ULTRASOUND ELASTICITY MEASUREMENTS AS A PREDICTOR FOR ARTERIOVENOUS FISTULA MATURATION

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A THESIS

Submitted to the graduate faculty of The University of Alabama at Birmingham,
In partial fulfillment of the requirements for the degree of
Master of Science Biomedical Engineering

BIRMINGHAM, ALABAMA

2011
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ABSTRACT

This research thesis examines the applicability of using ultrasound imaging to quantify arterial elasticity and assess potential of arteriovenous fistula maturation in chronic kidney disease (CKD) patients. Tissue-specific abnormalities have proven useful for identifying disease states within oncology, cardiovascular and musculoskeletal system. Using ultrasound-based imaging to evaluate arterial elasticity is a noninvasive and novel technique. It has the potential to contribute further insight into chronic kidney disease fistula failure and become a noninvasive prognostic indicator.

Reliable vascular access is critical for delivery of adequate hemodialysis treatment to CKD patients and to maintain long-term connections for dialysis. An arteriovenous fistula is a surgically generated direct anastomosis between a native artery and vein and is the preferred method available for reliable vascular access, yet up to 60% of fistula surgeries never entirely mature. Fistula maturity is based on the rate of blood flow that can be tolerated; 500 mL/min is considered successful maturation. In order to evaluate the potential of ultrasound to help determine fistula success, ultrasound mapping of the brachial artery is completed during pre-surgical evaluation of chronic kidney disease patients. In combination with echocardiogram and blood pressure measurements, an elastic modulus model allows estimation of vessel stiffness. Tracking fistula maturation
and completing histological analysis of vessel samples will confirm relationships. This data will be used in conjunction with ultrasound elastic modulus measurements to correlate possible explanations for fistula failure. A comprehensive database of vascular elastic modulus measurements on normal subjects is also needed to complete this study. This will assist in determining differences in CKD patients and normal subjects. This estimation of elastic modulus using ultrasound imaging will give additional arterial biomechanical information and has potential to be a successful addition to current predictors to help identify arteriovenous fistula maturation.

*Keywords*: arteriovenous fistula, chronic kidney disease, elasticity, elastic modulus, stress, strain
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ACKNOWLEDGEMENTS

I would like to thank the Department of Biomedical Engineering at University of Alabama at Birmingham and my research advisor and chair of my committee, Dr. Kenneth Hoyt, for his time and support on this project. Thank you to my committee members: Drs. Joel Berry, Michelle Robbin, Heidi Umphrey, and Donald Twieg for their time and help during this thesis research.

I would also like to thank and acknowledge the contributions from the Departments of Radiology and Medicine, specifically from Carl Abts, Dr. Mark E. Lockhart, and Dr. Michael Allon.

This research was supported by NIH grant RO1 DK085027-O1A1.
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LIST OF ABBREVIATIONS

AV: Arteriovenous

BP: Blood Pressure

CKD: Chronic Kidney Disease

Δ = change

E = Elastic Modulus

ε = strain

IMT: intima-media thickness

σ = stress
BACKGROUND AND SIGNIFICANCE

In the United States, chronic kidney disease (CKD) affects 26 million adults (National Kidney Foundation 2011). CKD is a progressive disease that takes months or years to develop, characteristically stemming from diabetes and high blood pressure. End stage renal disease patients are treated with hemodialysis, which allows for blood to flow into a dialysis machine, be filtered, and then return to the body purified. Reliable vascular access is critical for adequate hemodialysis treatment and for maintaining long-term connections for additional hemodialysis sessions (KDOQI 2006). An arteriovenous (AV) fistula is a direct anastomosis between a native artery and vein and is the preferred method available for reliable vascular access. This surgical connection between arterial and venous circulation puts pressure on the vein that it did not previously experience. In order for the vein to withstand the arterial pressure of the blood and accommodate the larger volume, it needs enlarging and maturation (Allon 2007). This surgical process of creating a passageway between an artery and a vein in the forearm or upper arm allows for CKD patients to undergo hemodialysis. The advantage of AV fistula use includes lower infection rates because no foreign material is involved in their formation. Additional AV fistula advantages are higher blood flow rates (which translates to more effective dialysis), and a lower incidence of thrombosis (Allon & Robbin 2002). Maturation of AV fistulas is determined by the blood flow rate required by hemodialysis, 300 mL/min. Other methods available for vascular access are grafts or catheters, yet surgically placed AV fistulas have shown to have the least chance for infections or clots, have the ability to tolerate repeated use, and survive the longest. Although this is true, up to 60% of surgically placed AV fistulas do not mature (Parmer et al. 2008, Dixon et al.
Medical ultrasound has become increasingly popular due to noninvasiveness, real-time imaging capability and low risk associated with exposure. Other encouraging characteristics that identify ultrasound as a valuable clinical imaging modality are its portability and low cost. These positive characteristics have also made ultrasound an emerging imaging modality in research. Diagnostic ultrasound imaging is currently used to visualize biological tissues such as tendons, muscles, joints, vessels and internal organs for pathology or lesions, as well as use in biopsies (Zagzebski 1996, Kremkau 2002). It is also used in obstetrics, musculoskeletal system, anesthesiology, cardiology and cardiovascular system, oncology, gastroenterology, gynecology, neurology, ophthalmology and urology (Zagzebski 1996, Kremkau 2002). The progression of ultrasound applications over the last decades has greatly increased and broadened into many diverse clinical fields. It is evident that there are more opportunities for ultrasound imaging that have not yet been explored. When establishing clinical imaging techniques, the ability to image and collect data in real-time is extremely important, as well as maintaining cost-effectiveness and accessibility for patients.

