

OBJECTIVE MEASUREMENT OF PERIPHERAL EDEMA AS SYMPTOMATIC OF CONGESTIVE HEART FAILURE

by

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Congestive heart failure is a type of cardiovascular disease that is often accompanied by excess fluid buildup in tissue, causing swelling of the extremities, known as peripheral edema. Assessing the severity level of pitting, or indentation, in peripheral edema can potentially provide insights about one's heart condition. When clinicians use digital manipulation to assess severity, the measurements are subjective. Objectifying measurements requires standardization so the severity score reported is both reliable and consistent across providers.

The HeartSMART system was developed to calculate the level of peripheral edema via four factors: the depth (displacement) of the skin, the force exerted on the skin, the surface temperature of the skin, and body weight. The specific aim of this project was to begin the process for developing an algorithm that could provide an overall standardized edema score based on these four parameters obtained from the HeartSMART system. Using the recorded force and displacement measurements from participants with varying levels of edema, we fit the collected data to a derivation of the standard linear solid model in order to establish edematous tissue properties. Additionally through clinical testing, we identified improvement opportunities to the device design to make it more user friendly.

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CONGESTIVE HEART FAILURE

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CHAPTER 1: INTRODUCTION

Cardiovascular Disease (CVD) is a condition that impacts the heart and blood vessels. CVD is the leading cause of death globally and, with stroke, CVD creates massive health and economic burdens [1]. According to AHA 43.9% of the US population is projected to have some form of CVD by 2030. AHA also projects that between 2012 and 2030 the direct medical costs of CVD will increase from \$396 billion to \$918 billion [2]. Americans die from CVD an average of 1 death every 40 seconds [3]. However, studies reveal that CVD can be reduced or prevented by decreasing risk factors such as high blood pressure and lack of exercise [4,5]. The 2020 Impact Goal of the American Heart Association states, “By 2020, [the goal is] to improve the cardiovascular health of all Americans by 20%, while reducing deaths from cardiovascular diseases and stroke by 20%” [2]. This goal introduces a new concept known as *ideal cardiovascular health* that includes four health behaviors (cessation from smoking, increased physical activity, healthy diet, and healthy body weight) and three health factors (cholesterol, blood pressure, and blood glucose). While medications are definitely important for managing CVD, dietary and lifestyle changes are necessary and recommended to all patients [2].

One type of CVD is congestive heart failure (CHF), during which the pumping action of the heart becomes compromised [6] and blood cannot maintain proper flow through the body. Consequently, blood builds up and increases pressure in the vessels, causing fluid to leak into body tissues. This excess fluid results in tissue swelling (edema) of the extremities [3,7]. Worldwide there are over 20 million people with CHF. Approximately 5.7 million Americans live with CHF according to the American Heart Association’s 2015 Statistical Report. On a yearly basis there is estimated to be 660,000 new cases of CHF and a mortality rate of 287,000 people. Upon diagnosis, half of CHF patients die within 5 years. Each year, there are 11 million physician visits focused on heart failure. When compared with the total of all forms of

cancer, heart failure results in greatest number of hospitalizations [2]. There is evidence that CHF can be managed with clinical intervention and self-care. Cardiac rehabilitation programs encourage CHF obese patients to lose weight through diet and exercise and CHF stable patients to participate in moderate aerobic exercise. Even with such changes, patients need to be motivated to provide self-care [3].

One indicator of CHF is peripheral edema, which is swelling in the soft tissues caused by an increase of the interstitial volume. The dynamics that result in this increase in volume are due to physiological processes in the heart and kidneys. Atrial-renal reflexes maintain total body volume in the normal range. Under normal conditions, an increase in atrial pressure prevents arginine vasopressin (AVP) release, decreases renal sympathetic tone, and promotes natriuretic peptides (ANP and BNP) release, all of which increase renal sodium and water excretion. However, in HF these normal reflexes are diminished due to the phenomenon of underfilling of the heart, during which blood backs up in the venous system and the effective arterial volume is decreased because of decreased cardiac output. Arterial volume receptors sense this attenuation in arterial filling (i.e. effective arterial volume) and trigger sympathetic nerve-mediated vasoconstriction of systemic and intrarenal arterioles in order to reestablish a normal ratio of cardiac output to vascular resistance. In addition, the impeding effects of the arterial stretch baroreceptors on the neurohumoral systems (such as AVP release) are lessened, increasing sodium reabsorption and AVP mediated water retention [8].

Because the presence of edema in the lower extremities is a useful diagnostic marker for the acuteness of the disease, the progression of CHF can be monitored over time with the progression of the severity level of edematous tissue. Changes in these patient conditions

are useful indicators to determine further intervention [9]. Even though edema is often a symptom of a more serious medical condition, the assessment process is only one indicator of a patient's condition and presence of peripheral edema may not always be a primary concern for the clinician. It is of significance to note that more patients are hospitalized for CHF due to increased fluid retention rather than severe breathlessness. Patients with greater levels of edema have more renal dysfunction and anemia and are more likely to have right heart failure [10].

The traditional standard for predicting imminent heart failure and preventing repeated hospitalization is fluid monitoring through edema assessment and daily weight [11]. Clinicians assess the level of edema by the amount of “pitting”, or indentation, in the skin, as shown in Figure 1 [12], as well as the time in seconds for skin rebound. Clinicians

assign a value between 1+ and 4+, inclusive, based on their experience and observation. The major issue with this digit press test to diagnose edema severity level is the subjective nature of the process. A cause for concern is that repeated measurements by different clinicians may be

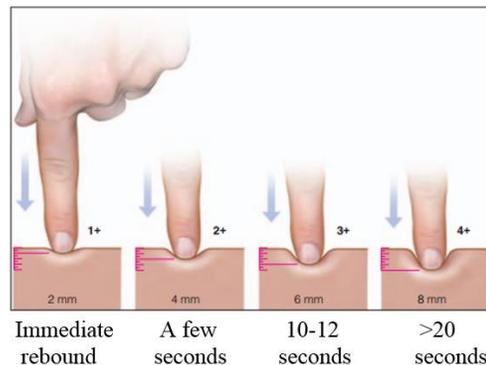


Figure 1. Levels of pitting edema [12].

inconsistent. Some clinicians rely on rebound time to determine the score while others focus primarily on depth of indentation. In spite of these concerns, digital manipulation remains the gold standard. Devices currently available to assess pitting edema remain expensive, unwieldy, or inaccurate [13]. Advancements in improved monitoring of such measurements, especially for in-home use, can improve patient outcomes and quality of life when dealing with chronic illnesses [14,15].

This thesis project focuses on design of an in-home monitoring system that can objectively measure peripheral edema. Furthermore, the system incorporates a standard linear solid (SLS) algorithm based on a viscoelastic tissue model. In this study, we have recorded force and displacement measurements from patients with varying levels of edema then fit this data to a SLS model in order to establish edematous tissue properties. The thesis contributes to biomedical engineering by providing a framework in which to determine the viscoelastic constants for peripheral tissue at differing levels of edema severity. Referencing the framework will allow a process for reducing subjectivity and thereby establishing a standardized measurement procedure for the severity of peripheral edema.

This thesis is organized into the following chapters. Chapter 2 summarizes a review of the literature of engineered peripheral edema measuring devices. Chapter 3 presents a detailed description of the HeartSMART system design and a preliminary validation study using foam. Chapter 4 provides an explanation for the application of a soft tissue model to edematous tissue and the hypothesis for the study. Chapter 5 describes the experimental methods for clinical data collection. Chapter 6 presents the results. Chapter 7 discusses the data analyses, improvement opportunities, and future direction for the HeartSMART system. Chapter 8 states the conclusions from the study.

CHAPTER 2: BACKGROUND

2.1 From Hospital to Home Care

Preventing and managing serious conditions such as obesity, diabetes, and heart disease are challenges for health care providers. With innovations in technology, opportunities exist for enhanced communication and prevention measures made possible through digital design and advancement [16,17]. In addition to improving (1) treatment and diagnosis, (2) communication, and (3) data retrieval with the use of mobile devices and apps, these same devices are a solution for self-care management. Rising healthcare costs are an additional incentive for self-care. In the U.S. healthcare spending has increased from 75 billion in 1970 to 2.6 trillion in 2010. It is predicted to reach 4.8 trillion in 2021 [18].

Heart failure is the top discharge diagnosis, accounting for 32 billion health care dollars [19]. The amount will only increase due to longevity and increasing survival rates of once deadly heart attacks. Because the finances are so monumental, healthcare providers are seeking better ways to enable patients to participate in their own self-care to lower health care costs [5].

Patients are being encouraged to accept more responsibility for their health in order to eliminate or shorten their hospital stays [20]. Due to the availability of improved treatment options and an increased awareness by the public of the benefits of healthy lifestyles, there are indications that hospitalization rates for chronic illnesses could decrease.

As the health care system continues to reward better health outcomes, mobile devices and apps can support this goal [14,21,22,23,24,25]. Studies provide evidence that patient care outcomes are impacted positively by mobile devices, such as reduced length of hospital stay [14, 23]. The healthcare system is now poised to enable individuals to participate in their own care (self-care). This shift in paradigm from reactive care to proactive and preventative care will

require devices adapted for home use as well as improved patient education. BlueCross BlueShield of North Carolina is now offering monetary incentives for participation in “My Active Health” and “Self-Assessments” [26]. Moving from clinic centered care to patient centered care means extending healthcare to the home and community [27].

There are a variety of patents and research studies published about digital devices that are used for the detection and management of cardiac associated diseases where edema is a symptom [13]; however, only the indentation (digital manipulation) method is included in standard clinical practice. Although “measuring internal properties of tissue, such as the water content, impedance, thermal energy or ultrasound or magnetic resonance imaging of the tissue provides accurate, quantitative representations of edema severity in tissue,” [13, p.9] these methods are “too expensive and unwieldy for using on a regular basis to assess edema” [13, p.10]. Other methods entail circumference measurements [28], water displacement [28], and impedance measurements [29]. However, these methods would not be considered for patient use at-home due to patients’ lack of training and ability to perform the tests on their own, which would be a requirement for an at-home device. Another published device, similar to the prototype investigated in this study, is a hand held version [13], which patients would not be able by themselves to maneuver successfully against their leg.

Investigations continue for the purpose of designing more affordable measurement devices [13], especially those compatible with home use, since in-home health care is predicted to improve the quality of care and reduction of healthcare costs. Proactive and preventative measures [27] will necessitate the development of equipment, procedures, and training that support patient-centered care [30]. For example, patients will need to acquire specific skills for following detailed instructions to assess the presence of edema as an indicator of their heart

failure disease, much like reading a thermometer to detect presence of a fever as a symptom of disease.

2.2 Significance

A daily monitoring system that would objectively monitor both weight and level of severity of edema to produce a consistent overall edema score would be an asset. The system would be wireless so health care professionals could continuously observe their patients from a remote location as well as provide patient feedback. The HeartSMART system is a vital tool that can be used by health care professionals to monitor heart failure progression and patients to improve their self-management skills. Continual use of this system will help individuals recognize how significant weight control and fluid monitoring is to their overall health and prevention of worsening conditions. Because the system is mobile and will be wireless, patients can use the device in their home while providers can monitor from a remote location. Information about disease management would be provided during the hospital stay to assist in preventing re-admittance in a health care facility, especially within 30 days of the last visit.

2.3 Previous Research

Reliable Methods for Assessing Peripheral Edema

Healthcare professionals use a variety of methods to gather data to assist in assessing the severity of edema. In 2009 Brodovicz et al. sought to compare the reliability of these measurements and the degree of correlation with the traditional clinical assessment of pitting depth and recovery. The methods were evaluated with 20 patients exhibiting a range of edema severity. Methods included patient questionnaire, ankle circumference, figure-of-eight (ankle circumference using eight ankle/foot landmarks), edema tester (plastic card with holes of varying size pressed to the ankle with a blood pressure cuff), modified edema tester (edema tester with

bumps), indirect leg volume (by series of ankle/leg circumferences), and foot/ankle volumetry by water displacement [31].

The investigation found that water displacement and ankle circumference had high inter-examiner agreement; however, drawbacks of water displacement methods include time required and implementation challenges. The subjective traditional assessment by nurse-performed assessments was correlated with the patient questionnaire, which suggests a questionnaire is a reliable and accurate method of assessing edema [31].

Devices that measure peripheral edema by probe depression measurements

A variety of devices have been patented to provide a reliable, accurate and quantifiable measure of a patient's edema that is user-independent by using probes that record displacement. The devices have been used to successfully collect measurements, but sample sizes were small. Other limitations included the variation in positioning and rate of application of force of the probe by different users [12] [[US Patent #8425433:2008](#)] [[U S Patent# 6186962B1: 2001](#)].

Devices that measure peripheral edema by tape measuring device

Those prototypes using an optical encoder, combined with a microprocessor and LCD, produced reliable and accurate measurements; however, limitations were the functionality of the internal assembly, the clip mechanism, and the power spring configuration [32].

When comparing spring tape and optoelectronic volumetry to measure leg and ankle circumference, advantages of the spring tape was the inexpensive cost and ease of use, but there was high user variance. The volumeter was the preferred choice. The study was limited in that the same investigator performed all measurements so inter-rater variability was not assessed. In addition, the study only tested healthy volunteers rather than patients experiencing limb swelling [33].

Another study investigating the delta in limb volume changes based on tape-measure measurements of limb circumference (girth) produced reliable results when girth measurements were completed with consistent tension and limb position and measurement sites were standardized [34].

Devices that measure peripheral edema by water displacement

A lower extremity is placed into a container filled with a displaceable medium, resulting in the displacement of a portion of the displaceable medium. The amount of the displaced portion is then determined and related to the volume of the lower extremity in the container. From the measured volume, the presence or absence of edema is determined. The measurement may be repeated to measure the progression of the edema [[US Patent#6077222: 2000](#)].

Devices that measure peripheral edema using a ratio of the extra-cellular to intra-cellular fluid

This device measures impedance for first and second body segments. An index for each body segment is calculated that is a ratio of the extra-cellular to intra-cellular fluid. The index ratio is used to determine the presence, absence or degree of tissue edema. A comparison is made with the index ratio of a reference [[US Patent#8744564 B2: 2005](#)].

Devices that measure peripheral edema by volume sensing

The perimeter of a peripheral extremity, like an ankle, is measured to obtain a perimeter value. The perimeter value is then compared to a control value and any difference is identified. The difference is then related to the presence of edema in the patient [13].

As an example of a commercial product based on this concept is the Perometer that ranges in cost from \$15,000 to \$30,000, a price that is too expensive for most hospitals. The patient must be mobile to sit or stand in the sensing area, thus only certain patients would benefit. The device scans the limb with infrared sensing and calculates limb volume.

Advantages are ease of use, no clean up, fast, view segments of a limb [US Patent#5891059 A: 1999].

Devices that measure peripheral edema by impedance measurement

The device measures bioelectrical impedance at a single frequency. Comparing the measurement recorded for the tissue compared with tissue unaffected by edema [US Patent#8233974 B2: 2004].

This device provides an impedance measurement, passing a high frequency current through the affected tissue via electrodes. It has a more limited patient compliance than other more simplistic methods [US Patent# 6714813: 2004].

Devices that measure peripheral edema by modeling relationships between tissue water content and thermal property of tissue

The device models the relationship between tissue water content and a thermal property of tissue that varies as a function of tissue water content. A thermal probe is placed in contact with tissue at a selected site and is energized to transfer thermal energy to the tissue. Tissue water content is calculated as a thermal property of tissue, which varies as a function of tissue water content. Edema is quantified as a function of the power used to heat tissue at a selected site and the thermal conductivity of tissue. For example, thermal diffusivity and thermal conductivity of the tissue increase as the water content of the tissue increases. The thermal response to the introduction of heat in a selected tissue sample or organ is a function of these properties [US Patent# 6488677: 2002].

