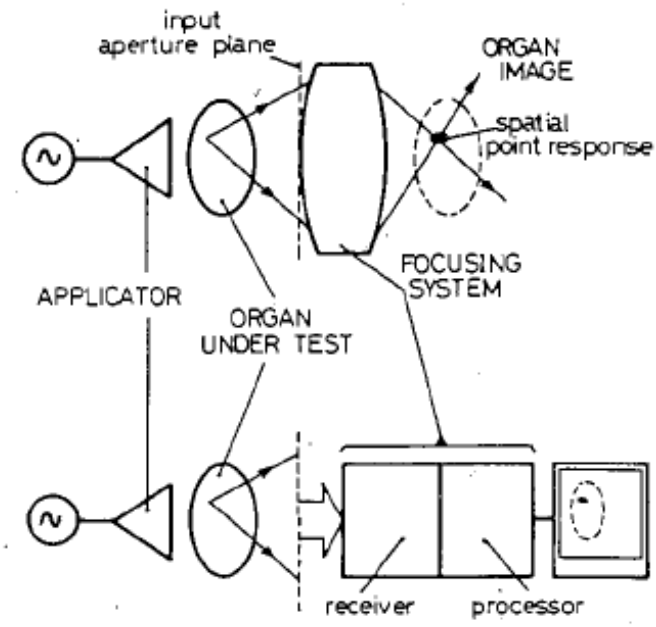

Figure 2. *Principle of microwave tomography.* A applicator or signal generator deliver electromagnetic wave to area to be imaged. The reflected electromagnetic wave is picked up by a receiver and processed to create reconstruction of area of interest. (Guerquin-Kern *et al*. 1985).

The microwave frequency, ranges from 300 megahertz to 300 gigahertz, is chosen due to the high contrast between tissue and biomaterial dielectric properties within this spectrum. In the microwave region, tissue and biomaterial dielectric properties can differ by about five fold, which would correspond to high contrast in the reconstructed image (Lezebnik, 2008). Microwave tomography is an emerging technology in tissue ischemia and cancer detection.

Advantages of this method include safety and high degree of contrast. In the microwave region, the energy of photons is small enough to avoid ionization effects, which means that the exposure to the electromagnetic field during imaging will not cause the tissue harm. Moreover,

the amount of exposure the field is comparable to that during appliance and cell phone use. The high degree of contrast in the reconstructed image due to large difference in tissue and biomaterial dielectric properties improves the specificity and selectivity in detecting failure within the biomaterial. In addition, data on dielectric properties of various materials are readily available in the literature or can be measured easily.

Microwave tomography however has several disadvantages. The greatest disadvantage comes from the fact that microwave tomography is still at its infancy and relatively unavailable outside the world of academic research. The complexity of building a microwave tomography apparatus is beyond our skills and currently, there exists no laboratory group on campus that owns a full fledge microwave tomography apparatus. Mathematical analysis is possible however to theoretically test the degree of reflected wave, and with it the contrast in the reconstructed image, upon collision with tissue-biomaterial interface. Another disadvantage of this method is that tissue dielectric properties can be very sensitive to changes in physiological condition which would result in highly complex calibration procedure.

III. Elastography

Elastography is a medical imaging technology that can contrast different materials based on differences in stiffness. Based on an ultrasound technique, it uses echoes of high frequency sound waves. As high frequency sound waves penetrate the skin and hit various organs and tissues significant amount of the original waves will be reflected back from the boundaries of tissues and objects that have different acoustic impedances. These reflected sound waves, echoes, can be collected and processed to reconstruct images of organs and tissues in which the sound waves have penetrated. The difference between the elastogram and sonogram (the image created using normal ultrasound) is an additional image taken during pressure application by the

transducer. During pressure application, each type of tissue behaves differently according to its relative stiffness. Combinations of these two images will therefore produce an image with a higher contrast than a typical sonogram, as illustrated in figure 2.

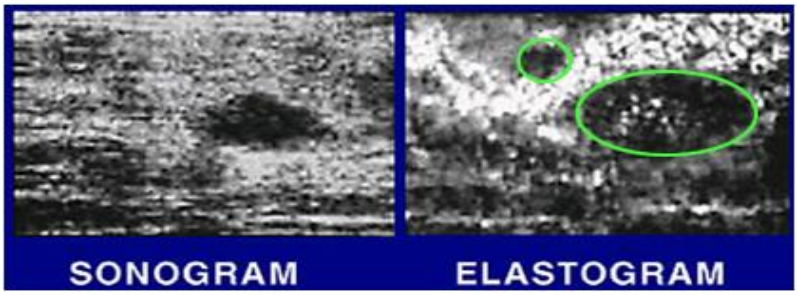

Figure 3. *Comparison of sonogram and elastogram*. In the sonogram, malignant tissue is shown in darker shade. After an elastogram is obtained, a larger and more defined area of the malignant tissue is observed as well as a smaller secondary growth. (Layton, 2006).