Noninvasive imaging modalities begin with an external source emitting a signal into the body, which then produces a propagating signal to measure and record the biological responses. Sound is mechanical energy that is transmitted by pressure waves in a material medium, therefore ultrasound utilizes high frequency sound waves and echoes to create images. Medical ultrasound utilizes frequencies around 1-20 MHz, while normal audible sound is between 20 Hz to 20 kHz (Zagzebski 1996, Kremkau 2002). Ultrasound
begins with a transmitting transducer, a piezoelectric element, which converts electrical energy into pressure waves and acoustic energy. This energy produced from the transducer creates mechanical vibrations, which in turn generates sound waves, or ultrasonic pulses to travel through a medium. In general, the waves change depending on the medium, or tissue, they are propagating through. Biological substances have different speeds at which the ultrasound waves travel, averaging around 1540 m/s for soft tissue (Zagzebski 1996). As the waves propagate through tissue, the tissue’s acoustical impedance cause pulses to return to the transducer as an echo signal. Ultrasound striking a smooth tissue boundary produces a reflection which is dependent on the acoustical impedance of the boundary where the two tissues create the boundary (Zagzebski 1996, Kremkau 2002). Ultrasound measures the transmit time for a signal to travel to a reflecting interface and return an echo to the transducer; therefore travel time allows for distance calculations. Echo images are recorded as a function of depth (A-line) for each element of the transducer. Each of these A-lines is sequentially recorded for all transducer elements in order to create a two dimensional grayscale image (B-mode). This B-mode or brightness mode is known as a sonogram. Resolution and image clarity is dependent on wavelength as the penetration of an ultrasound wave is proportional to the wavelength. At higher frequencies, ultrasound images will have increased resolution, but the penetration depth the ultrasound can reach decreases (Zagzebski 1996, Kremkau 2002). In general, ultrasound imaging gives us the ability to derive structural and mechanical information from within the body.

The field of elasticity imaging has proven useful in analyzing differential changes in tissue to characterize irregularities. Compliance, the ability of an elastic body to
deform under an applied load, is a measurable parameter within elasticity imaging. Compliance is widely accepted as a descriptor of vascular tissue health. The variance between the elastic properties of materials can be measured through elastic modulus calculations. Elastic modulus is determined through measurements of stress and strain. In vascular applications, the stress is intrinsically provided by cardiovascular pulsations from the patient or subject studied (Fromageau et al. 2003, Mai et al. 2002, Weitzel et al. 2005, 2009). As strain on the vessel wall increases for a given stress field, the elastic modulus decreases, which is proportional to increasing compliance. This is due to collagen fibers engaging in order to maintain the wall shape (Wagenseil & Mecham 2009, Greenwald et al. 1997). Basic theory from engineering mechanics points us to the conclusion that the stiffer the material, or tissue, the less deformation will occur under an applied stress. This information can be applied to biological elastic modulus models to characterize vascular biomechanics in clinical applications.

Changes in elasticity have been shown to identify abnormalities within biological tissues, and imaging these elastic properties has become a pivotal point of many research efforts. Clinical applications include cancer detection and therapeutic monitoring, vascular elasticity for circulatory regulation, tendon analysis in musculoskeletal system and altering skin elastic properties in plastic surgery (Bercoff et al. 2003, Hall et al. 2003 Weitzel et al. 2005, Ahn et al. 1991, Sharma and Maffuli 2005). Elasticity imaging and tissue characterization has become a popular field to estimate the elastic properties of tissue, which are known to change with certain diseases. Ultrasound is a well-known imaging modality for the vascular system (i.e. monitoring blood flow, locating blockages or abnormalities, detecting blood clots and evaluating surgical procedures) due to its high
temporal resolution and the ability to image small changes in vessel motion (Danpinid et al. 2010, Mackenzie et al. 2002, Laurent et al. 2006, Hartley et al. 1997, Harvey et al. 2002). It has been shown that ultrasound can be used to track vessel wall motion and amount of overall vessel deformation (Pirat 2006). Increasing the range of applications for which ultrasound can effectively be used is an important field of interest for clinical evaluation of CKD patients.

Estimation of structural components of the arterial wall using ultrasound allows derivation of structural and mechanical information. This information, in combination with vascular biomechanics, gives the ability to estimate elastic modulus calculations. Vessel anatomy shows clear distinctions between arteries and veins. Arteries are thick-walled pressure vessels that transport blood actively away from the heart using contractions to move blood flow and have the ability to withstand high amount of pressure (Willis 1982). Veins carry blood to the heart with passive blood flow and are thin-walled vessels that are not created to withstand high amount of pressure (Willis 1982). When an AV fistula is surgically created, there is an increased stress on the veins. Those veins are then required to bear the load of arteries, which they are not designed in nature to take on this additive stress. Using vascular biomechanics and ultrasound imaging, an approximated approach to arterial elasticity will be constructed.

In pre-fistula assessment, ultrasound is currently used to image and map the brachial artery. Introduction of ultrasound mapping has had positive impacts on increasing fistula placement, but has not decreased the fistula non-maturation rate (Allon et al. 2001, Robbin et al. 2000, 2002). With institutions recording up to 60% of AV fistula surgeries failing to mature (Dixon et al. 2006, Asif et al. 2008, Dember et al. 2008,
Allon et al. 2001, Miller et al. 1999), it is suspected that pre-existing vascular irregularities, which are not accounted for in preoperative mapping, are reducing the chance for maturation. Patients who successfully underwent the preoperative ultrasound vascular mapping qualified for AV fistula surgery with the following characteristics: diameter of the candidate artery must be at least 2 mm, and diameter of the candidate vein must be at least 2.5 mm (Silva et al. 1998, Malovrh 1998, 2002, Korten et al. 2007, Parmar 2007). The depth of the artery and vein to the surface of the skin was also analyzed for ease of needle access during hemodialysis and to ensure absence of vein stenosis or thrombosis.