Devices that measure peripheral edema by 3D imaging

Five healthy subjects participated in a study using low-cost sensors for leg edema detection as a method for home monitoring to prevent or reduce re-hospitalization. 3D camera-

based images were correlated with body weight and leg circumference to detect and quantify leg edemas. The results suggest further investigation [35].

Devices that measure inhomogeneous soft tissues in patients with peripheral edema

A hand held stiffness meter was designed to evaluate factors that affect indentation responses of inhomogeneous soft tissues (skin, adipose tissue, muscle) on the experimental indentation responses recorded by the stiffness meter.

The study suggested that a 3D model, instead of the present 2D model, is needed for a more realistic simulation of the soft tissue behavior under indentation. The 3D model may be created by using MR or CT imaging [28] [[US Patent # 8,147,428: 2005](#)].

Devices that measure foot edema by dielectric electro-active polymer sensors

For continuously monitoring foot edema, this model showed that DEAP (dielectric-electro-active polymer) sensors are suitable for use in wearable monitoring systems. They allow for very limited pressure on the foot, which allows for valid measurements. Because the sensing values follow the same pattern during pump-in/pump-out phase, but shift on both amplitude and phase, measurements were reported as reliable. Future work should consider designing an advanced data analyzing algorithm with a suitable calibration of each measurement [36].

Impact of monitoring systems and response training

A heart failure (HF) training program (SMART- for symptom monitoring and response to decrease uncertainty surrounding the meaning of symptoms experienced) was investigated for increase in patients' ability to recognize and respond to changes in HF symptoms. Participants received weight scales and a HF self-care booklet written at the 6th to 8th grade. Intervention participants received 4 additional education modules. The training appeared to have an early but not sustained benefit, which meant no difference in 90-day event-free survival between groups.

Improvement in self-care maintenance and confidence scores in the intervention group was greater but not significant. Effective self-care, with daily symptom monitoring and knowledgeable decision-making about symptoms appears to help patients with HF maintain an acceptable quality of life and avoid repetitive hospitalizations [37].

No differences in hospitalization rates were reported between control and treatment groups that experienced heart failure program care versus heart failure program care plus the AlereNet system (Alere Medical, Reno, Nevada). There was a 56.2% reduction in mortality for patients randomized to the AlereNet group, even though both groups received specialized and aggressive heart failure care. The intervention appeared to improve survival rates [38].

In a third study no differences were reported between the treatment (usual care plus a medication compliance device linked to a Web-based monitoring system) and control (usual care only). At baseline and 3 months, there were no differences reported between groups as to self-care behaviors, pill counts, 6-minute walk-test distance, or Functional Class. Yet, quality of life improved significantly for the treatment group. Patients in the compliance device group had 94% compliance with taking medication, 81% compliance with daily blood pressure monitoring, and 85% compliance with daily weight monitoring compared to 51% and 79% for blood pressure and weight monitoring, respectively, in the control group [39].

Conclusion

The review indicates that there is no one preferred device to measure severity levels of peripheral edema. Limitations of the studies included small sample sizes, using only healthy participants, lack of testing by more than one user, and challenges in use of method or device. In this thesis study a total of 30 healthy and CHF subjects exhibiting different levels of edema were tested. In addition, prior to subject testing, the force and displacement sensors were validated

with foam testing to determine baseline measurements of force and displacement as they correlate to the simulated level of edema. Healthcare providers continue to use the method of indentation with their hands which results in a subjective scoring and a lack of reliability between providers as to the degree of peripheral edema in patients. The development of a standardized method will enhance the continuity of care and increase the ability of providers to predict exacerbations of heart failure.

CHAPTER 3: DEVICE DESIGN AND FUNCTION

3.1 Design Overview

An illustration of the HeartSMART system components is shown in Figure 2. Our device utilizes mechanical and electrical components that can provide more accurate and repeatable

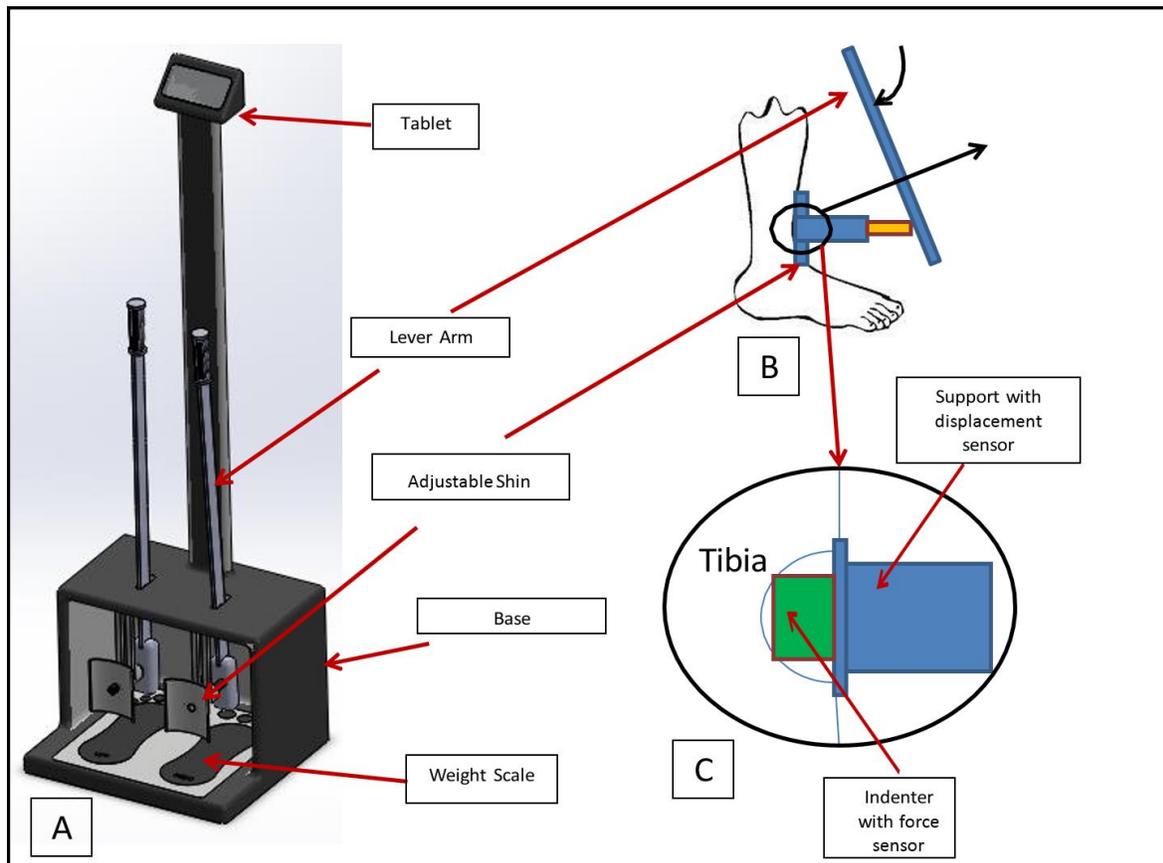


Figure 2. HeartSMART system components; A) Overall design, B) zoom-in on the indentation method, and C) a zoom-in on the indenter.

measurements compared to the current digit press test executed in the clinic.

3.2 Mechanical Components

The mechanical components include a base, indentation device, adjustable shin rest, and lever arm. The base, which is constructed from acrylic sheets, provides housing for the weight scale and structure for the other components. The base is large enough to allow the subject to

stand for weight measurement and sit for edema measurement. The indentation device consists of the indenter that slides over a support attached to a shin guard. The shin guard can be adjusted to account for variations in subject heights. A displacement sensor is housed inside the support and a force sensor is attached to the end of the indenter. The original housing design is captured in a sketch shown in Appendix A. The indenter, support and shin guard were designed in SolidWorks and later 3D printed. The lever arm is used to push the indentation device into the subject's leg.

3.3 Electrical Components

The displacement sensor chosen is the Subminiature Gauging DVRT, as shown in Figure 3. The Subminiature Gauging DVRT® consists of a ruby bearing and hardened stainless steel ball that guide the spring-loaded tip. The sensor exhibits sub-micron resolution, linear analog output, and ease of use. This displacement sensor can measure up to 10 mm, which is



Figure 3. Displacement sensor, SG-DVRT-8-SK1.

above the expected maximum displacement of 8mm for a level 4+ edema patient. The force sensor chosen is the Honeywell FS101 Pressure Sensor, as shown in Figure 4. It is a peizoresistive-based



Figure 4. Fore sensor, FS01.

force sensor that provides an accurate and stable output over an operating range of 0 to 1.5 pounds, with a maximum force of 7 pounds. The sensor was chosen because of its small size, low cost, and low noise. One of its common applications is load and compression sensing.

The displacement and force sensors are connected to a National Instruments Elvis II+ circuit board. The circuit board is connected to a Dell laptop with LabView Software, as shown in Figure

5. Voltage readings from the displacement sensor are converted into displacement readings in millimeters and voltage readings from the force sensor are converted into force readings in pounds. Data collected is stored as Microsoft Excel files for further analysis.

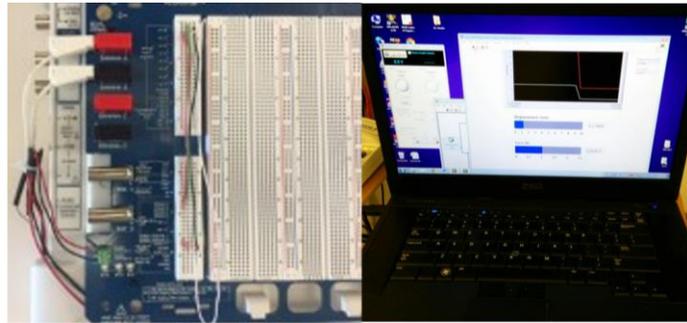


Figure 5. NI Elvis II+ circuit board and laptop with LabView

The Withings wireless weight scale is an electronic blue-tooth enabled scale that records subject weight. The Exergen Temporal Scanner Infrared Thermometer is a separate component used to collect patient skin temperature on the forehead and leg.

3.4 Mobile Application Development

Concurrently, development of a mobile application (app) is in progress. The app will collect, analyze, and store data from the displacement and force sensors and the weight scale in order to determine severity levels of edema. A Sparkfun IOIO-OTG circuit board, as shown in Figure 6, will replace the NI Elvis II+ circuit board, the designed app will replace the LabView software, and the

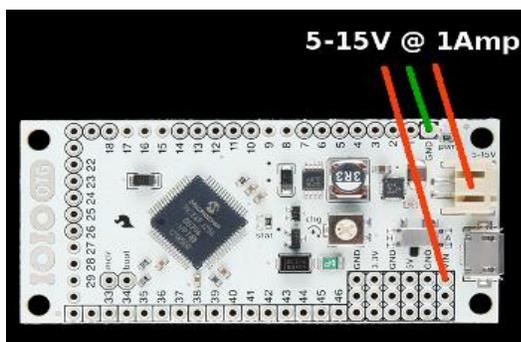


Figure 6: IOIO-OTG circuit board.

2013 Nexus 7 tablet will replace the laptop. The Sparkfun IOIO board connects with the Android operating system KitKat 4.4.4 through a USB or Bluetooth connection and can be controlled by an Android app via Java programming language API (application programming interfaces). The IOIO

board has one MCU (micro controller unit) that serves as a USB host and deciphers commands from the app. The IOIO board can be used with Digital Input/Output, PWM, Analog Input, I2C, SPI, and UART control. The IOIO board can be used with the V3.04 bootloader, which interfaces

with Android devices over a Bluetooth connection via an USB Bluetooth dongle attached to the board.

3.5 Foam Study

The main purpose of the foam study was to validate the force and displacement sensors with foam sample testing to determine baseline measurements of force and displacement as they correlate to the simulated level of edema. Foam samples consisting of high-density memory foam were tested on the HeartSMART system. Squares of foam were cut to different thicknesses and soaked in vegetable oil. The varying thicknesses were representative of the different levels of edema. Vegetable oil was used as the most



Figure 7. Foam testing setup

representative liquid for soft tissue models. Dr. Sonya

Hardin, an edema specialist, verified that the samples did indeed represent the different levels of edema. Table 1 illustrates the foam thickness associated with each edema level. The setup for testing is shown in Figure 7. A lower leg model consisting of a cylindrical PVC pipe stabilized with

concrete in a foil pan was used to hold each piece of foam in the shin guard. Each foam sample was tested on the device three times. The detailed testing protocol is described in Appendix B.

Results showed that as the simulated level of edema increased (i.e. the foam thickness

Table 2. Foam testing results

Foam Thickness	0.25"	0.50"	0.75"	1.00"	1.25"
Average Maximum Displacement (mm)	1.774	4.470	9.751	9.752	9.751
Standard Deviation (mm)	0.077	0.325	0.001	0.001	0.001
Average Force (lb)	5.093	4.900	4.317	4.453	4.743

Table 1. Edema correlation to foam thickness

Edema Level	Foam Thickness	Sample #
None	0.25"	1
1+	0.50"	2
2+	0.75"	3
3+	1.00"	4
4+	1.25"	5

increased), the depth of indentation increased. Table 2 illustrates the collected data. It is important to note that the

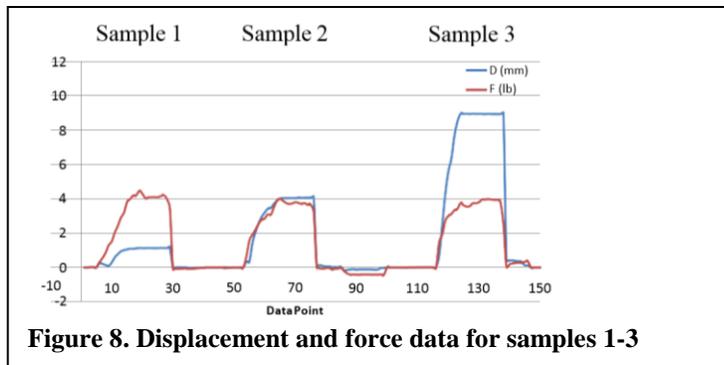


Figure 8. Displacement and force data for samples 1-3

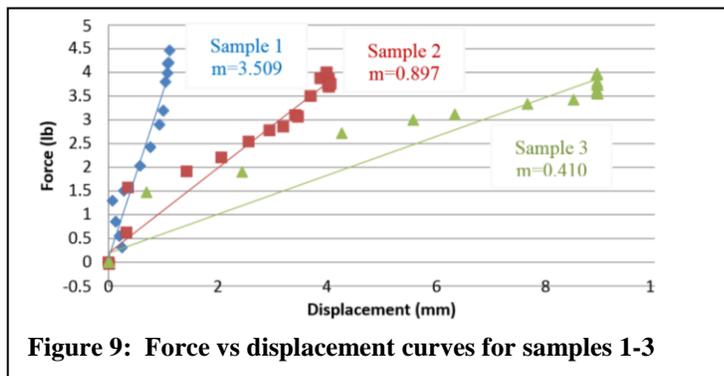


Figure 9: Force vs displacement curves for samples 1-3

maximum displacement of the sensor (9.75 mm) was reached for the 0.75 inch, 1.00 inch and 1.25 inch thick sections of foam. Because the pitting seen in the severest cases of edematous tissue in human subjects is 8 mm, it is expected that maximum displacement of the sensor will not be reached during patient testing. Figure 8 represents the force and displacement data for the first models.