Elastography is currently being widely researched to detect breast cancer. Since cancerous cells are naturally much stiffer than normal and benign cells, any malignant growths can be easily detected by pressure application since little deformation will be seen and the corresponding image will be noticeably different than normal tissues on the elastogram (Itoh, K. *et al*, 2006). For example in fig.2 above, the sonogram shows a dark circle that is suspected to be cancerous tissue, while the elastogram proves that it is malignant since it does not undergo deformation like the surrounding normal and benign tissues. It is observed that the tumor is significantly bigger than the initial suspicion. In addition, there is an additional small tumor on the upper left hand corner of the primary one (Layton, 2006).

Certain biomaterials will undergo conformational changes as they reach failure (Ambay, 2008). Therefore we propose to test the possibility of using elastography to detect this change to verify the intactness of the biomaterial. Elastography is proven to be very sensitive (up to 10%

contrast) and therefore, even a slight deformation in the embedded material due to applied pressure during elastography testing will be detectable. Moreover, since practically every hospital is already equipped with at least one ultrasound system, and there are several professors who are conducting research on elastography on campus, we will be able to get access to these systems and run preliminary testing using a simple phantom. By examining different transducers and pressure sensors on phantoms with various stiffness, we will determine the optimal wavelength to detect failure in the embedded biomaterial. If the method proves to give promising results, it will help reduce cost for patients, since each elastography scanning costs approximately $100 - $200. Moreover, the result will be available for immediate diagnosis, and appropriate treatment can be given as needed.

However, the technique also has some disadvantages. The ultrasound system itself is very expensive (approx. $250,000) and in addition, accommodation of elastography will require multiple transducers and additional pressure sensor. It is also a complicated technique to be integrated into a hand-held device as required by our client. Moreover, the result must be interpreted by a trained technician, and this may cause additional expenses for the patients.

Design Evaluation

In selecting a final method to detect failure in biomaterials, we created a matrix with six criteria weighted based on their importance to design constraint. Feasibility plays the most important role in our method selection since it is highly imperative for us to gain access to the technology in order to test the ability of the method to detect biomaterial failure within the allotted time. Accuracy and cost are weighted heavily and equally since the motivation of this project is both to reduce cost and increase accuracy from the current methods used to detect

failure in biomaterials. In addition, the equal weighing corresponds to the fact that we will not sacrifice accuracy for the sake of cost.

Each alternative method was evaluated on a scale out of ten for each criterion with a maximum tabulated score of 10 for the perfect method. The result of this evaluation is shown in Table 1.

Table 1. Design matrix used to evaluate alternative technologies

Category	Weight	Impedance Spectroscopy	Elastography	Microwave Tomography
Feasibility	.30	1	9	8
Accuracy	.20	1	7	9
Cost	.20	9	7	5
Availability	.10	8	8	2
Non-Invasiveness	.15	6	8	8
Accessibility	.05	8	6	6
Total		4.4	7.8	6.9

After rating all three alternative technologies, we found that the elastography scored the highest based on its feasibility and availability. Therefore, this method will be pursued throughout the rest of the semester.

Testing and Results

Per suggestion of Professor Timothy Hall, we decided to conduct basic mechanical testing in order to obtain fundamental information regarding whether any difference in properties

might be detectable using elastography. After several consultations with Professor Vanderby, Professor Lakes, and Hirohito Kobayashi, we settled on stress and relaxation testing. This test is mainly done to observe the viscoelastic behavior of our biomaterial. Since elastography contrast materials based on differences in stiffness, we can use the result of this test to get a rough estimate of the material's stiffness. In addition, we should be able to see the change in the viscoelastic behavior betweenthe intact and failed biomaterial

Viscoelasticity is the property of materials that exhibit both viscous and elastic behaviors when undergoing deformation. Viscous material resists strain linearly with time when a stress is applied, while elastic material strain instantaneously when deformed and return quickly to its original state once the stress is removed. Viscoelastic materials demonstrate both of these properties when exposed to stress and consequently will exhibit a characteristic shape of logarithmic function in its force versus time curve.