Ultrasound assessment of blood flow characteristics determines maturation of a fistula. Hemodialysis filters blood and returns it to the body at a blood flow of 300 mL/min (Miller et al. 1999). For hemodialysis to correctly function, the blood flow rate is increased compared to that needed for dialysis in order to maintain the blood flow through the vessels during dialysis without vessel collapse (Robbin et al. 2002). An AV fistula is considered mature if it can undergo hemodialysis and support a blood flow of at least 500 mL/min for an extended period of time of three months (Miller et al. 1999, Robbin et al. 2002). There is currently a lack of information regarding the mechanics of fistula maturation. Ultrasound-based elasticity measurements can be used to identify biomechanical properties of tissue and may prove effective for characterizing vascular fibrosis, which is believed to negatively impact fistula maturation. The ability to use ultrasound to better characterize vascular health and evaluate AV fistula surgery potential for CKD patients is an important contribution to vascular access research. It has potential
to decrease extraneous surgical procedures and provide insight into why up to 60% of surgically placed AV fistulas are failing to mature.

The goal of this thesis project is to investigate the use of ultrasound to noninvasively estimate the elastic modulus of human brachial arteries and assess potential in determining likelihood of AV fistula maturation in CKD patients. Future translational objective is to increase the successful percentage of surgically placed AV fistulas in CKD patients by using elastic modulus quantifications as an additional predictor to current standards. Therefore, we hypothesize that noninvasive elastic modulus measurements using ultrasound images will be a successful addition to current predictors to help identify AV fistula maturation. This hypothesis will be tested by the following specific aims:

Specific Aims

1. Construct an arm stabilization device for preoperative ultrasound mapping of brachial artery to use concurrently with the existing equipment
2. Using vessel tracking software, model the elastic modulus of the brachial artery using systolic and diastolic pressure measurements. Model the changes in human, strain, stress, and elasticity error.
3. Collect and create a database of normal (non-CKD) elastic modulus measurements to find synopsis of brachial artery elasticity measurements to create a normalization standard. Correlate elasticity to demographic characteristics.
THEORY

When a thick-walled vessel contracts and expands, there is movement in three distinct directions: radial, cylindrical and longitudinally across the z plane as seen in Figure 1. The stress along the z plane is considered insignificant, yet the radial and circumferential stresses both significantly add to total stress on the vessel (IIT Kharagpur 2011).

![Figure 1. Stress occurs along three planes of an artery: radial ($\sigma_r$), circumferential ($\sigma_\theta$), and along the z axis ($\sigma_z$). Both $\sigma_r$ and $\sigma_\theta$ contribute significantly to vessel stress.](image-url)
Using Lame’s equation for thick-walled cylinders where $\sigma_r$ is the radial stress, $p_i$ is the pressure on the inside of the vessel, $p_o$ is the pressure on the outside of the vessel, $r_i$ is the inner radius, and $r_o$ is the outer radius, the radial stress can be calculated using the following equation:

$$\sigma_r = \frac{p_i r_i^2 - p_o r_o^2}{r_o^2 - r_i^2} + \frac{r_i^2 r_o^2 (p_o - p_i)}{r_o^2 - r_i^2} \frac{1}{r^2} \quad (1)$$

The circumferential stress can also be calculated from Lame’s equation where $\sigma_\theta$ is the radial stress, $p_i$ is the pressure on the inside of the vessel, $p_o$ is the pressure on the outside of the vessel, $r_i$ is the inner radius and $r_o$ is the outer radius. This is detailed in Equation (2).

$$\sigma_\theta = \frac{p_i r_i^2 - p_o r_o^2}{r_o^2 - r_i^2} - \frac{r_i^2 r_o^2 (p_o - p_i)}{r_o^2 - r_i^2} \frac{1}{r^2} \quad (2)$$

Using estimated measures of pressure and radius, we are able to estimate the radial and circumferential stress acting on the arterial wall using Equation (1) and (2). This estimation shows that a large portion of the stress is resulting from the circumferential stress. A detailed example of Lame’s equation and estimated variables is shown in the Appendix A.
For our purpose of estimation of the elastic properties of a material, an estimation of stress and strain on the vessel wall is calculated. For cylindrical blood vessels there are two assumed constraints. The vessel wall of arteries can be considered incompressible when subjected to physiological pressure and load, and therefore preserve vessel wall cross-sectional area during diastole and systole (Weizsacker and Pinto, 1988, Carew et al. 1968). This preservation results in a change in wall thickness from systole to diastole. This is possible to assume because arteries are 90% water and water is an incompressible liquid (Fine and Mellero, 1973, Shaul et al, 1990, Smuskiewicz, 2007). It is also assumed the z-axis strain is uniform throughout the wall and held constant. With assumptions made of a simply linear elastic medium, a thin cross-sectional image of the artery can be analyzed for strain measurements using changes in intima-medial thickness (IMT) during peak systole and diastole. Because ultrasound measurements are captured at one infinitesimal plane along the vessel wall, assumptions of incompressibility allow a thin cross-sectional slice of artery to be used in this analysis (Figure 2). The cross-sectional area remains constant within each plane during systole and diastole. An extended example of this is shown in Appendix B. All artery samples are considered isotropic along this plane when evaluated for elastic modulus (Weizsacker and Pinto, 1988).
A standard curve of pressure versus diameter of the vessel wall is shown in Figure 3. The diameter of the arterial vessel wall is proportional with IMT measurements. As the diameter of the vessel increases to peak systole, the vessel wall and IMT are at its minimal thickness. Using the derivative of the function as the linear approximation for the relationship between pressure and vessel wall diameter over a small region of interest, the application of a simple elastic modulus equation is used (Figure 3). Assuming a homogenous, isotropic, linear elastic medium, the modulus of elasticity for the vessel wall is estimated as the ratio of vascular stress to strain.
The elastic modulus of biological tissues is known to be a nonlinear function of stress and strain. In order to analyze the relationship between arterial stress and strain, the function is linearized. The elastic property of a material are thought of as a response to an outside force and is measured in terms of elastic modulus, \( E \) (kPa). The elastic modulus, \( E \), is the slope of the stress-strain curve of an object,