As level of edema increases the displacement due to the approximately same amount of force increases. The relationship between the force and displacement was investigated by applying a trend line to the force application portion of the curve, as shown in Figure 9. The test results demonstrate that the device works well and is ready for data collection on human subjects.

CHAPTER 4: EDEMA CLASSIFICATION USING SLS TISSUE MODEL

4.1 Application of the Standard Linear Solid (SLS) Model

Bone and soft tissues, including blood vessels, nerves, muscle, fat, and skin, have viscoelastic properties. In addition, edematous tissue exhibits viscoelastic characteristics. One property of viscoelastic materials is that they enable large deformations [40]. This property is the basis for edema measurements recorded by healthcare providers; however, as previously stated, visual diagnosis alone results in high intra- and inter-provider variability. For the purpose of eliminating the need for multiple sensors and to obtain objective measurements of edema levels, a material model can be developed to examine creep (which is increased deformation under a constant applied load), dependence on rate of loading, and dependence on history of force application [40]. Maintaining these measurements across providers and across multiple measurements will maintain consistency in readings for the purpose of improving diagnosis and treatment [13].

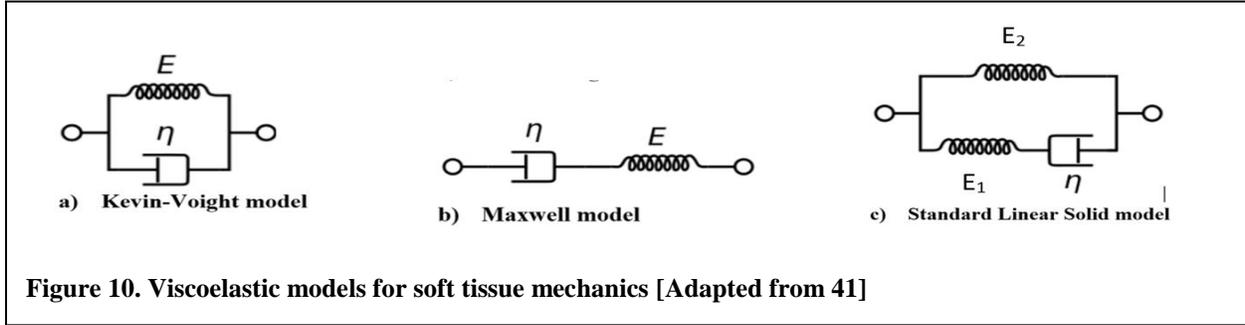
A simple model of soft tissue can be represented by its resistive property, i.e. the mechanical resistance R . Resistance can be calculated as shown in equation 1,

$$R = \frac{P}{v} \quad (1),$$

where P is the pressure applied to the surface of the tissue and v is the velocity (i.e. the rate of change of displacement of the tissue). Excess interstitial fluid buildup in edematous tissue changes the properties of the tissue.

More sophisticated models contain multiple components. The elastic response can be modeled with linear springs E_n and the viscous characteristic can be modeled with dampers η_n .

Figure 10 illustrates several configurations for soft tissue modeling. Fitting collected



experimental data from the sensors to a model allows for determination of edematous tissue properties thereby providing alternative measures for edema [41].

Based on the design of the HeartSMART system, the standard linear solid (SLS) model was best suited to determine edematous tissue properties. Fitting the experimental data to this model was the first step in developing an algorithm that could provide an overall standardized edema score for each user. One assumption of the model is that the stress applied to the tissue is constant. However, in this study, the applied stress was not constant. Therefore, the model must be modified to account for changing stress. Appendix C provides the derivation to the solution for creep when the stress applied to the tissue is not constant. The final equation used in the data analysis is shown in equation 2, where ε is the strain, a_1 is the slope of the force over time, t is time, $u(t)$ is the unit step function, η_1 is the damping coefficient, and E_1 and E_2 are the two spring constants.

$$\varepsilon(t) = \frac{a_1}{E_2} t \cdot u(t) + a_1 \frac{\eta_1}{(E_2)^2} u(t) - a_1 \frac{\eta_1}{(E_2)^2} e^{\frac{-E_2 E_1}{\eta_1 (E_2 + E_1)} t} \quad (2)$$

Because force and displacement data was collected on each participant using the HeartSMART system, the data can be plugged into equation 2 to solve for the three constants, η_1 , E_1 and E_2 .

4.2 Hypothesis for the Classification of Edema

The hypothesis is that in determining the values of η_1 , E_1 and E_2 for each participant and

grouping the values according to the level of edema, a classification system can be created and used to predict the level of edema of future participants. To clarify, an analogy for color determination is used. Color in programming languages is represented by a red, green and blue component. The output color is a combination of these three colors, with values commonly ranging from 0 to 255 for each component. In this study, color is comparable to the edema score while the red, green, and blue components are comparable to η_1 , E_1 and E_2 . The first step is to determine what numerical values of η_1 , E_1 and E_2 correspond to each edema level. Because the values will vary from patient to patient, an average and range for each constant must be established for each edema level. The next step is to conduct a blind study by testing another sample of participants with the clinician assigned edema score not revealed until the end of the study. Applying equation 2 to the collected data and determining the values of η_1 , E_1 and E_2 for each participant, the edema score can be predicted. By comparing the predicted scores and the clinician assigned scores, the process can be validated.

CHAPTER 5: CLINICAL DATA COLLECTION

5.1 Subject Participation

During clinical data collection, the HeartSMART system was implemented to collect measurements from the lower legs of subjects. Subjects were recruited to collect data on the HeartSMART system prototype. In the process of selecting subjects, the NIH Outreach Notebook for the Inclusion, Recruitment and Retention of Women and Minority Subjects in Clinical Research (October 2001) and Increasing Diversity in Clinical Research (The Endocrine Society, 2007) was employed. Healthy subjects on and off the East Carolina University campus

were notified of the study. Students attending East Carolina University were not allowed to participate in the study; only faculty and staff on campus were contacted. In order to collect data on HF patients, Dr. John Cahill of the East Carolina University Heart

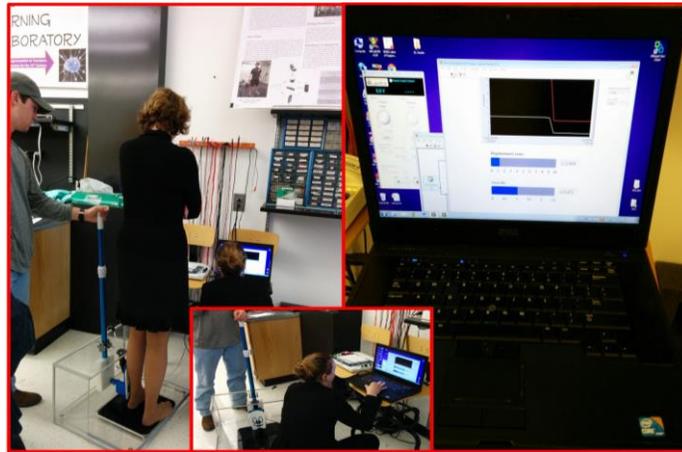


Figure 11: Setup for subject testing

Institute (ECHI) discussed the study

with his patients to determine if they were interested in participating. Heart failure subjects were required to meet the following criteria: alert, oriented, and understood the English language; 40 years or older; understood and were capable of providing consent; diagnosed with heart failure and classified using the New York Heart Association (NYHA) functional class (I, II, III, or IV; as documented by the cardiologist) and community dwelling. In order to collect data on geriatric patients, Dr. Candace Harrington of the Monk Geriatric Center discussed the study with her patients to determine if they were interested in participating. Geriatric subjects were required to

meet the following criteria: alert, oriented, and understood the English language; 40 years or older; understood and were capable of providing consent. Heart failure and geriatric subjects could not have the following conditions: cognitive impairment; impaired hearing as documented in the medical record or by observation and documented history of chronic mental illness. After interest was expressed from either a healthy subject, HF subject, or geriatric subject, the subject will meet with a research assistant to sign up for the study. Figure 11 illustrates the setup for patient testing.

Sample size initially depended on the number of consenting subjects. Sample size was based on subject volume accessibility in the clinic and is restricted by budget size. The total number of subjects tested was 30. Clinician edema scores were collected in addition to other demographic information to that the sample pool consisted of a diverse group of individuals. Table 3 in Chapter 5.3 illustrates the diversity in the sample population.

5.2 Implemented Subject Protocol

Testing begins with the tester collecting the subject's forehead and peripheral skin temperature. Next, the subject steps on the scale and his/her weight is recorded. Then the subject places his/her leg into the device. The tester pulls on the indentation lever, causing the indentation device to press into the subject's skin at an approximate force of 4 lb. At this force, the skin indents to a certain depth. Measurements are taken on the lower anterior and lateral parts of both legs. The indentation procedure is performed a minimum of 3 times at each position. Displacement (mm) and force (lb) measurements are recorded and stored with LabView and Microsoft Excel, respectively. The testing protocol has been approved by the ECU UMCIRB. A detailed, step-by-step procedure is explained in Appendix D. The most recent approved amendment to the IRB is provided in Appendix E.

5.3 Summary of Subject Data

A total of 30 subjects participated in the edema study. A variety of category data were collected on each participant to potentially be used in the data analyses. Clinician edema score, age, gender, race, and weight are displayed in Table 3. Any information blocked out in Table 3 was a result of no data collection on the category at the particular point in time during the study.

Table 3. Subject data

Subject	Clinician Edema Score	Age	Gender	Race	Weight (kg)	Weight (lb)	Data Breakdown			
							No. of Participants	% of Participants	Average Age	Std Dev Age
P17	0	53	M		147.4	325.8				
P18	0	66	M		91.1	201.3				
P20	0	88	F	C	72.2	159.6				
P21	0	90	F	C	48.6	107.4				
P22	0	66	F	AA	126	278.5				
P23	0	67	M	AA	84.8	187.4	6	29%	72	14.40
P2	1	69	M		101.1	223.4				
P6	1	40	M		130	287.3				
P8	1	77	M		81.5	180.1				
P10	1	63	F		94	207.7				
P11	1	47	F		95.8	211.7				
P12	1	67	M		93.4	206.4	6	29%	61	14.11
P5	2	64	M		120.3	265.9				
P7	2	61	M		92.4	204.2				
P13	2	39	F		122	269.6				
P14	2	63	F		116.6	257.7				
P15	2	76	F		95	210.0	5	24%	61	13.43
P1	3	76	F		97	214.4				
P3	3	60	M		92.4	204.2				
P9	3	88	M		61.6	136.1				
P19	3	93	M	C	77.1	170.4	4	19%	79	14.68
Total							21	70%	67	15.15
H1	NA		M	C	94	207.7				
H2	NA		F	C	78.4	173.3				
H3	NA		M	C	96.2	212.6				
H4	NA		F	C	64.4	142.3				
H5	NA	45	M	AA	131.2	290.0				
H6	NA	42	F	AA	152.3	336.6				
H7	NA	51	F	C	71.1	157.1				
H8	NA	49	F	C	108.4	239.6				
H9	NA	60	F	C	57.2	126.4				
Total							9	30%	49	6.88

*M: Male; F: Female; C: Caucasian; AA: African American

*NA: All healthy subjects exhibited no edema

*No data could be collected on subjects P4 and P16 because the force sensor was not working

Table 3 shows an equal distribution of male and female participants with both Caucasian and

African American representation. The number of participants in each edema level category (level 0, level 1+, level 2+, and level 3+) ranged from 4 to 6 with average ages in the 60s and 70s.

There were a total of 9 healthy subjects (control) with an average age of 49.

Although other data were collected, including surface skin temperatures and force and displacement measurements, these data are not included Table 3. An analysis of the surface skin temperature correlation to edema level is shown in Chapter 6.1 in Figure 12. Appendix F provides Excel worksheets of force and displacement data with calculations of E_1 , E_2 , and η_1 as pertinent to the SLS model. Table 4 in Chapter 6.2 provides an overall summary of these calculated values.

CHAPTER 6: RESULTS

6.1 Data Analyses

The HeartSMART system was developed to calculate the level of peripheral edema via four factors: the depth (displacement) of the skin, the force exerted on the skin, the surface temperature of the skin, and body weight. To determine the extent of the relative contribution of each, this section presents the analyses of the data. Refer to Appendix D for participant testing protocol.

Figure 12 exhibits the number of participants in each weight category per edema level. The significance of this figure is to illustrate that each edema level consisted of participants with

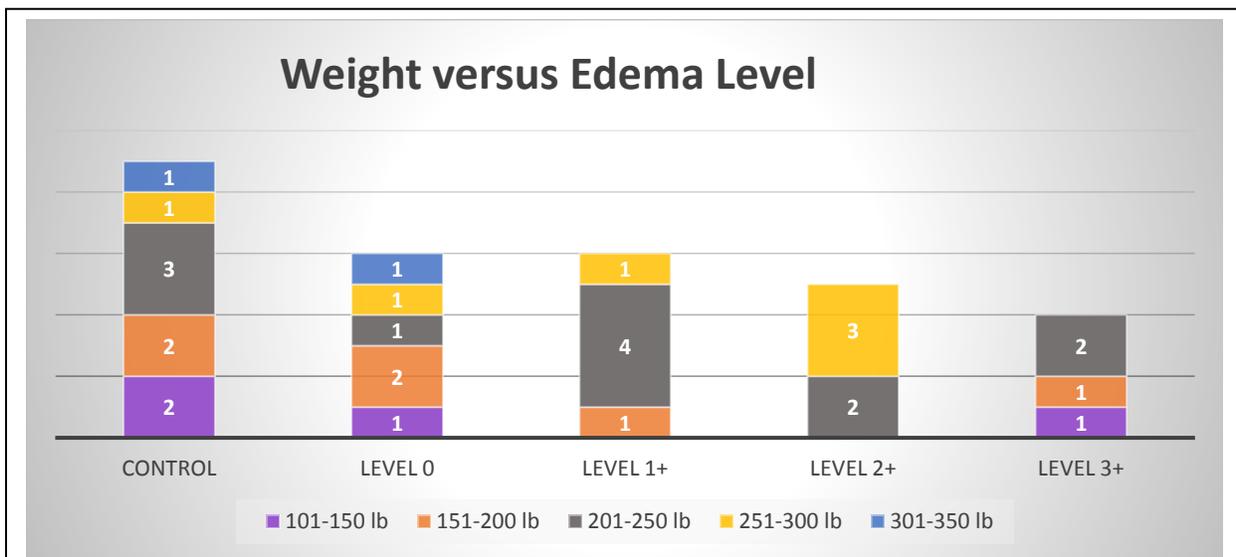
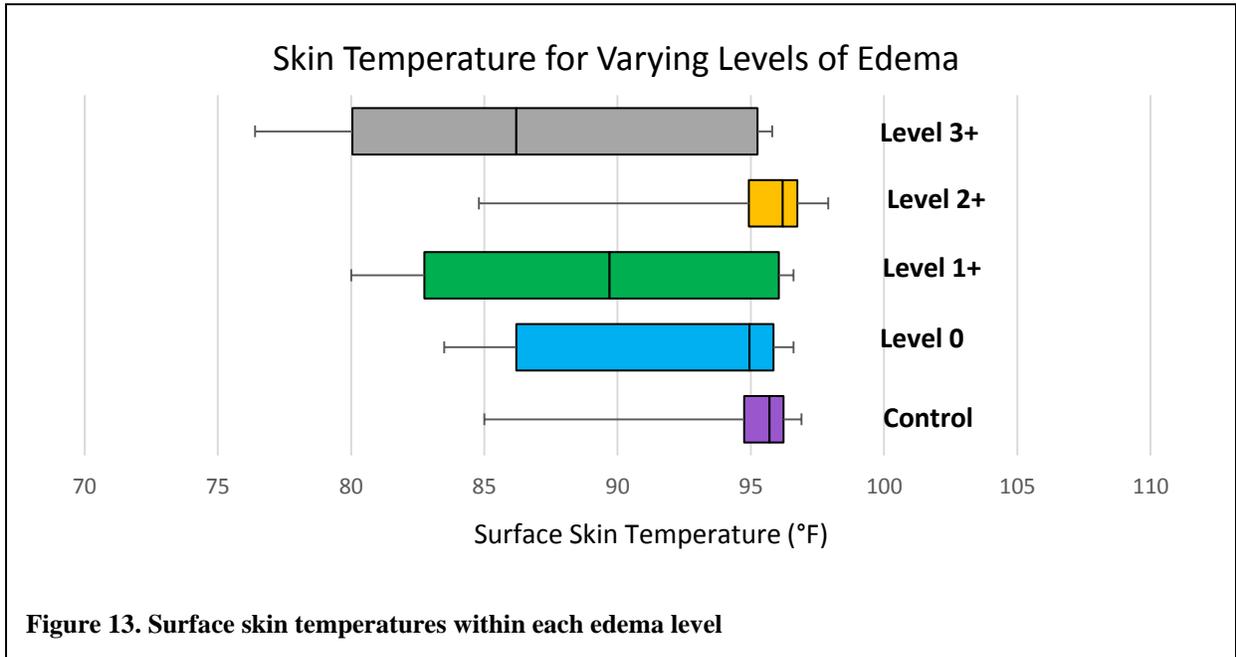


Figure 12. Weight distribution of participants within each edema level

varying weight levels. One of the events that occurred during the study that is not indicated in Table 3 is that participant P1 and P15 are the same person. It appears that by merely losing weight (4.4 lb), the patient's edema level changed from a 3+ to 2+.