The set up of our test is shown in figure 4 below. We set the deformation of the biomaterial to be 15% of its original height. The original height of our sample was measured to be 37 mm, therefore we controlled the deformation to be 5.5 mm. The decrease in stress or load is recorded over prolonged period of time as the material relaxes to its original state. The result of this test is shown in figure 5.

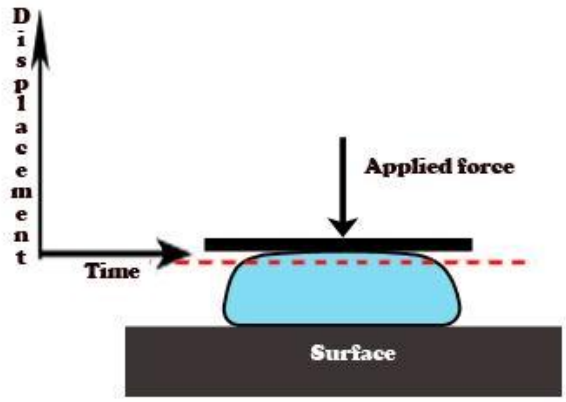

Figure 4. *Stress and relaxation testing diagram.* The testing machine was set up to compress the biomaterial up to 85% of its original height. The changes in force as the biomaterial relaxes to its orignal state was then recorded.

We observed the viscoelastic behavior from the force versus time graph. The sudden increase of force that is accompanied by a logarithmicdecrease of force in magnitude as the material recovers to its original state is the characteristic of a viscoelastic material. The information gathered from this testing was used to calculate the structural stiffness of the material (force divided by displacement): 4000 N/m.

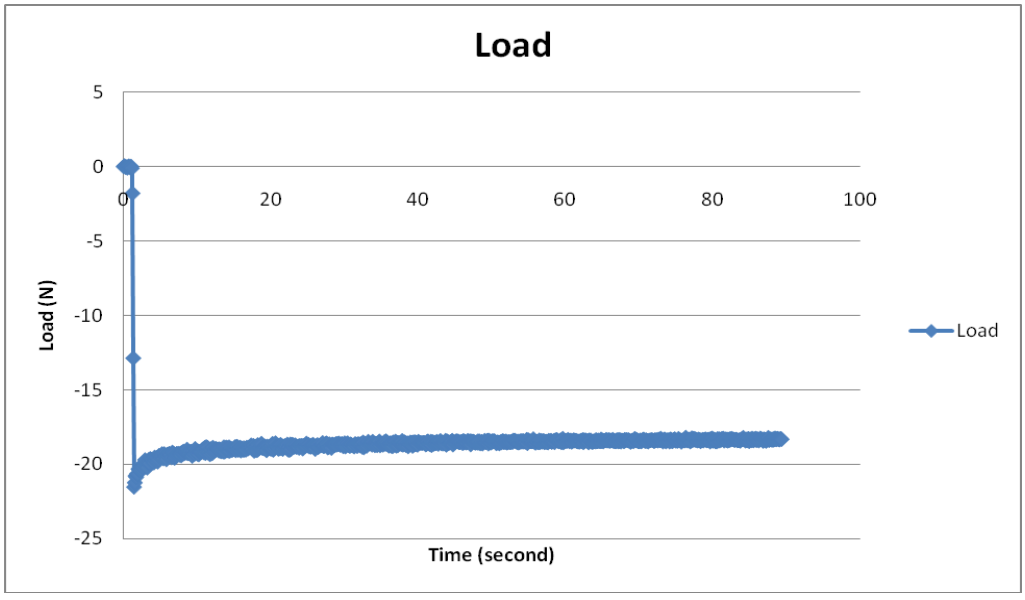

Figure 5. *Result of stress and relaxation testing.* From the plot of time versus force response as the biomaterial relaxes, we observed viscoelastic response characterized by the logarithmic decrease of force in magnitude.

Originally, we had planned to conduct this same test on the failed biomaterial. The idea being that we would used the test that we had conducted as the baseline measurement. However, we were unable to obtain a phantom that mimics the in vivo environment of the biomaterialon time. Withoutthe phantom, we will not be able to collect any physically meaningful data for the failed biomaterial. The reason being the fact that an embedded failed biomaterial will be contained by its surrounding tissue. A result of a test without a restricting environment will be significantly different than that of embedded biomaterial.

Design proposal

Based on the design matrix, we have chosen to develop a design that applies elastography technique to detect the changes in stiffness of the biomaterial as it reaches failure. Since the access to ultrasound-based testing was very limited, we took advantage of mechanical testing to simulate elastography detection of the changes in biomaterial viscoelastic response as it reaches failure. The following idea is not necessarily a design but more of a proposal and future work since we were not able to confirm it experimentally.