\[
E = \frac{\sigma}{\varepsilon}
\]  

where \( \sigma \) is the stress or pressure of an object in kPa, and \( \varepsilon \) is the strain of an object measuring the dimensionless change in deformation (Fung 1993). A young’s modulus model is used to measure the overall elastic modulus of a material. Elastic modulus is measured by an application of stress, and the subsequent strain resulting from the applied force.
For our purpose, stress is taken as the difference between systolic and diastolic pressure measurements (prior to ultrasound imaging). This estimated stress is a combination of radial and circumferential stress. Stress measurements from blood flow result in perpendicular pressure on the vessel wall and denoted as:

\[ \sigma = \Delta BP \]  

(4)

where \( \Delta BP \) represents the change in blood pressure of the patient between maximum systolic and diastolic measurements (Kim et al 2004, Weitzel et al 2005). This change in blood pressure is converted from mmHg to kPa. Extravascular pressure is assumed to be insignificant or zero.

Assuming that vascular tissue is incompressible, the IMT cross-sectional area will be preserved in systole. Tissue strain is derived from changes in IMT measurements (between systole and diastole) as follows:

\[ \varepsilon = \frac{\Delta IMT}{IMT} \]  

(5)

where \( \Delta IMT \) is measured by the difference in IMT at the peak systole and peak diastole and IMT is the original diastolic measurement. In a traditional sense, strain is measured at one distinct point, and this estimation analyzes the average change in length across an infinitesimal plane. Strain measurements are unitless and thought of as a change resulting from applied force or pressure.
The elastic modulus is estimated as the ratio of stress to strain as stated in Equation (3) and demonstrated in Figure 4.

Employing ultrasound imaging, with a spatial resolution of 16.7 µm/ pixel, and vascular biomechanics, assuming incompressibility, isotropic and a linear-elastic medium, an estimation of the elastic modulus of the brachial artery was calculated. Although simplified, this theory uses a basic equation to estimate the elastic modulus of the brachial artery. This estimation will help derive an assessment of expected AV fistula maturation in dialysis patients. This information is projected to improve the quality of

\[
E = \frac{\sigma}{\varepsilon} \\
\sigma = \Delta \text{BP} \\
\varepsilon = \Delta \text{IMT}
\]

*Figure 4.* As the cardiac cycle moves from peak systolic pressure to peak diastolic pressure, the IMT changes. This change in IMT allows calculation of strain. Blood pressure (BP) acts perpendicular on the vessel wall and allows stress calculations. Elastic modulus is measured by an application of stress, and the subsequent strain resulting from the applied force.
patient prognosis because it may help to reveal an underlying biomechanical basis for the failure of fistula maturation.
ARM STABILIZATION DEVICE

Aim 1: *Construct an arm stabilization device for preoperative ultrasound mapping of brachial artery to use concurrently with the existing equipment*

METHODS

An arm stabilization device was needed that can attach to the current hospital equipment used during ultrasound brachial arterial mapping. It was necessary that it can be easily transportable, cleaned and stored between ultrasound mappings. Important characteristics include the adaptation to the variety of patients, the ability to disinfect between patients, and the capability for the sonographers to have full access of the brachial artery to scan. This device was utilized to minimize motion during both preoperative and normal subject ultrasound mapping the brachial artery. The IMT measurements are very small (micrometer range) and the ability to reliably track changes in IMT measurements ultimately impacts the ability to calculate elastic modulus.

RESULTS

Successful arm stabilization was created for preoperative ultrasound mapping of brachial artery (Figure 5). This apparatus is able to be used concurrently with the existing equipment in the UAB hospital and Kirklin clinic to minimize motion during ultrasound mapping.
In construction, a foam material is used inside a 120 degrees radius stiff plastic shell to allow molding to the patients arm while still allowing for complete imaging access to the brachial artery. This apparatus was covered in vinyl plastic to allow for easy and complete cleaning between patients. The apparatus is positioned and fastened on top of a moveable arm rest to ensure patient comfort during ultrasound procedure.

Figure 5. The arm stabilization device for vessel wall tracking prevents movement and adds comfort to the patient. This device which coincides with current mapping protocols is shown in attached to current equipment utilized.
Aim 2. Using vessel tracking software, model the elastic modulus of the brachial artery using systolic and diastolic pressure measurements. Model the changes in human, strain, stress, elasticity error.

METHODS

Modeling is needed to investigate the extent and range of measurement error during tissue elasticity measurements. Using custom programs developed using the software package Matlab (Mathworks Inc, Natick, MA), modeling vascular stress, strain and elastic modulus error will give better insight into the accuracy of vascular elasticity analysis using ultrasound. When imaging, a sonographer attempts to image perpendicular to the vessel to visualize the largest cross-sectional plane possible. A family of curves is shown for the transverse margin of error for transducer. This shows how error manifests for different IMT values. Oblique errors in the transducer placement are also modeled. Stress, strain and elasticity curves were simulated modeling errors that can occur for different values of IMT, stress and elastic modulus. If an error occurs at an early time point in measuring elastic modulus, the likelihood of receiving an accurate elasticity measurement decreases.