Figure 13 illustrates the surface skin temperatures where the force and displacement measurements were taken. On average, more of the participants in the healthy and level 2+ groups had warmer skin temperatures compared to the other groups. In fact, the median for healthy and level 2+ were similar (95.7°F and 96.2°F, respectively). Although the median for



level 0 (94.95°F) was comparable to healthy and level 2+, the range of temperatures had greater variance. When considering level 1 and level 3, the median dropped (89.7°F and 86.2°F, respectively) and the range increased. From this plot, one could deduce that on average, participants with edema level 3+ will have cooler surface skin temperatures compared to lower levels of edema. It is interesting to note that in a 2016 study conducted by Oya et al. there was evidence of low temperature skin surfaces in areas exhibiting subcutaneous edema [43].

Table 4 provides a summary of the calculated averages and standard deviations for the slope of the force curve and η_1 , E_1 and E_2 at each testing location on the leg for the corresponding edema level. To better visualize these data, Figures 14-28 contain bar charts.

Table 4. Summary of force slope, E_1 , E_2 , and η_1 values

Location: Front of Left Leg

Control (Healthy Subjects; No Edema)				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.0	2,108,338	52.3	20.1
Total Standard Deviations	0.5	869,414	6.9	3.0
Edema Level: 0				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	3.5	3,577,110	68.9	47.0
Total Standard Deviations	1.0	4,475,202	54.9	15.9
Edema Level: 1+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.4	3,755,309	26.9	8.9
Total Standard Deviations	1.2	6,714,545	11.2	2.9
Edema Level: 2+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	3.1	1,575,836	18.3	9.2
Total Standard Deviations	1.7	1,232,253	7.2	5.8
Edema Level: 3+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	3.0	1,551,191	19.4	9.9
Total Standard Deviations	1.4	1,946,346	5.8	5.6

Location: Side of Left Leg

Control (Healthy Subjects; No Edema)				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.8	2,084,255	14.3	6.7
Total Standard Deviations	1.1	809,173	2.5	3.3
Edema Level: 0				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.7	3,032,282	19.6	7.6
Total Standard Deviations	0.7	3,229,144	4.9	3.0
Edema Level: 1+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.6	6,397,778	43.4	20.3
Total Standard Deviations	0.9	5,255,159	13.0	14.1

Edema Level: 2+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	3.0	1,518,882	18.7	11.4
Total Standard Deviations	2.0	1,496,963	7.2	8.1
Edema Level: 3+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.4	1,957,078	10.1	7.2
Total Standard Deviations	1.3	2,280,181	4.8	7.0

Location: Front of Right Leg				
Control (Healthy Subjects; No Edema)				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	3.1	2,625,398	63.3	18.6
Total Standard Deviations	1.4	2,090,086	47.0	12.9
Edema Level: 0				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	3.3	1,213,612	24.6	9.7
Total Standard Deviations	1.2	1,248,658	11.6	8.5
Edema Level: 1+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.2	1,391,898	16.9	7.1
Total Standard Deviations	0.9	1,211,250	6.0	5.0
Edema Level: 2+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	5.4	5,662,163	28.0	16.4
Total Standard Deviations	6.3	4,421,763	13.0	7.9
Edema Level: 3+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.7	1,941,973	30.3	10.3
Total Standard Deviations	1.5	2,604,442	5.4	5.4

Location: Side of Right Leg				
Control (Healthy Subjects; No Edema)				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	3.2	3,784,776	45.6	24.6
Total Standard Deviations	1.3	82,218	8.8	8.8
Edema Level: 0				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.6	6,357,948	30.8	9.5
Total Standard Deviations	1.0	6,322,928	15.1	6.0

Edema Level: 1+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	2.8	1,234,951	18.2	16.4
Total Standard Deviations	1.2	1,188,190	9.0	2.6
Edema Level: 2+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	4.7	1,414,067	28.8	9.2
Total Standard Deviations	2.5	2,605,600	10.6	8.6
Edema Level: 3+				
	$\Delta F/\Delta T$	E_1	E_2	η_1
Total Averages	3.0	2,202,599	15.2	9.4
Total Standard Deviations	2.8	1,953,846	9.4	5.8

Figures 14 -25 represent the data summarized in Table 4. Figures 14-17 show the average η_1 value for each of the four leg locations for each group of edema level participants. Figures 18-21 show the average E_1 value for each of the four leg locations for each group of edema level participants. Figures 22-25 show the average E_2 value for each of the four leg locations for each group of edema level participants. The data are displayed in the following order on each graph: Control (Healthy), Level 0, Level 1+, Level 2+, and Level 3+. Note that N represents the number of runs, where a run is defined as each time the indentation device is pushed into the participant's leg and then released.

*N represents number of runs in the following charts, Figures 18-25.

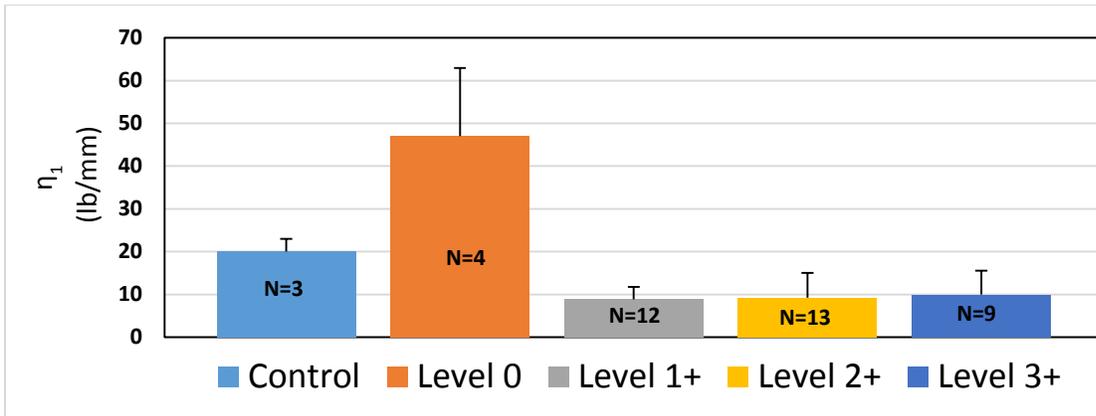


Figure 14. η_1 for the front location of the left leg

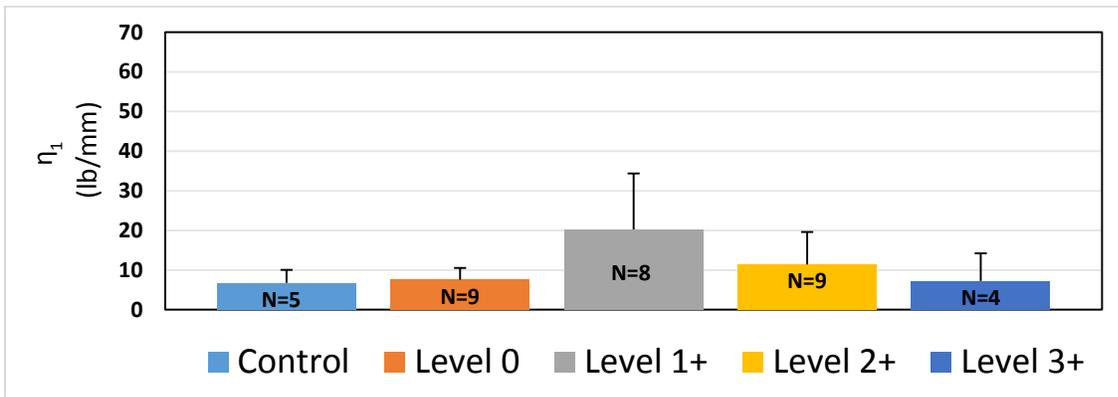


Figure 15. η_1 for the side location of the left leg

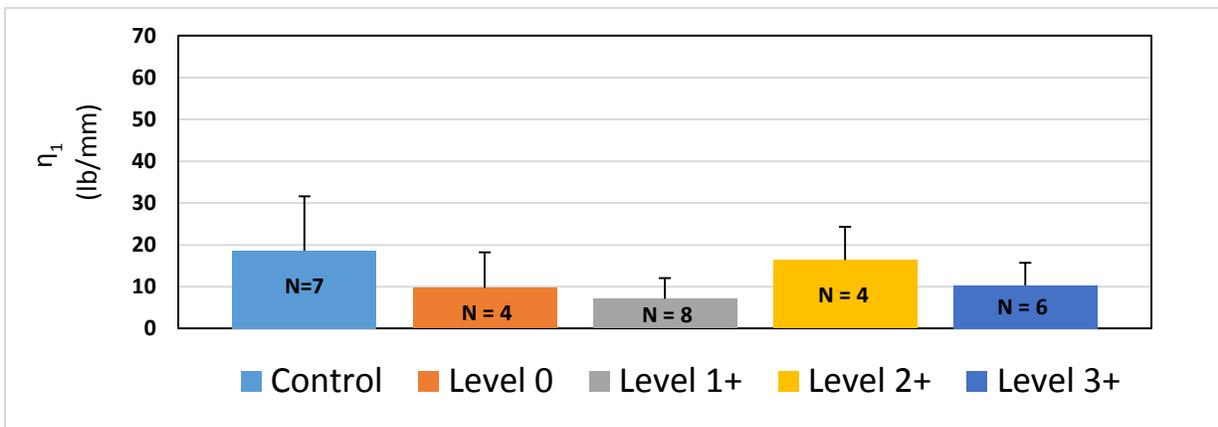


Figure 16. η_1 for the front location of the right leg

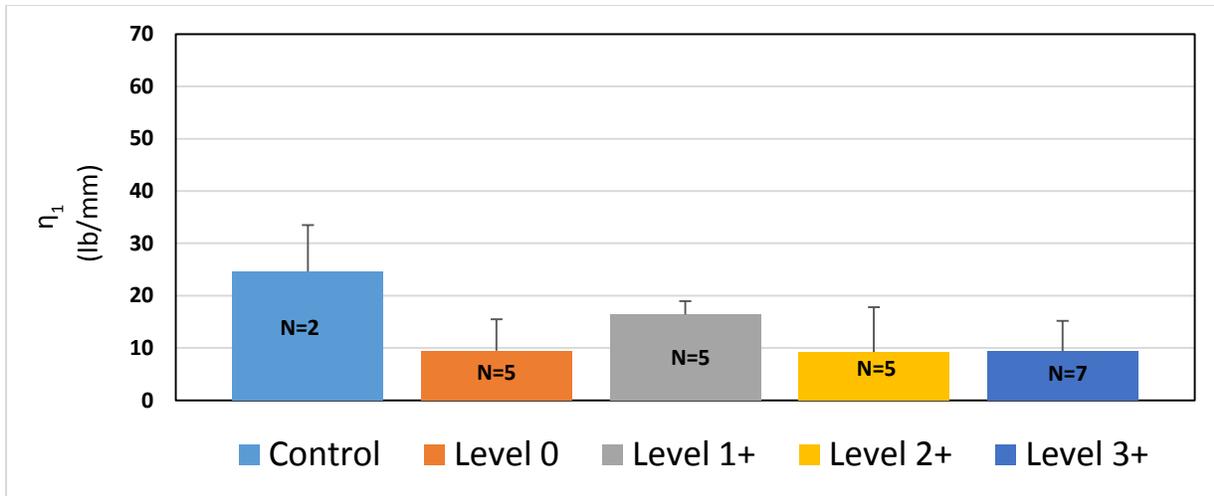


Figure 17. η_1 for the side location of the right leg

After a thorough review of all the force and displacement data collected, the front left side of the leg provided the most reliable data and had the largest sample size when compared to the other three locations. Therefore, the front left location will be used when establishing the classification system for a standardized edema score. Figure 14 shows that there is a difference in η_1 values when comparing tissue with no edema versus tissue with edema. After performing t-test analyses and Wilcoxon statistical tests, there was a statistically significant difference between Control/Level 0 and Levels 1,2,3 and between Level 0 and Levels 1,2,3 for the front left location (p-value equal to 0.01 and 0.02, respectively). There was a statistically significant difference between Control/Level 0 and Levels 1,2,3 and between Level 0 and Levels 1,2,3 for the side left location (p-value equal to 0.01 and 0.02, respectively). There was not a statistically significant difference for the other two locations.