First of all, we would like to corporate the phantom designed by Professor Ernie Madsen to our mechanical testing. Since the phantom will imitate the physiological environment closely, we would be able to test the viscoelastic responses of the implant as it is still intact and as it is damaged within the body. The data collected while it is still intact will be used as a base line for comparison. Then, we would conduct series of testing, naminglystress-relaxation test, strain-time dependence test and creep test, for quantitative data on degree of failure. There are several variables that we must consider, which are the severity of failure and its position on the biomaterial. Currently, there is no literature statistic showing the minimum degree of damage that can be detected non-invasively, while our client would like to know as soon as there are any

abnormalities. Based on the information given to us by Professor Lakes, mechanical testing could only detect the difference in viscoelastic response when the rupture has a size of centimeter scale, while elastography would be able to show the changes in micrometer scale (Lakes, 2008).

After we are able to confirm the feasibility of our hypothesis on mechanical testing, we will integrate our data into ultrasound-based testing. Hopefully in the period of six months from now, the ultra sound probe with a pressure sensor will be available for our testing and design. With elastography, we would also conduct series of testing similar to our mechanical testing to quantify the data and determine the minimum sensitivity that elastography can achieve. Ultrasound based systems are currently available in any hospital, so we will be able to conduct our *in vivo* testing for more reliable conclusion.

Since elastography is a technique that still depends on image interpretation, we would like to design a hand-held device that could eliminate this dependency and only give us signals indicating the state of the material, meaning intact of failed. The device will then be incorporated into clinical setting. Furthermore, we would like to design a device that is similar to a home glucose meter, in which each patient can own one for a more frequent self-testing than the recommended semi-annual check up

Limitation

While working on this project, we faced several limitations, which hindered us from finishing our project. First of all, according to Professor Hall, this project requires a developing ultrasound transducer with an integrated force and pressure sensors. Unfortunately, this transducer would not be in market for another 6 months to 2 years. This new transducer will

allow us to determine the pressure and force applied on the area of interest while elastography is performed. This transducer will be the main component in designing a simple handheld device.

Also, due to the limited access to ultrasonic system, we were unable to test our hypothesis experimentally. Additionally, most important information related to this project were not available to us due to intellectual property , therefore we did not have data on the basic properties of the biomaterial, as well as the results of various experiments done by multiple parties who are involved in this project. In conclusion, this project will require a long term research in order to ultimately design the desirable hand held device.

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Project Design Specification

May 6th, 2008

Team Members: Rexxi Prasasya, Chou Mai, Hyungjin Kim

Problem Statement: A variety of biomaterials are currently being installed and embedded within biological system. The wear and tear of these biomaterials will cause changes to its intrinsic properties. Currently, a parameter and device with high specificity and selectivity in detecting failure within embedded biomaterials are unavailable. The goal of this project is to determine a specific property of biomaterial that changes as it reaches failure. We will determine a method to detect and quantify this change in property non-invasively. In the long term, we are hoping to design a device that will exploit these properties difference..

Client Requirements:

1. Detect a specific property change on the biomaterial, regardless of the host response.
2. Determine a proper, non-invasive method to detect the differences in property determined in item one.
3. Method should be operable by a primary physician without consultation with expert, such as radiologist.

Design Requirements:

1. Physical and Operational Characteristics

a. Performance Requirements- Used frequently as a part of routine check-up.

b. Safety- The method must be non-invasive. Method and product use may require FDA approval.

c. Accuracy and Reliability- Precisely determine the state of the biomaterial quantitatively and deliver qualitative output (answer) to the physician.

d. Shelf Life- N/A.

e. Operating Environment- The method must be compatible with hospital environment.

d. Ergonomics- N/A.

e. Size and Shape- N/A.

f. Weight- N/A.

g. Materials (for testing procedure)- Gelatin, biomaterials sample, apparatus depending on the method use.

f. Aesthetics N/A

2. Method Characteristics:

a. Quantity- One working and well tested method by the end of the semester.

b. Target production cost- $1500 for the initial testing of the method.

c. Testing procedure- Initial qualitative and quantitative testing should be done on phantom.

d. Output- Method should be able to quantitatively determined failure and convert the result to a qualitative answer for the primary physician.

3. Miscellaneous:

a. Standards and Specifications- Obtain FDA approval.

b. Customer- The customer (primary physician) will use the product on daily basis.

c. Patient-related concerns- Maximum cost of $500 per check-up.

d. Competition- MRI and X-ray scans.