For all subjects, potential AV fistula surgery patients and normal subjects, ultrasound data is collected by mapping the brachial artery using a Philips iU22 scanner (Bothell, WA) equipped with a L17-5 transducer. The forearm is stabilized for ultrasound imaging to minimize any discomfort or patient motion. The subject remains in an upright position during the exam. Simultaneous echocardiogram (EKG) recordings verified
ultrasound data was collected during 10 separate cardiac cycles. Arterial Health prototype software (Siemens, Mountain View, CA) is used to determine IMT of the arterial wall during both end systole and diastole (Figure 6). Patient EKG data helped determine these extreme states of vessel distension and contraction. The diameter of the vessel determines the true state of distension and contraction in the vessel, yet this correlates with the EKG data at the brachial artery. The vessels dictate how the EKG wave pulses as blood courses through the vascular system. The pressure wave in the distal artery is delayed from the

![Figure 6](image.png)

Figure 6. Intima-medial thickness (IMT) measurement software is shown which is used to calculate measurements and changes in IMT during peak systolic and diastolic pressure. The lumen and IMT of the vessel are highlighted.

QRS wave, and timing of maximum distension is located approximately at the T wave of the cardiac cycle (Bertino et al. 2007). CKD patient and normal subject data matches up identically with previous results showing the brachial artery at peak systole during the T wave of the cardiac cycle. This information can then be used for patient analysis and
guiding IMT measurements. Elastic modulus measurements are acquired for six cardiac cycles for each subject and recorded as mean ± SE. Patients undergo a vascular anatomy preoperative mapping with ultrasound imaging to ensure suitable anatomy for AV fistula surgery.

RESULTS

A custom model for vessel tracking, which was based on elastic modulus equation, was successfully completed. IMT measurement software used to track vessel wall motion is shown in Figure 6. As the cardiac cycle moves from peak systolic pressure to peak diastolic pressure, the IMT changes as illustrated in Figure 4. The range of elasticity values found was consistent with that produced found in the literature (50-300 kPa range) (Danpinid et al. 2010). Measurement error was calculated and graphed for experimental errors. Transducer displacement can occur during evaluation and brachial artery mapping from slight movement by either the subject or the sonographer (human error). As shown in Figure 7, slight angulations of the transducer can increase the experimental IMT measurement, yet the blood pressure remains acting perpendicular on the vessel wall. As the distance of the transducer (past perpendicular to the vessel wall) increases, the IMT appears larger than actual. This causes a rise in variability from displacement of the transducer.
Transducer displacement from maximum arterial diameter and resulting angle measurements for various IMT measurements was simulated (Figure 9a). As the IMT value decreases in patients and subjects, transducer error is more prominent.

Figure 7. Ultrasound transducer is shown in ideal location (perpendicular to vessel wall) in order to calculate accurate IMT measurements. If an error in the angle of the transducer occurs, the measured IMT can be inaccurately calculated as shown.

\[ IMT = \text{Measured IMT} \cos \theta \]
Oblique error movements from the sonographer results in augmented IMT measurements towards the periphery of the ultrasound image (Figure 8). This error is minimized by IMT measurements consistently acquired in the middle of the ultrasound image and ultrasound images are only used if the brachial artery is shown longitudinally across the entire image. If the transducer becomes oblique, a transverse section of the artery will be shown as the ultrasound image, instead of a longitudinal section, and the sonographer corrects for this at the time of the study. The IMT measurement is the average over the section measurement, therefore the average could be slightly inflated, yet the change in IMT over the IMT is the measurement used for strain calculations. Therefore, oblique error measurements in this study are considered negligible because they are beyond the spatial resolution capabilities conducted by the ultrasound machine used and are well within the standard deviations of each patient.

Figure 8. Ultrasound transducer is shown in ideal location (perpendicular) with IMT measurements consistent across the image (left). During oblique error, augmented IMT measurements are seen towards the periphery of the ultrasound images, while the center of the ultrasound images is the actual IMT measurement (right).
Error in stress measurements could occur due to blood pressure increasing at the time of measurement. Error in measurement versus percent error was calculated for cases of high to low stress levels (Figure 9b). At lower changes in stress, estimation/measurement errors in this stress calculation play a more pronounced role due to the low magnitude and noise contributions. When the change in stress for a subject is large, small errors do not affect the total percent error as much as when the patient has a lower change in stress due to a higher signal-to-noise ratio. Because the IMT
measurements themselves are so low, it is difficult to precisely compute the small changes in IMT, or strain. Strain measurements are taken over six cardiac cycles, which allows for a more precise calculation and standard deviation to be calculated. Measurements are considered more accurate due to minimizing fluctuations due to noise. Error in measurement is calculated for low to high levels of strain and error vs. percent error is shown (Figure 9c). As IMT in subjects and patients increase, less percent error occurs for small measurement inaccuracies. Error measurements versus percent error for elastic modulus are seen in Figure 9d. Lower values of elastic modulus show error at a greater level than higher values of elastic modulus.
NORMAL SUBJECT DATABASE

**Aim 3.** Collect and create a database of normal (non-CKD) elastic modulus measurements to find synopsis of brachial artery elasticity measurements to create a normalization standard.

**METHODS**

Normal subjects (i.e. non-CKD patients) (N = 50) were analyzed for arterial mappings in the same methodology as CKD patients awaiting fistula surgery. All methods were approved by Institution Review Board (IRB) at University of Alabama at Birmingham. Vessel wall motion throughout the cardiac cycle can be used to calculate an estimate of the biomechanical properties of that vessel. Using custom software, changes in vessel wall thickness can be normalized by blood pressure measurements to determine vessel elastic modulus. A study in CKD patients will be pursued in order to further validate the ability to use the computer software to track vessel wall and IMT motion, as well as this estimated approach to arterial elastic modulus. Ultrasound-based elastic modulus measurements are applicable to many areas of research. It is expected that a normal database of elastic modulus of the brachial artery could have future potential with prediction of outcome of fistula surgery and cardiac applications. Using previously described methods, this is a noninvasive study using 5-10 sec clips of conventional grayscale ultrasound images taken in healthy subjects to test and validate a computer algorithm that tracks brachial artery IMT motion to calculate elastic modulus. It is hoped that a database of arterial elastic modulus normal values for vessel wall movement in
healthy subjects will help us better understand the distensibility of the brachial artery. This data is compared to patients with severe health problems, such as CKD.