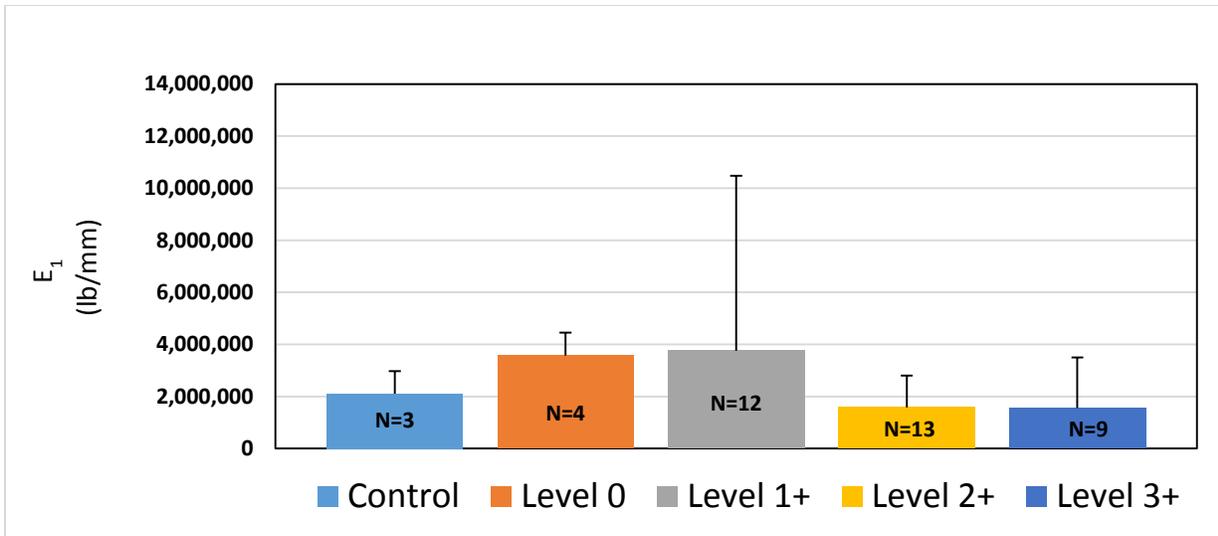


Figure 18. E_1 for the front location of the left leg

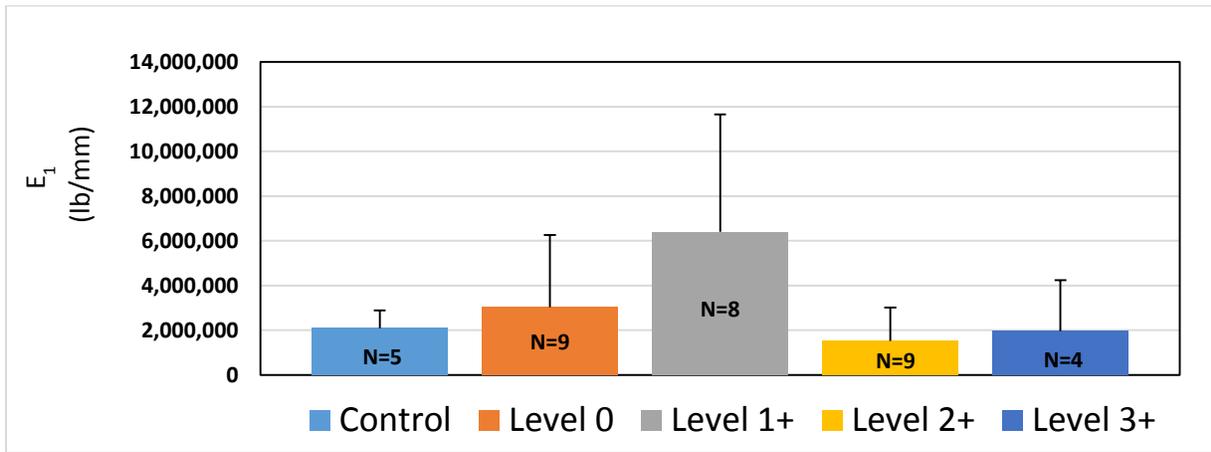


Figure 19. E_1 for the side location of the left leg

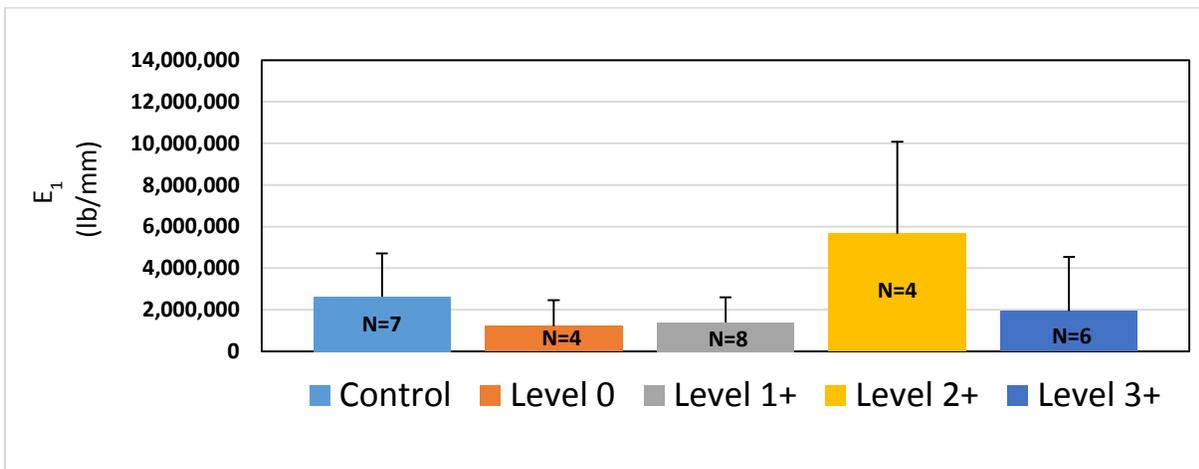


Figure 20. E_1 for the front location of the right leg

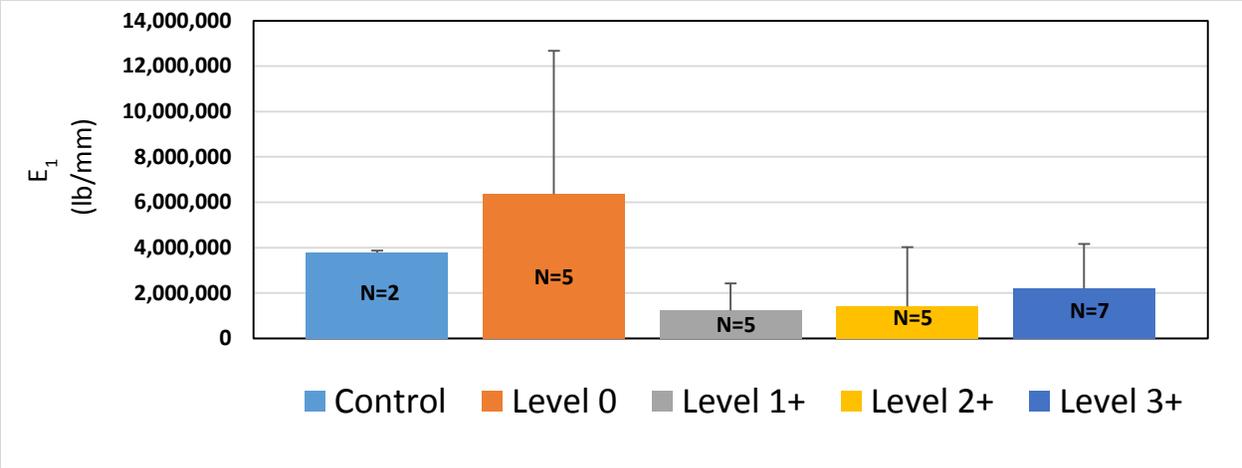


Figure 21. E₁ for the side location of the right leg

Figures 18-21 illustrate that the values of E₁ are significantly large, with the smallest value approximately 2,000,000 lb/mm, indicating that the spring is extremely stiff for tissue with no edema and edematous tissue. After performing t-test analyses and Wilcoxon statistical tests, there was not a statistically significant difference between Control/Level 0 and Levels 1,2,3 or between Level 0 and Levels 1,2,3 for all locations.

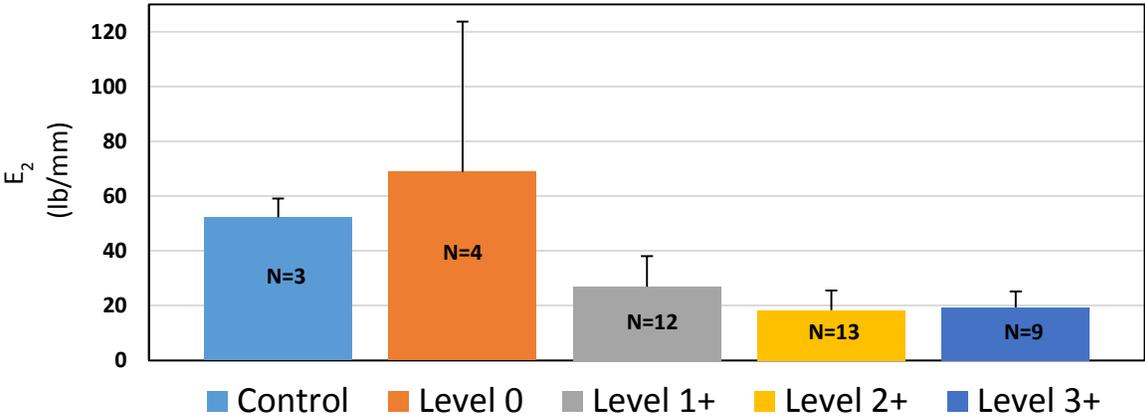


Figure 22. E₂ for the front location of the left leg

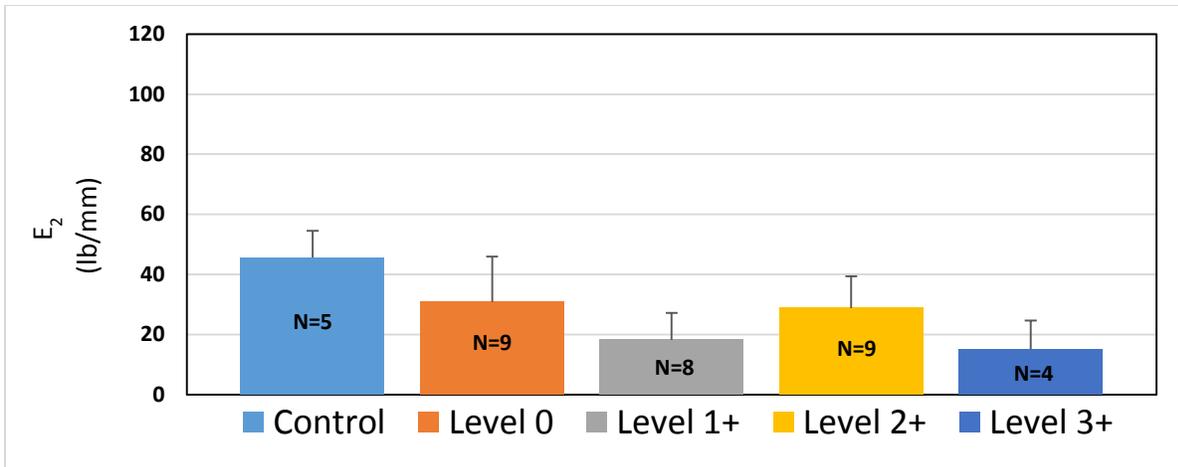


Figure 23. E_2 for the side location of the left leg

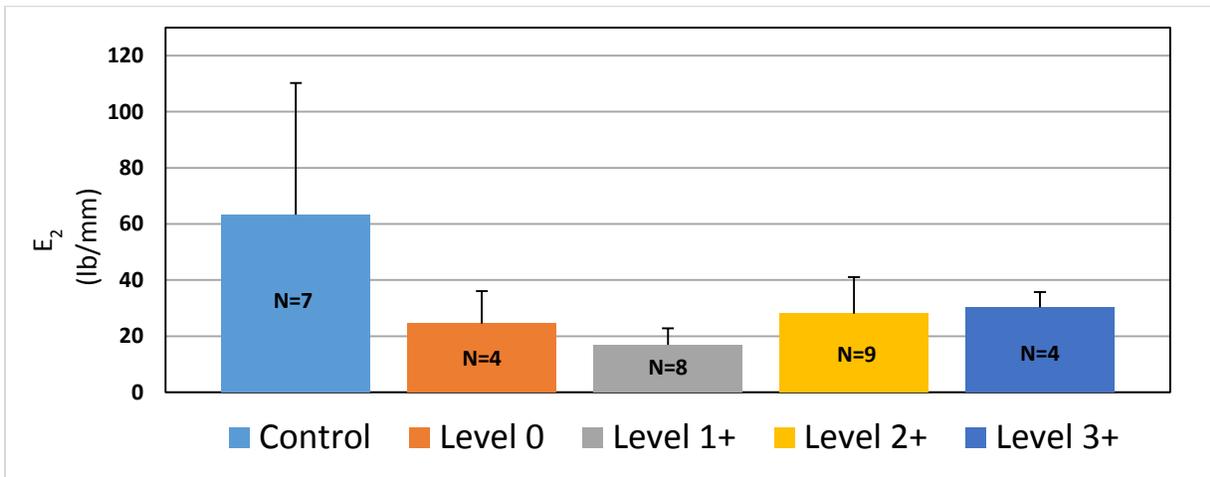


Figure 24. E_2 for the front location of the right leg

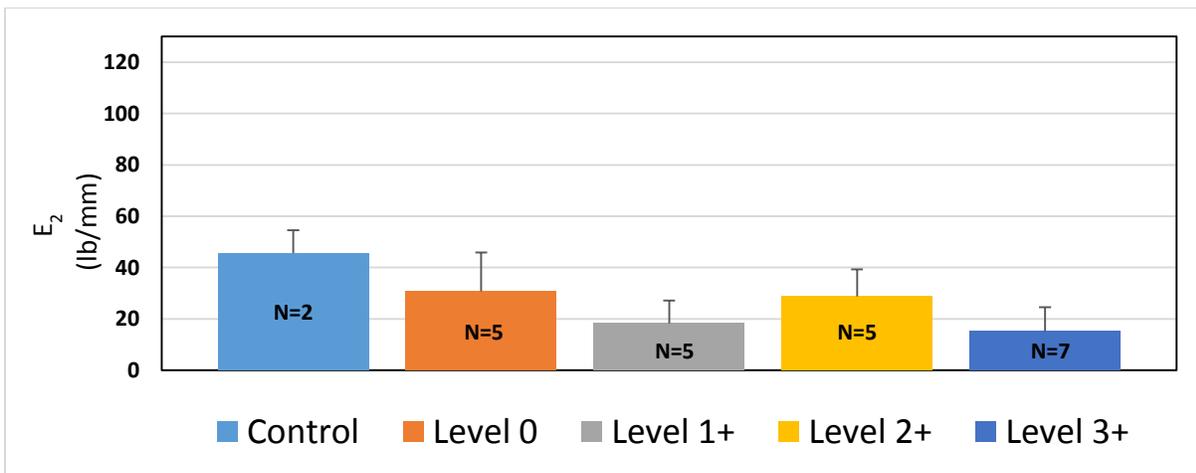


Figure 25. E_2 for the side location of the right leg

Figure 22 shows that there is a difference in E_2 values when comparing tissue with no edema versus tissue with edema for the front left and side left locations. After performing t-test analyses and Wilcoxon statistical tests, there was a statistically significant difference between Control/Level 0 and Levels 1,2,3 for the front left location (p-value equal to 0.04) but not a statistically significant difference between Level 0 and Levels 1,2,3 for the front left location. There was a statistically significant difference between Control/Level 0 and Levels 1,2,3 and between Level 0 and Levels 1,2,3 for the side left location (p-value equal to 0.01 and 0.04, respectively). There was not a statistically significant difference for the other two locations (front right and side right).

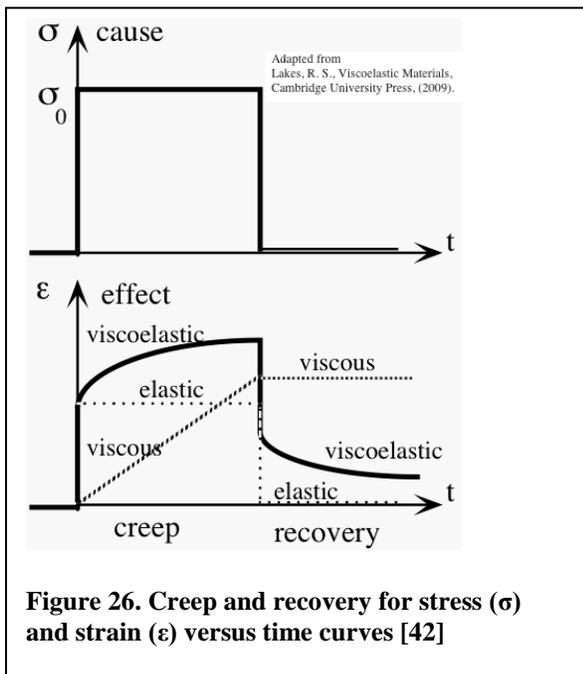
6.2 Edema Rankings

Due to the fact that the front left location provided the most reliable data, the η_1 and E_2 values from this location will be used for the classification system. This classification distinguishes between edematous tissue and tissue without edema. Because the values of E_1 were so large, this spring can be removed from the model and replaced with a rigid bar. The configuration of the model then changes from the SLS model to the Kevin-Voight model, as previously shown in Figure 10.