Data was summarized as mean ± SE. Statistical analyses were performed using the software package SAS 9.2 (SAS, Cary, NC). Linear regression analysis is conducted to correlate elastic modulus with subject characteristics. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Preliminary results in normal healthy (non-CKD) patients (age range 20 to 65, mean age of 43) are used to establish a database for comparison to patients scheduled for AV fistula surgical placement. To date, normal patient brachial artery elasticity measurements (N = 50) are found to be 100.85 ± 8.1 kPa, ranging from 39.3 to 267.7 kPa. The relatively low standard error demonstrates feasibility and indicates low variability in healthy brachial arterial elastic modulus measurements. Because it has been proven that vessel compliance does decrease with age, it is important to show this characteristic within our normal population group (Mitchell et al. 2004, Greenwald et al. 2007). Normal subjects showed significant linear correlation between age and elastic modulus ($R^2 = 0.14$, $p = 0.017$). The range of IMT for normal subjects is 0.100 to 0.249 µm, with an average of 0.169 µm. A total of 50 normal subjects over a range of ages were deemed sufficient to complete the evaluation of normal elastic modulus.
Aim 4. Collect and create a database of CKD patients waiting to undergo fistula surgery. Correlate elasticity to patient characteristics and demographic data. Assess patient results and histology in comparison to preoperative elasticity measurements. Monitor until complete maturation or failure.

METHODS

Using previously described methods, CKD patients (N = 75) received a preoperative ultrasound scan of the brachial artery. After proper assessment of fistula compatibility, the patient, if applicable, underwent fistula surgery. Those patients who undergo AV fistula surgery will be analyzed and followed until complete fistula maturation or failure. At the time of access surgery, the surgeon will obtain small specimens of the artery and vein used to create the access. The specimens will be placed in a container with a fixative, labeled with an identifier, and stored for tissue processing. The artery is treated with trichrome stain, which includes three colored components; only two are utilized at this time. Trichrome stain produces red color in keratin or muscle fibers, marking normal artery red, after staining with red acid dyes. Medial fibrosis is stained blue through methyl blue staining. The sample is then scanned using a Bioquant imaging system (Image analysis Corporation, Nashville, TN) which determines the total area that is stained red, and the total area that is stained blue. Representative pictures of elastic artery stain and Biquant imaging system are shown in Figure 14. The percent of medial fibrosis (total area stained blue) is calculated. Correlation of elastic modulus measurements to fibrosis scores, systolic pressure and demographic data was conducted.
Data was summarized as mean ± SE. Statistical analyses were performed using the software package SAS 9.2 (SAS, Cary, NC). Linear regression analysis is conducted to correlate elasticity with patient characteristics. Two sample independent $t$-tests are used to assess differences between normal and CKD patient data. Analysis of variance (ANOVA) statistical testing is used to evaluate elastic modulus differences in various elastic modulus groups. A Pearson rank correlation test was used to analyze relationships between in elastic modulus and fibrosis, blood pressure and age. A $p$-value of less than 0.05 was considered statistically significant.

RESULTS

Elastic modulus measurements in patients prior to AV fistula surgical placement (age range 34 to 76, mean age of 56) were between the range of 47.04 and 266.5 kPa, averaging at 129.89 ± 6.44 kPa. CKD patients’ arterial elasticity showed no correlation to age ($R^2 < 0.001, p = 0.829$) as seen in Figure 10. There were also no differences between male and female vascular modulus estimates ($p = 0.63$) with males averaging 138.46 kPa and females averaging 126.65 kPa.
The range of IMT measurements in CKD patients are 0.130 to 0.387 µm, averaging at 0.224 µm. A total of 26 patients successfully underwent AV fistula surgery. To date, only four fibrosis scores have been completed. There was high correlation between elasticity and fibrosis, yet not significant due to small numbers ($R^2 = 0.94$, $p = 0.16$).

Elastic modulus measurements in patients prior to AV fistula surgical placement were significantly higher than normal subjects ($p = 0.01$). Average change in blood pressure was significantly higher in CKD patients than normal subjects, comparing 68.04 ± 2.36 to 48.38 ± 2.12 mmHg ($p = 0.002$). Systolic blood pressure also showed significant increase in CKD patients compared to normal subjects ($p < 0.001$), as well as diastolic blood pressure ($p = 0.02$) (Figure 11).
There was significantly increased IMT in CKD patients, compared to normal subjects averaging CKD patients at 0.227 µm and normal subjects at 0.169 µm ($p < 0.001$). Using both normal and CKD patient data, it was shown that there is a significant correlation between elastic modulus and systolic blood pressure ($R^2 = 0.23$, $p < 0.001$) as seen in Figure 12.

*Figure 11.* Blood pressure (mmHg) measurements shown between CKD patients and normal subjects. Significant differences are seen in change in blood pressure ($p = 0.002$), systolic blood pressure ($p < 0.001$), and diastolic blood pressure ($p = 0.02$).
A review of unopened (pre-surgical) artery, unopened vein and vein post fistula creation was completed to ensure that this did not play a role in fistula maturation.