CHAPTER 7: DISCUSSION

7.1 Rationale and Application

Clinicians and researchers investigating management of HF voice interest in tools and models that assist with improved diagnostic capability, and thus advancements in treatment of associated health issues. The importance of self-care management behaviors to overall health are becoming increasingly known. For these reasons, the potential of the HeartSMART system deserves thoughtfully designed investigations. This thesis project focused on design of an in-home monitoring system that can objectively measure peripheral edema. Furthermore, the system incorporates a standard linear solid (SLS) analysis based on a viscoelastic tissue model. In this study, we have recorded force and displacement measurements from participants with varying levels of edema then fit this data to a SLS model in order to establish edematous tissue properties. Fundamental to this project is the knowledge that human tissues exhibit significant viscoelastic effects. These effects are measurable. Phenomena in viscoelastic materials that can be measured are as follows: (1) creep, in which strain increases with time if stress is constant; (2)



relaxation, in which stress decreases with time if strain is constant; and (3) effective stiffness, which relies on application rate of the load [42]. An example of the phenomenon of creep, as shown in Figure 29, is a placing a 1,000 lb security safe in the attic. When the stress of the safe is first applied to the floor, the floor will displace a small amount. Over time, the floor will displace more, even though the weight of

the safe remains the same.

In this study, stress could not be held constant, and therefore manipulations to the model were necessary. Using the SLS model, the constants η_1 , E_1 , and E_2 were calculated. Findings showed significantly high values E_1 , indicating that a relatively large amount of force was necessary to cause little displacement.

7.2 Recommended Improvements

Through clinical testing, we discovered improvement opportunities to the device design to obtain more reliable data and make the device more user friendly in a clinical and home setting, such as:

- Allow patient to sit instead of stand during testing
- Redesign indentation lever so participants will not use it as a means to support themselves during body weight measurements; also make the lever automated
- Affix a temperature sensor onto the device instead of using a thermometer
- Move force sensor inside displacement housing to prevent damage to the sensor
- Secure the device on a wall instead of using a standalone to increase stability and enhance ease of use

7.3 Future Direction

Further study is necessary to elaborate on the device design and algorithm to determine a deeper meaning of the parameters. Conducting a breadth study of a minimum of a hundred participants across many different edematous tissue types could demonstrate whether the model can predict level of edema in an objective manner. In addition, retesting the same participants would provide greater insight on measurement consistency.

The next step is to use the data from the analyses to predict the edema score for another

sample of participants. By comparing the predicted scores and the clinician assigned scores, the process can be validated.

Based on the design of the system, the skin rebound time could not be captured. Future prototypes are under discussion that would include sensors that could measure this parameter.

CHAPTER 8: CONCLUSION

The HeartSMART system is a vital tool that can be used by health care professionals to monitor heart failure progression and by patients to improve their self-management skills. Continual use of this system will help individuals recognize how significant weight control and fluid monitoring is to their overall health and prevention of worsening conditions. The goal of collecting force and displacement data from the sensors and using these measurements to derive the constants η_1 , E_1 and E_2 for each level of edema was met.

The importance of implementing the tissue model cannot be overemphasized despite some of the unexplainable findings. Increasing the sample size, repeating the study on the same group of participants, and improving the system design as suggested in Chapter 7.2 all have the potential to achieve a higher modeling accuracy. A more informed focus, per findings from this study, is suggested to take into consideration more subtle changes in tissue properties.

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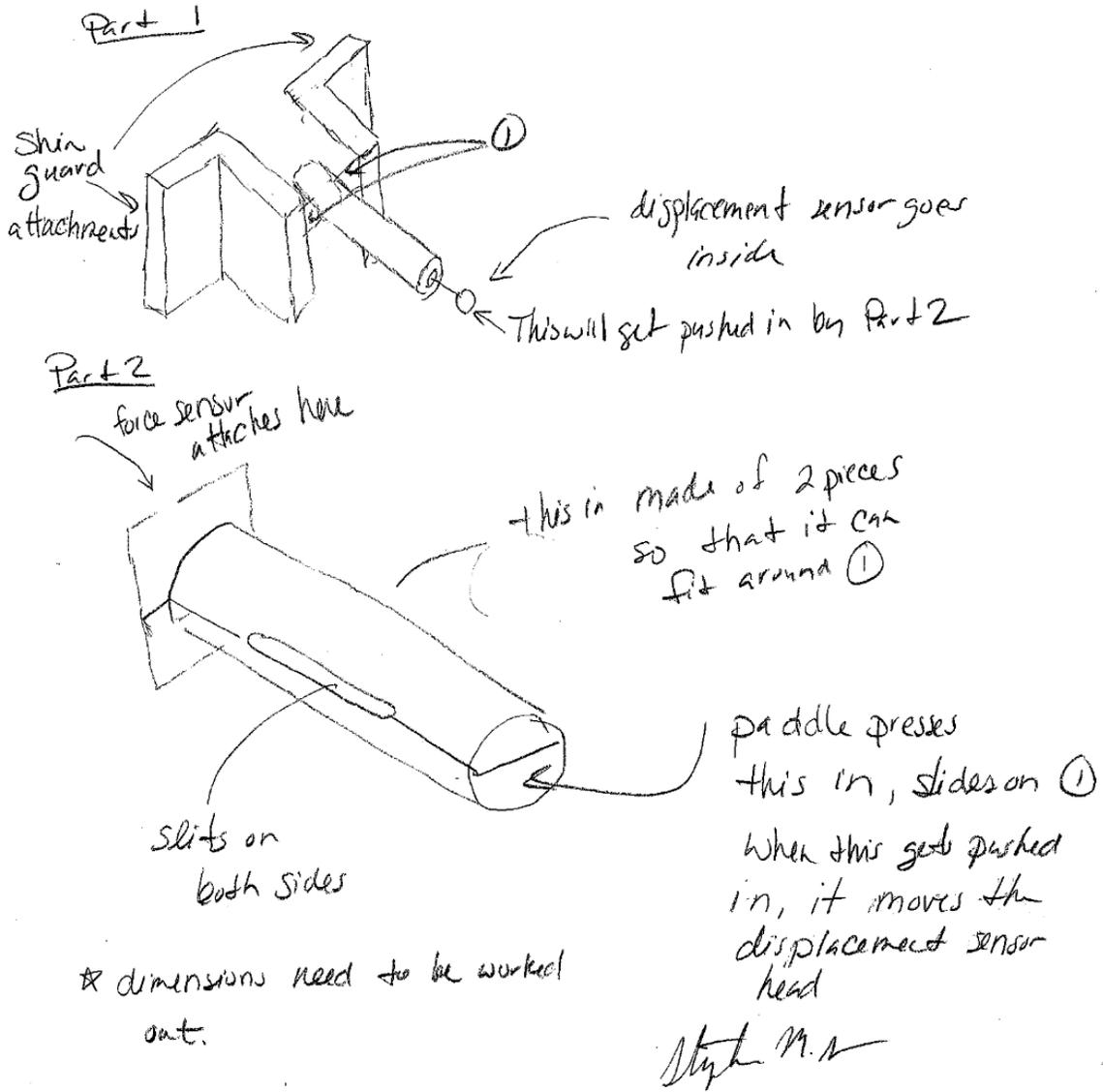
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APPENDIX A: SENSOR HOUSING DESIGN SKETCH

Original work by Dr. Stephanie George

1/28/15

Edema - sensor housing



APPENDIX B: FOAM PROTOCOL

Materials	Quantity
Airtex high-density foam: 1 inch x 15 inch x 17 inch	1
Food Lion large rectangle plastic storage container: 76 fluid ounces	3
Ziploc freezer bag: 1 quart	5
Stanley 1-blade utility knife	1
Crisco pure vegetable oil: 1 gallon	1
Hefty EZ Foil all-purpose pan: 13.25 inch x 9.625 inch x 2.75 inch	1
PVC cylindrical pipe: 3 inch diameter	1
Quikrete concrete mix: 50 pound bag	1
Hacksaw	1
Durabuilt measuring tape: 12 feet	1
Sharpie pen	1
Hot glue gun with glue	1
Sunbeam household iron	1

Lower Leg Model Design

1. Cut a 3 inch diameter PVC pipe to a length of 18 inches with a hacksaw.
2. Mix approximately 25 pounds of concrete with water per the manufacturer's instructions and fill the EZ foil pan with the mixture.
3. Immediately place the PVC pipe upright in the center of the pan and hold until the mixture sets (approximately 20 minutes).
4. Allow mixture to dry overnight.

Foam Model Design

1. Cut six 4 inch x 4 inch pieces of foam using the box cutter. Using the Sharpie, label the samples on the top and bottom "1" through "5." Label the sixth sample as "E" for extra.
2. Set sample 4 to the side. Relabel as "1.00 inch."

3. Measure 0.25 inches deep on sample 1 and mark around each edge with the Sharpie. Use box cutter to cut the 1 inch thick sample to 0.25 inches thick. Dispose of the leftover 0.75 inch thick piece. Relabel sample as “0.25 inches.”
4. Measure 0.50 inches deep on sample 2 and mark around each edge with the Sharpie. Use box cutter to cut the 1 inch thick sample to 0.50 inches thick. Dispose of the leftover 0.50 inch thick piece. Relabel sample as “0.50 inches.”
5. Measure 0.75 inches deep on sample 3 and mark around each edge with the Sharpie. Use box cutter to cut the 1 inch thick sample to 0.25 inches thick. Dispose of the leftover 0.25 inch thick piece. Relabel sample as “0.75 inches.”
6. Measure 0.25 inches deep on sample E and mark around each edge with the Sharpie. Use box cutter to cut the 1 inch thick sample to 0.25 inches thick. Dispose of the leftover 0.75 inch thick piece. Hot glue this 0.25 inch sample to sample 5 and relabel as “1.25 inches.”
7. Place the “0.25 inch” sample and “0.50 inch” sample in one large rectangle container. Fill the container with 38 fluid ounces of vegetable oil and cover with the lid. Allow the samples to soak in the oil overnight.
8. Place the “0.75 inch” sample and “1.00 inch” sample in one large rectangle container. Fill the container with 38 fluid ounces of vegetable oil and cover with the lid. Allow the samples to soak in the oil overnight.
9. Place the “1.25 inch” sample in one large rectangle container. Fill the container with 38 fluid ounces of vegetable oil and cover with the lid. Allow the sample to soak in the oil overnight.
10. Remove each piece of foam from the oil filled containers and allow 30 seconds to drain out excess oil.
11. Place each sample individually in a Ziploc bag. Cut each bag to allow 0.125 inches around each edge of the foam. Seal around all four edges of each bag with an iron.
12. Lay sealed foam bags flat on a table until testing with the lower leg model and HeartSMART system commences.

Device Setup

1. Run the LabView Force and Displacement Program (LFDP) on the university laptop.
2. Plug in the NI Elvis II+ circuit board into the power supply. Connect the laptop to the circuit board with the USB cable. Turn on the circuit board.
3. Place the base of the HeartSMART system on the floor. Check the force sensor and displacement sensor connections to the circuit board by running the LFDP. Troubleshoot if necessary.
4. Close and restart the LFDP in preparation for foam testing.

Foam Testing

1. Position the lower leg model (as described above) in the shin guard of the HeartSMART system.
2. Record the foam thickness of sample 1 (0.25 inch) in the LFDP.

3. Take the "0.25 inch" foam sample and place it between the shin guard and lower leg model. Ensure sample is positioned such that the indentation device will make contact with it.
 4. Immediately run the LVDP to prevent loss of oil from the center of the sample.
 5. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
 6. Repeat step 5 two more times. Stop the LFDP.
- *Note: Displacement (mm) and force (lb) measurements for each of the three runs are automatically recorded and stored with LabView and Microsoft Excel software, respectively. Each time the LFDP is started and stopped, a new excel file is created.
7. Remove foam sample from in between shin guard and lower leg model.
 8. Record the foam thickness of sample 2 (0.50 inch) in the LFDP.
 9. Take the "0.50 inch" foam sample and place it between the shin guard and lower leg model. Ensure sample is positioned such that the indentation device will make contact with it.
 10. Immediately run the LVDP to prevent loss of oil from the center of the sample.
 11. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
 12. Repeat step 11 two more times. Stop the LFDP.
 13. Remove foam sample from in between shin guard and lower leg model.
 14. Record the foam thickness of sample 3 (0.75 inch) in the LFDP.
 15. Take the "0.75 inch" foam sample and place it between the shin guard and lower leg model. Ensure sample is positioned such that the indentation device will make contact with it.
 16. Immediately run the LVDP to prevent loss of oil from the center of the sample.
 17. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
 18. Repeat step 17 two more times. Stop the LFDP.
 19. Remove foam sample from in between shin guard and lower leg model.
 20. Record the foam thickness of sample 4 (1.00 inch) in the LFDP.
 21. Take the "1.00 inch" foam sample and place it between the shin guard and lower leg model. Ensure sample is positioned such that the indentation device will make contact with it.
 22. Immediately run the LVDP to prevent loss of oil from the center of the sample.
 23. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
 24. Repeat step 23 two more times. Stop the LFDP.
 25. Remove foam sample from in between shin guard and lower leg model.
 26. Record the foam thickness of sample 5 (1.25 inch) in the LFDP.
 27. Take the "1.25 inch" foam sample and place it between the shin guard and lower leg model. Ensure sample is positioned such that the indentation device will make contact with it.

28. Immediately run the LVDP to prevent loss of oil from the center of the sample.
29. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
30. Repeat step 29 two more times. Stop the LFDP.
31. Remove foam sample from in between shin guard and lower leg model.

Post Testing

1. Create a new folder labeled with the date of testing.
2. Move the five excel files (0.25 inch, 0.50 inch, 0.75 inch, 1.00 inch, and 1.25 inch) to the folder for future data retrieval and analysis.

APPENDIX C: SLS FINAL EQUATION DERIVATION

The following derivation first illustrates the solution for creep when a constant stress is applied to the tissue, such that $\sigma(t) = \sigma_0$. The derivation then illustrates the solution when $\sigma(t)$ is not constant, such that $\sigma(t) = a_1 t$, where a_1 is the slope of the stress.

Given stress $\sigma(t)$ and strain $\varepsilon(t)$, the relationship between the two can be represented as $\hat{\sigma} = \mathbf{E} \hat{\varepsilon}$ in the Laplace domain, where \mathbf{E} is related to the configurations of the spring constants E_n and damping coefficients η_n .