Figure 12. Elastic modulus (kPa) vs. Systolic Blood Pressure (mmHg) in all subjects (normal and CKD patients). Elastic modulus and systolic blood pressure showed significant positive correlation ($R^2 = 0.23, p < 0.001$).

Figure 13. Elastic modulus (kPa) vs. diameter (mm) of unopened artery, unopened vein, post fistula vein in CKD patients. No significant correlations were shown.
There were no significant trends in any of the data (Figure 13). Comparison to AV fistula outcome and remaining histological measures of vascular fibrosis are pending.

![Figure 14](image-url)

*Figure 14.* Example of histological stain of a piece of severe fibrotic artery, fibrosis shown in blue (left) and example of stained artery (62% medial fibrosis shown in blue) using the Bioquant imaging system (right).

Seventy-five patients have completed pre-operative AV fistula mappings of the brachial artery. This was deemed sufficient to analyze differences between our preliminary data sets of CKD patients and normal subjects. To date, 30 patients have undergone fistula surgery. One patient has had complete fistula failure (140 kPa elastic modulus), and three patients are currently using their fistula access for hemodialysis (96 kPa, 64 kPa, and 161 kPa). None of these patients have reached three months of fistula use.
There is currently no universal application of specific cut-offs on vessel anatomy, vessel distensibility, and vessel mechanics in order to optimize fistula use (Weitzel et al. 2008). Recommendations are made from ultrasound mapping on vessel size and location for each university. It is essential that a universal technology is established to create standard practices to increase percentage of successful AV fistula surgeries in CKD patients. Using ultrasound as a noninvasive method to accurately measure mechanical structures within the body of various disease developments has great promise in the imaging field (Weitzal et al. 2005). Investigating the use of ultrasound to noninvasively measure the elastic modulus of human brachial arteries in CKD patients has great potential to give further explanation as to why AV fistulas may not mature. Ideally, future translational significance will be shown by increasing the successful percentage of surgically placed AV fistulas in CKD patients. Quantifying elastic modulus measurements of the brachial artery in normal subjects and CKD patients, along with demographic information, will also give a database for reference to assess the likelihood of AV fistula maturation.

Using imaging modalities to measure tissue elasticity has proven to be beneficial in discovering and characterizing irregularities in the body (Hoyt et al. 2008, Weitzel et al. 2008). Specifically, arterial stiffness, end-stage renal disease and impaired glucose intolerance has been shown (Duprez & Cohn 2010). Elastic modulus measurements also have potential to be a predictor for cardiovascular events in the general population. Patients with hypertension (arterial stiffness) have provided information about the functional and structural vascular changes at various levels in the vascular system: the
aorta, the muscular conduit arteries, the peripheral branches, and the microvascular components (Duprez & Cohn 2010). It is essential for medical practices to use as minimally invasive techniques as possible to monitor and quantify arterial stiffness in order to minimize discomfort for the patient. Ultrasound is ideal due to its portability, real-time capability and noninvasive nature. Feasibility of using ultrasound to directly measure vessel elasticity has been proven in phantoms using strain imaging (Korte et al. 1997). Currently, measurements of arterial elasticity index can be completed in ml/mmHg depending on the size of the artery using a tonometer, HDI/PulseWave CR-2000 System (Kehda et al. 2009). Kehda et al. (2009) showed a significant difference between mature and failed fistulas in the small arteries along with a linear correlation between elasticity index and systolic blood pressure. This validates results found in this study, which shows significant correlation between elastic modulus and systolic blood pressure ($R^2 = 0.23, p < 0.001$).

It has become beneficial to create an imaging modality to monitor compliance of arterial vessels. Using ultrasound to quantify the elastic modulus of vascular walls through IMT measurements and blood pressure will help characterize overall compliance of the brachial artery, which in turn could give substantial information regarding CKD patients and potential of AV fistula maturation. Due to the fact that ultrasound mapping is currently used in pre-surgical evaluation of AV fistula patients, it is a cost-effective imaging component to implement for gaining additional information.

Measurements show that as you increase error in the earlier phases of arterial elastic modulus measurements, there is a more pronounced increase in variability in the later phases. It is essential to calculate strain measurements over multiple cardiac cycles,
as it ensures more reliable and precise numbers which reduces error when further calculating elastic modulus values. Limitations to the study can occur at the stress measurement level. Only one blood pressure measurement is taken per subject, due to ease and convenience for patients and subjects. Ideally, the subject’s blood pressure would be monitored over a period of time and an average or median value would be used for elastic modulus calculations.

Spatial resolution calculated from the ultrasound post-scan converted images collected clinically can give additional insight into error measurements. There will always be measurement variability due to human error within ultrasound imaging, yet because the measurements are small, it is also necessary to have adequate spatial resolution in order to appropriately measure small changes. Spatial resolution was estimated at 16.7 μm/pixels using the post-scan converted images. The range of IMT measurements were found to 130 to 387 μm, averaging 224 μm for CKD patients. The range of IMT for normal subjects is 100 to 249 μm, with an average of 169 μm. Although the spatial resolution is sufficient to calculate the smallest changes shown, this is also a limitation. Stiffer vessels, whose change in IMT is less pronounced, shows increased measures of variability. As spatial resolution is increased, it is assumed measurement variability will decrease proportionally.