In a typical creep experiment, $\sigma(t) = \sigma_0 H(t)$, where σ_0 is constant and $H(t)$ is a unit step function defined as

$$H(t) = \begin{cases} 0 & t < 0 \\ 1 & t \geq 0 \end{cases}$$

The Laplace transformation of $H(t)$ is

$$L\{H(t)\} = \frac{1}{s}$$

so the Laplace transform of $\sigma(t)$ is

$$\hat{\sigma} = \frac{\sigma_0}{s}$$

$$\text{Thus, } \hat{\varepsilon} = \frac{\hat{\sigma}}{\mathbf{E}} = \frac{\sigma_0}{s\mathbf{E}}$$

In time domain,

$$\varepsilon(t) = \sigma_0 L^{-1}\left\{\frac{1}{s\mathbf{E}}\right\}$$

For the SLS system,

$$\mathbf{E} = \frac{(E_1 + E_2)\eta_1 s + E_1 E_2}{\eta_1 s + E_1}$$

$$\sigma(t) = \mathbf{E}_0 L^{-1}\left\{\frac{\mathbf{E}}{s}\right\} = \mathbf{E}_0 L^{-1}\left\{\frac{(E_1 + E_2)\eta_1 s + E_1 E_2}{s(\eta_1 s + E_1)}\right\}$$

Using partial fraction expansion,

$$\frac{(E_1 + E_2)\eta_1 s + E_1 E_2}{s(\eta_1 s + E_1)} = \frac{k_1}{s} + \frac{k_2}{s + \frac{E_1}{\eta_1}} = \frac{k_1\left(s + \frac{E_1}{\eta_1}\right) + k_2 s}{s\left(s + \frac{E_1}{\eta_1}\right)}$$

Solving for k_1 and k_2 ,

$$\frac{(E_2 + E_1)\eta_1 s + E_2 E_1}{s(\eta_1 s + E_1)} = \frac{(E_2 + E_1)s + \frac{E_2 E_1}{\eta_1}}{s(s + \frac{E_1}{\eta_1})} = \frac{(k_1 + k_2)s + \frac{k_1 E_1}{\eta_1}}{s(s + \frac{E_1}{\eta_1})}$$

$$\frac{E_2 E_1}{\eta_1} = \frac{k_1 E_1}{\eta_1} \rightarrow k_1 = E_2$$

$$E_2 + E_1 = k_1 + k_2 \rightarrow k_2 = E_1$$

$$\text{Therefore, } \frac{(E_2 + E_1)\eta_1 s + E_2 E_1}{s(\eta_1 s + E_1)} = \frac{E_2}{s} + \frac{E_1}{s + \frac{E_1}{\eta_1}}$$

Therefore, $L^{-1}\left\{\frac{\mathbf{\epsilon}}{s}\right\} = E_2 + e^{-\frac{E_1}{\eta_1}t} = R_0(t)$, where $R_0(t)$ is the relaxation function.

For creep, the compliance function $J_0(t)$ can be defined as

$$J_0(t) = L^{-1}\left\{\frac{1}{s\mathbf{\epsilon}}\right\}, \text{ where}$$

$$\mathbf{\epsilon} = \frac{(E_2 + E_1)\eta_1 s + E_2 E_1}{\eta_1 s + E_1}$$

For a constant stress, the strain with respect to time,

$$\begin{aligned} \epsilon(t) &= \sigma_0 L^{-1}\left\{\frac{1}{s\mathbf{\epsilon}}\right\} \\ &= \sigma_0 L^{-1}\left\{\frac{\eta_1 s + E_1}{s[(E_2 + E_1)\eta_1 s + E_2 E_1]}\right\} \end{aligned}$$

Using partial fraction expansion,

$$\frac{\eta_1 s + E_1}{s[(E_2 + E_1)\eta_1 s + E_2 E_1]} = \frac{1}{E_2 + E_1} \frac{1}{s} + \frac{E_1}{\eta_1(E_2 + E_1)} \frac{1}{s[s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}]}$$

$$\frac{A}{s} + \frac{B}{s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}} = \frac{(A + B)s + A \frac{E_2 E_1}{\eta_1(E_2 + E_1)}}{s[s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}]}$$

$$A = \frac{1}{E_2}$$

$$B = \frac{1}{E_2 + E_1} - \frac{1}{E_2} = \frac{-E_1}{E_2(E_2 + E_1)}$$

$$\frac{1}{s\mathbf{\epsilon}} = \frac{1}{E_2} \frac{1}{s} + \frac{\frac{-E_1}{E_2(E_2 + E_1)}}{s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}}$$

$$J_0(t) = \frac{A}{s} + \frac{B}{s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}} = \frac{(A + B)s + A \frac{E_2 E_1}{\eta_1(E_2 + E_1)}}{s[s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}]}$$

$$A = \frac{1}{E_2}$$

$$B = \frac{1}{E_2 + E_1} - \frac{1}{E_2} = \frac{-E_1}{E_2(E_2 + E_1)}$$

$$\frac{1}{s\mathcal{E}} = \frac{1}{E_2} + \frac{\frac{-E_1}{E_2(E_2 + E_1)}}{s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}}$$

$$J_0(t) = L^{-1}\left\{\frac{1}{s\mathcal{E}}\right\} = \frac{1}{E_2}u(t) - \frac{E_1}{E_2(E_2 + E_1)}e^{-\left(\frac{E_2 E_1}{\eta_1(E_2 + E_1)}t\right)},$$

where $u(t) = 1$ at $t \geq 0$

In a typical creep experiment, $\sigma(t)$ is constant. However, $\sigma(t)$ was not constant in this study. Instead, $\sigma(t)$ is about like a ramp function, with $\sigma(t) = a, t$, where a , is the slope of the stress versus time curve. The Laplace transform in this case, therefore, is $\hat{\sigma} = \frac{a_1}{s^2}$, and the equation becomes

$$\varepsilon(t) = L^{-1}\left\{\frac{a_1}{s^2}\mathcal{E}\right\}. \mathcal{E} \text{ remains the same.}$$

$$\frac{1}{s^2\mathcal{E}} = \frac{\eta_1 s + E_1}{s^2[(E_2 + E_1)\eta_1 s + E_1 E_2]} = \frac{\frac{1}{E_2 + E_1}s + \frac{E_1}{\eta_1(E_2 + E_1)}}{s^2\left[s + \frac{E_1 E_2}{\eta_1(E_2 + E_1)}\right]}$$

Using partial fraction expansion,

$$\begin{aligned} \frac{A}{s^2} + \frac{B}{s} + \frac{C}{s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}} &= \frac{A\left[s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}\right] + Bs\left[s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}\right] + Cs^2}{s^2\left[s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}\right]} \\ &= \frac{(B + C)s^2 + \left[A + B\frac{E_2 E_1}{\eta_1(E_2 + E_1)}\right]s + A\frac{E_2 E_1}{\eta_1(E_2 + E_1)}}{s^2\left[s + \frac{E_2 E_1}{\eta_1(E_2 + E_1)}\right]} \end{aligned}$$

From the constant term: $A = \frac{1}{E_2}$

From the 1st order term: $A + B \frac{E_2 E_1}{(E_2 + E_1) \eta_1} = \frac{1}{E_2 + E_1}$

$$B = \frac{\frac{1}{E_2 + E_1} - \frac{1}{E_2}}{\frac{E_2 E_1}{(E_2 + E_1) \eta_1}} = \frac{\eta_1}{E_2^2}$$

From the 2nd order term: $B + C = 0$

$$C = -B = -\frac{\eta_1}{E_2^2}$$

Taking the inverse Laplace transform,

$$\varepsilon(t) = L^{-1} \left\{ \frac{a_1}{s^2 \mathcal{E}} \right\} = \frac{a_1}{E_2} t u(t) + a_1 \frac{\eta_1}{E_2^2} u(t) - a_1 \frac{\eta_1}{E_2^2} e^{-\frac{E_2 E_1}{\eta_1 (E_2 + E_1)} t}$$

APPENDIX D: DEVICE TESTING PROTOCOL

Device Setup

5. Run the LabView Force and Displacement Program (LFDP) on the university laptop.
6. Plug in the NI Elvis II+ circuit board into the power supply. Connect the laptop to the circuit board with the USB cable. Turn on the circuit board.
7. Place the base of the HeartSMART system on the floor. Check the force sensor and displacement sensor connections to the circuit board by running the LFDP. Troubleshoot if necessary.
8. Close and restart the LFDP in preparation for participant testing.

Participant Testing

1. Greet and introduce yourself to the participant, who is either a healthy subject or patient (Patients were brought to the testing room by the healthcare provider. Healthy subjects were informed of the study either through a university email or an announcement at the Monk clinic).
2. Once participant is seated, explain step by step all pages of the “Informed Consent to Participate in Research” and “UMCIRB HIPAA Privacy Authorization” forms. Note: For healthy subjects, only the “Informed Consent to Participate in Research” form is required.
3. Ask participant if he/she has any questions and answer accordingly. Give the participant the appropriate forms to initial and sign.
4. Verify participant has initialed at the bottom of every page of the informed consent form. Verify participant has printed and signed his/her name and dated the last page of the informed consent. Verify patient has printed and signed his/her name and dated the last page of the HIPAA form.
5. Assign participant a number. Note: All future references to the participant from this point on will only be associated with the assigned number and not the name in order to protect participant identity.
6. Collect the participant’s forehead temperature with the thermometer. Record the temperature in the Participant Data excel file.
7. Enter the participant’s assigned number in the LFDP.
8. While seated, have the participant remove his/her shoes.
9. Collect the participant’s weight by having him/her stand on the Withings scale. Record the weight in the LFDP.
10. Allow participant to sit on a roller chair. Collect the skin temperature of the outside lower portion of the participant’s left leg. Record the temperature in the LFDP.
11. Place the outside lower portion of the participant’s left leg in the shin guard. Verify the participant’s leg is aligned correctly with the indentation device so that contact with the skin will occur. Verify the participant is resting his/her leg in the shin guard and is not pushing against the shin guard.
12. Record the testing location (side of left leg) in the LFDP.
13. Run the LVDP.

14. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
15. Repeat step 14 two more times. Stop the LFDP.

*Note: Displacement (mm) and force (lb) measurements for each of the three runs are automatically recorded and stored with LabView and Microsoft Excel software, respectively. Each time the LFDP is started and stopped, a new excel file is created.

16. Allow participant to remove his/her leg from the shin guard.
17. Collect the skin temperature of the front lower portion of the participant's left leg. Record the temperature in the LFDP.
18. Place the front lower portion of the participant's left leg in the shin guard. Verify the participant's leg is aligned correctly with the indentation device so that contact with the skin will occur. Verify the participant is resting his/her leg in the shin guard and is not pushing against the shin guard.
19. Record the testing location (front of left leg) in the LFDP.
20. Run the LVDP.
21. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
22. Repeat step 21 two more times. Stop the LFDP.
23. Allow participant to remove his/her leg from the shin guard.
24. Collect the skin temperature of the front lower portion of the participant's right leg. Record the temperature in the LFDP.
25. Place the front lower portion of the participant's right leg in the shin guard. Verify the participant's leg is aligned correctly with the indentation device so that contact with the skin will occur. Verify the participant is resting his/her leg in the shin guard and is not pushing against the shin guard.
26. Record the testing location (front of right leg) in the LFDP.
27. Run the LVDP.
28. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
29. Repeat step 28 two more times. Stop the LFDP.
30. Allow participant to remove his/her leg from the shin guard.
31. Collect the skin temperature of the outside lower portion of the participant's right leg. Record the temperature in the LFDP.
32. Place the outside lower portion of the participant's right leg in the shin guard. Verify the participant's leg is aligned correctly with the indentation device so that contact with the skin will occur. Verify the participant is resting his/her leg in the shin guard and is not pushing against the shin guard.
33. Record the testing location (side of right leg) in the LFDP.
34. Run the LVDP.
35. Push on the lever arm and apply a maximum force between 4 and 5 pounds. Hold at this force for 1 to 3 seconds. Release the lever arm.
36. Repeat step 35 two more times. Stop the LFDP.

37. Allow participant to remove his/her leg from the shin guard.
38. Assist participant to a non-roller chair and have him/her put on his/her shoes.
39. Thank the participant for his/her time and willingness to participate in the study. Escort participant to the location of their healthcare provider.
40. While at the clinic, record the healthcare provider assigned edema score in the Participant Data.xls file.

Post Testing

3. Create a new folder labeled with the date of testing.
4. Move the participant's four excel files (side of left leg, front of left leg, front of right leg, side of right leg) to the folder for future data retrieval and analysis.
5. For IRB purposes, take participant informed consent and HIPAA forms to committee member, Dr. Stephanie George, for secure storage.

APPENDIX E: IRB AMMENDMENT APPROVAL

UMCIRB 14-0001: “Comparison of sensor and provider generated edema measurement”

approval letter is shown below.



EAST CAROLINA UNIVERSITY
University & Medical Center Institutional Review Board Office
4N-70 Brody Medical Sciences Building · Mail Stop 682
600 Moye Boulevard · Greenville, NC 27834
Office 252-744-2914 · Fax 252-744-2284 · www.ecu.edu/irb

Notification of Amendment Approval

From: Biomedical IRB
To: [Stephanie George](#)
CC:
Date: 3/15/2016
Re: [Ame4 UMCIRB 14-000153](#)
[UMCIRB 14-000153](#)
Comparison of sensor and provider generated edema measurement

Your Amendment has been reviewed and approved using expedited review for the period of 3/15/2016 to 6/16/2016. It was the determination of the UMCIRB Chairperson (or designee) that this revision does not impact the overall risk/benefit ratio of the study and is appropriate for the population and procedures proposed.

Please note that any further changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. A continuing or final review must be submitted to the UMCIRB prior to the date of study expiration. The investigator must adhere to all reporting requirements for this study.

Approved consent documents with the IRB approval date stamped on the document should be used to consent participants (consent documents with the IRB approval date stamp are found under the Documents tab in the study workspace).

The approval includes the following items:

Document	Description
Flyer(0.01)	Recruitment Documents/Scripts
Healthy Consent Form(0.04)	Consent Forms
Patient Consent Form(0.04)	Consent Forms
Provider/Student Consent Form(0.03)	Consent Forms
Study Protocol(0.05)	Study Protocol or Grant Application

The Chairperson (or designee) does not have a potential for conflict of interest on this study.

IRB00000705 East Carolina U IRB #1 (Biomedical) IORG0000418
IRB00003781 East Carolina U IRB #2 (Behavioral/SS) IORG0000418

APPENDIX F: DATA SAMPLE FILES OF PATIENT 6

Raw data collected and analyses were performed on each participant. Figures 27-32 illustrate such for patient 6.

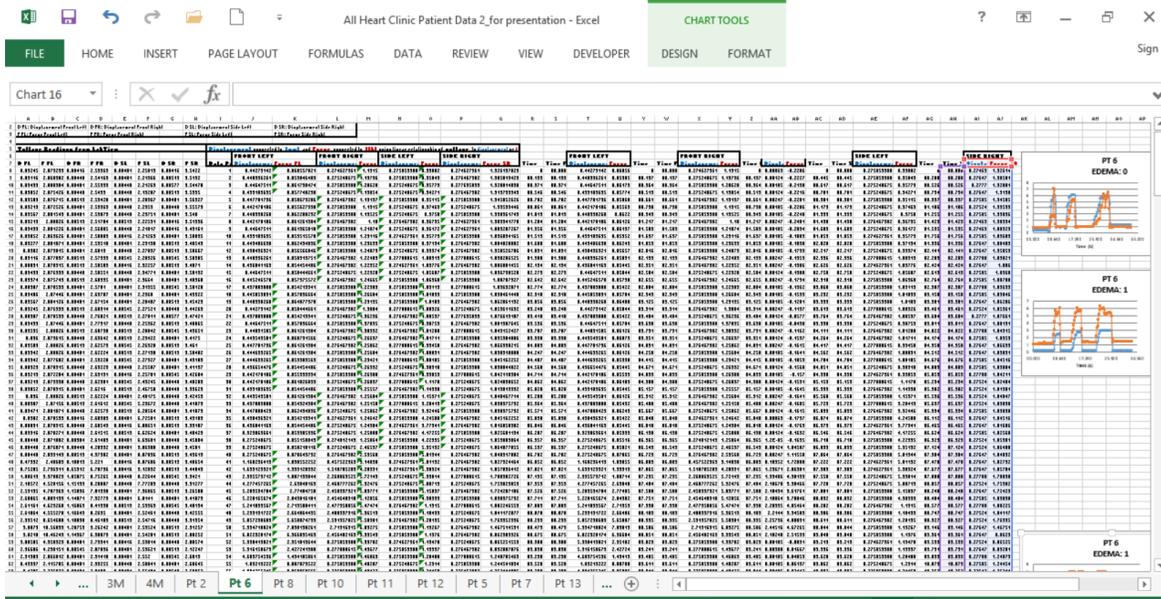


Figure 27. Sample worksheet of force and displacement raw data

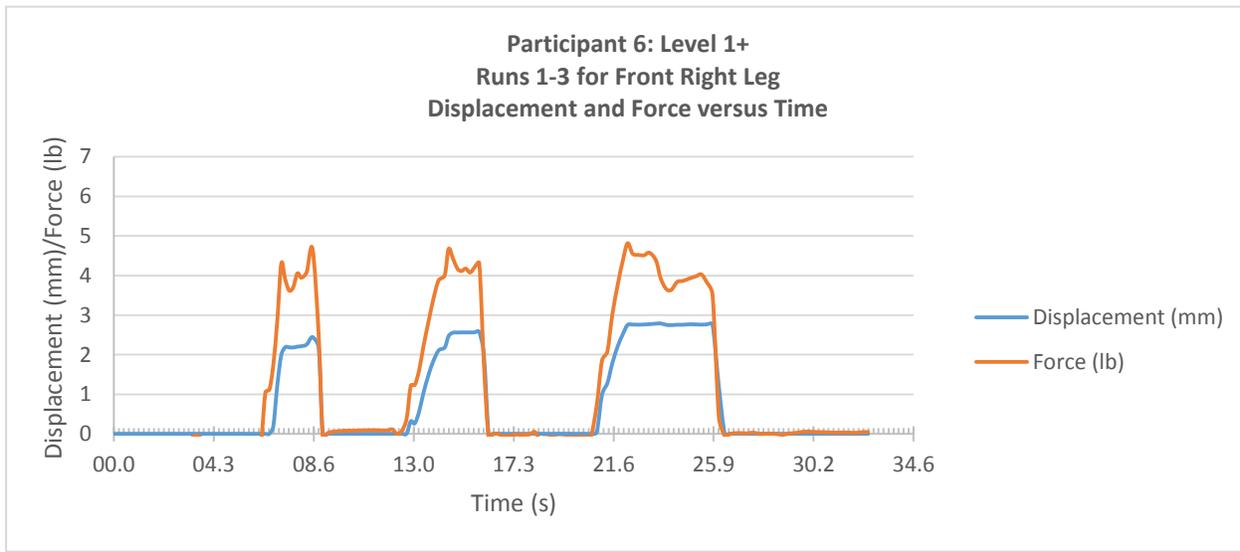


Figure 28. Example of displacement and force versus time curve

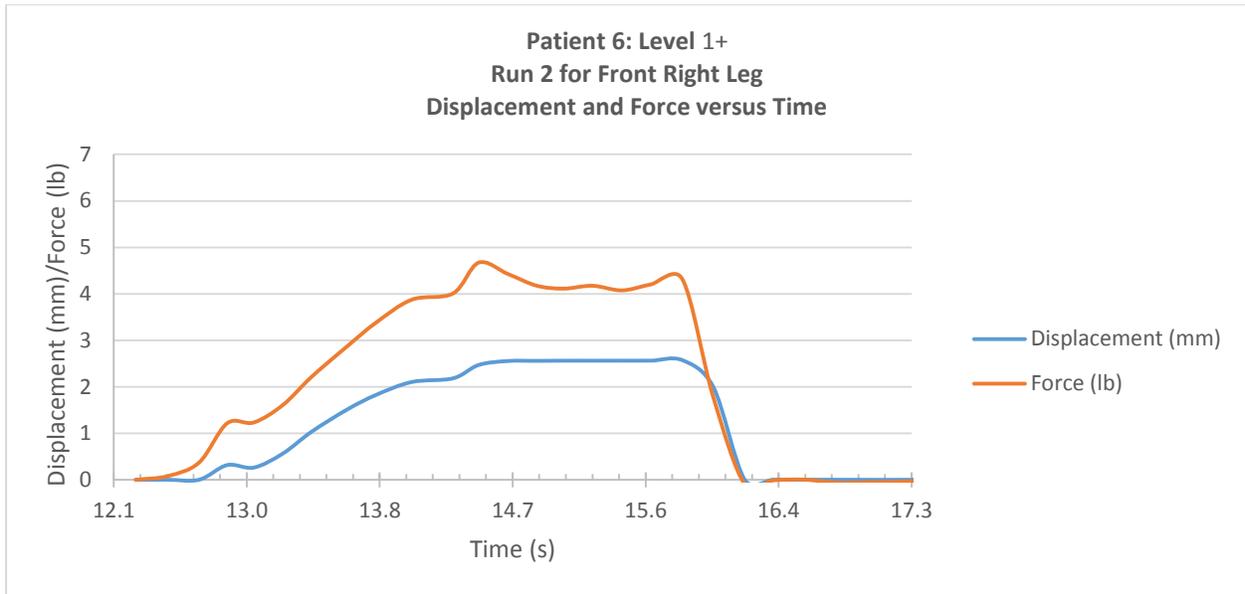


Figure 29. Example of one run of displacement and force versus time curve

Weaver_Displacement and force slopes_June 26 - Excel

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	
1																							
2	FL	Begin	Time	6.702	Displacement	0.275	6.702	Force	0.871	Slope (D)	Slope (F)		FR	Begin	Time	6.723	Displacement	0.276	6.365	Force	1.251	Slope (D)	Slope (F)
3		Run	End	8.239	5.857	8.239	5.65			3.631750163	3.109303839			Run	End	7.404	2.461	7.404	5.325		3.208516887	3.92107796	
4		1												1									
5			Time		Displacement		Force		Slope (D)	Slope (F)	0.85614				Time		Displacement		Force		Slope (D)	Slope (F)	
6		Begin	13.701	0.839	13.701	1.08								Begin	12.651	0.276	12.239	1.517					
7		Run	End	15.738	6.019	15.738	5.053		2.542955326	1.95041728	0.76699			Run	End	14.467	2.744	14.467	6.188		1.359030837	2.096499102	
8		2												2									
9			Time		Displacement		Force		Slope (D)	Slope (F)					Time		Displacement		Force		Slope (D)	Slope (F)	
10		Begin	24.958	1.413	24.958	1.225								Begin	20.868	0.318	20.612	1.437					
11		Run	End	27.713	5.526	27.993	4.029		1.49292196	0.923887974				Run	End	22.2	3.023	22.2	6.331		2.030780781	3.08186398	
12		3												3									
13																							
14																							
15																							
16	SL												SR	Begin	Time	17.993	Displacement	0.277	16.6	Force	1.294	Slope (D)	Slope (F)
17			No data could be collected on this location											Run	End	19.633	3.188	17.591	7.038		1.775	5.796165489	
18														1									
19															Time		Displacement		Force		Slope (D)	Slope (F)	
20														Run	End	Bad Run				#DIV/0!	#DIV/0!		
21																							
22																							
23														2		Time		Displacement		Force		Slope (D)	Slope (F)
24														Begin	31.581	0.275	31.064	1.704					
25														Run	End	32.998	3	31.581	7.038		1.923076923	10.3172147	
26														3									
27																							
28																							
29																							
30																							

Figure 30. Sample worksheet of force slopes and displacement slopes

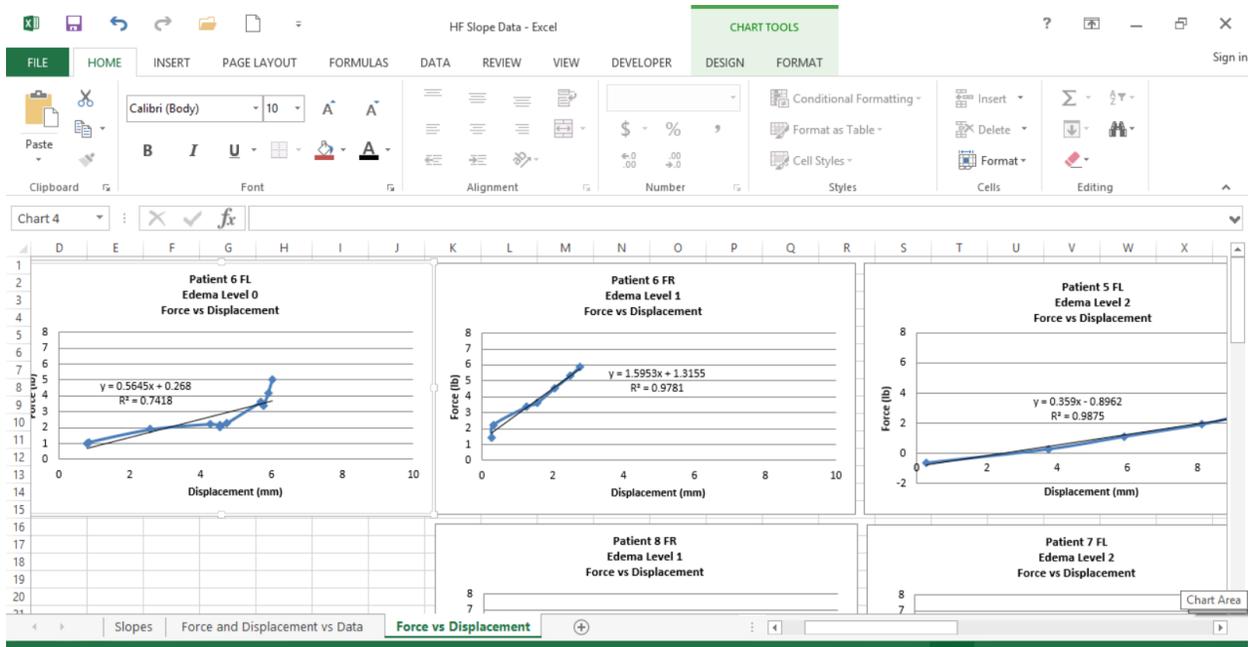


Figure 31. Sample worksheet of force versus displacement curves with slopes

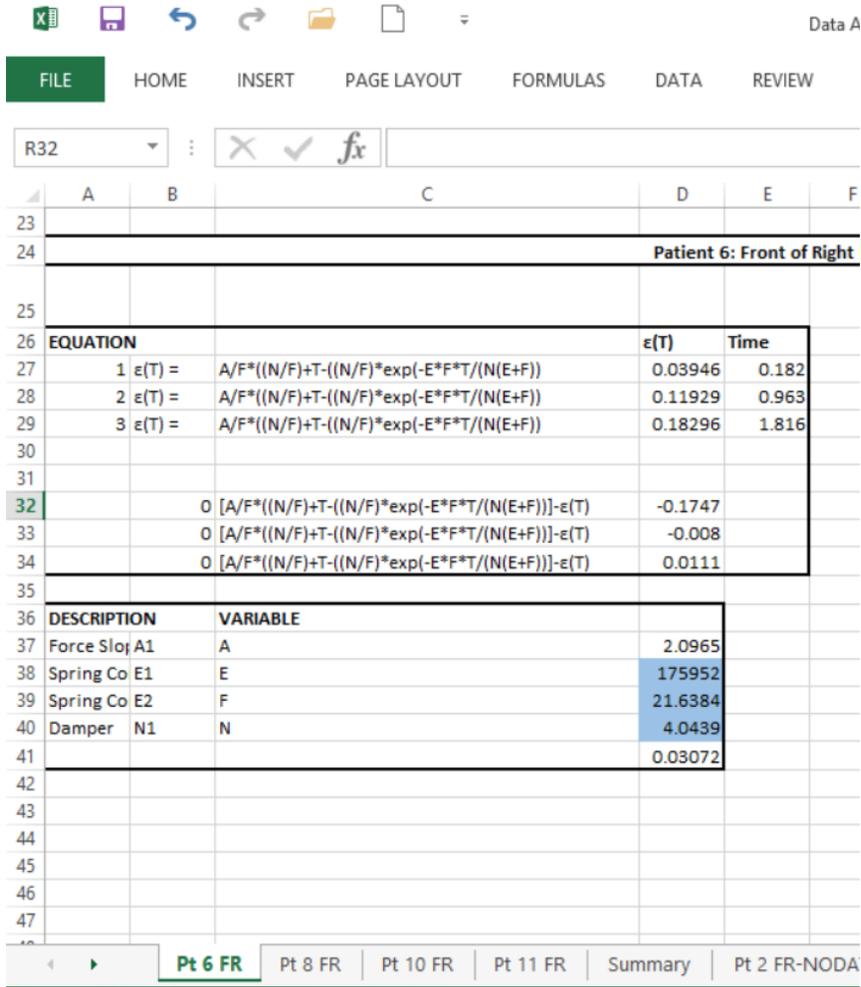


Figure 32. Sample worksheet of SLS analysis

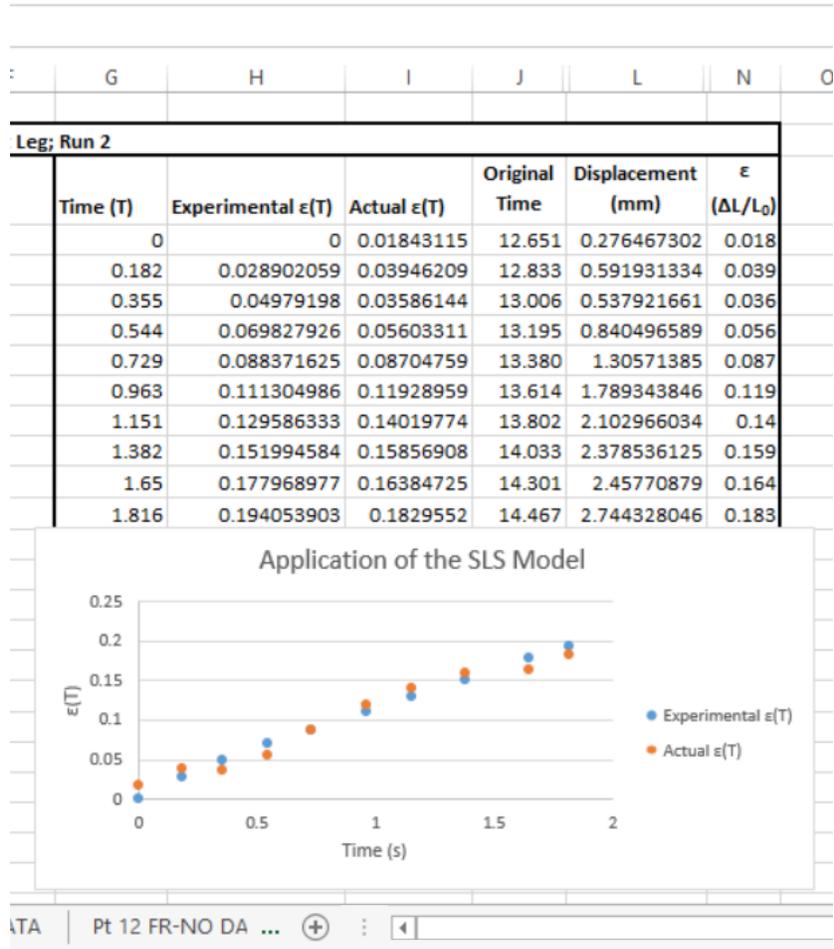


Figure 32 Continued. Sample worksheet of SLS analysis