Preliminary results found significant differences between elastic modulus of CKD patients and normal subjects ($p = 0.01$). There were also significant differences in blood pressure changes between systole and diastole for CKD patients and normal subjects ($p = 0.01$) as seen in Figure 11. It is anticipated that with further information, a limit can be set (currently we anticipate that limit around 150 kPa) which will state that once the arterial
elastic modulus is above that level of stiffness, a fistula will not be placed due to increased probability of non-maturation (Figure 15). To further analyze the data, three main distinctions of arterial elastic modulus were created: low values of elastic modulus (high compliance) showing measurements less than 100 kPa, mid-range elastic modulus of 100-150 kPa, and high values of elastic modulus (low compliance) measurements greater than 150 kPa. Upon the stratification of normal patient population, 68.85% remained in the low elastic modulus group, with 21.95% in the mid-range arterial elastic modulus group, and 12.20% in the high elastic modulus group. In CKD patients, arterial compliance scores show 30.51% patients in the low elastic modulus group, 38.98% in the mid-range group, and 30.51% in the high elastic modulus as seen in Figure 15. As elastic modulus increases, stiffness of the vessels increases (Greenwald 2007). It is suspected that the group with abnormally high elastic modulus measurements will correlate with those patients whose fistulas do not reach maturation.

Figure 15. Elastic modulus measurements in CKD patients and normal subjects are separated into three categories: low, medium and high elastic modulus. CKD patients exhibit significantly higher elastic modulus values compared to normal subjects ($p = 0.01$).
Current preliminary results show as vessel stiffness increases (shown by an increase in elastic modulus measurement), fibrosis correspondingly increases ($R^2 = 0.94$, $p = 0.16$). As indicated by Kheda et al. (2009) in a prospective cohort study, it was speculated that low compliance also promotes development of stenosis. It has also been shown that arterial stiffness is significantly influenced by the presence of arterial calcifications (Guerin et al. 2000). In addition to influences on vessel compliance, stiffening of vessels, as well as calcification of vessels, can be a result of increased age (Stein et al. 2004, Benetos et al. 2002, Guerin et al. 2000). Vascular compliance is dependent on the composition of elastic fiber and collagen. As a person ages, the ratio of collagen to elastic fiber increases within arteries, causing increased stiffness (Levy 2001). CKD patients arterial elasticity showed no apparent correlation to age ($R^2 = 0.001$, $p = 0.83$), as well as no difference between males and females ($p = 0.63$). Because we know that on average there should be increased vessel stiffness with age, results indicate that there is an additional outside effect causing the observed increased elastic modulus values in some CKD patients. Embracing the limitations, there is evidence to believe that fistula non-maturation can be predicted in part by ultrasound-based elasticity of the brachial artery.
CONCLUSION

Presented are significant results which lead us to conclude ultrasound can be used to noninvasively measure the elastic modulus of the brachial artery in humans. Results revealed a significant difference between CKD patients' and normal subjects' elasticity measurements. A vascular arterial elasticity database has potential in helping determine whether CKD patients will have complete AV fistula maturation. As the preoperative elastic modulus of the vessel is quantified in AV fistula surgery patients, there is information that will help lead to an improved evaluation as to whether the patient will be able to develop a mature fistula. Tracking these CKD patients, and further evaluating the histological analysis, will give a more complete answer. This decision is expected to improve the prognosis of fistulas maturing to completion in patients undergoing this surgery. Future potential is to improve percentage of fistula maturations, which will decrease the number of unnecessary surgeries. It is hypothesized that those patients that undergo fistula surgery that remain in the high elastic modulus group, will have an increased fibrotic score as well as a decreased likelihood of fistula maturation.

This thesis detailed a method of using ultrasound measurements to estimate the elastic modulus of the brachial artery. This technique analyzed both CKD patients and normal subjects and revealed significant differences between the groups using ultrasound measurements. Ultrasound elasticity measurements introduce preliminary evidence suggesting elastic modulus estimates could play a role in determining AV fistula maturation. Future analysis will further evaluate this clinical technique in determining AV fistula maturation by investigating in depth the relationship between vascular physiology, pertinent demographic information, and ultrasound elasticity estimation.
FUTURE WORK

The detailed analysis of arterial vessel elasticity to evaluate fistula maturation is an estimate of elastic modulus from clinically received ultrasound imaging data. This technique is an efficient way to analyze arterial elasticity, yet there are several limitations and future work would be widespread translation of this work. Advance model development, including information such as vascular blood flow kinetics and more detailed stress measurements, could improve elastic modulus measurements. Increasing the imaging frequency during brachial artery ultrasound mappings would fundamentally increase the image resolution, thereby decreasing measurement errors. Other future work could include incorporating three-dimensional (3D) ultrasound to allow collection of more complex information during an examination.

Clinically, CKD patients enrolled in this study will be tracked until complete maturation or failure. Using ultrasound to measure elasticity has potential as an additional predictor to evaluate patient response to AV fistula surgery. This technique could eventually help predict which vessels are more likely to yield a successful AV fistula, which could decrease the number of unnecessary surgeries.
This project is a part of a larger study that is investigating many aspects of fistula non-maturation. From 2010-2015, there will be a total of 100 participants recruited per year for a total of 500 in five years. Experiments identified to study features of vessels that may predict failure to mature include looking at thickening of the wall of the artery or vein and proliferation of cells within the artery and vein. The current funded study includes many of these multitudes to evaluate the ability of vessel abnormalities to predict failure of AV fistula new vascular access. Elasticity is one specific component to this larger study, and is the only aspect that is under evaluation for this thesis.
REFERENCES


APPENDIX A

Lame equation for thick-walled vessels:

Assuming the following variables:

Pressure, interior = \( p_i = 120 \) mmHg
Radius, interior = \( r_i = 4 \) mm
Pressure, outside = \( p_o = 20 \) mmHg
Radius, outside = \( r_o = 5 \) mm

Using Equations (1) and (2) from the text for radial stress (\( \sigma_r \)) and circumferential stress (\( \sigma_\theta \)) as shown below:

\[
\sigma_r = \frac{p_ir_i^2 - p_or_o^2}{r_o^2 - r_i^2} + \frac{r_o^2r_i^2(p_o - p_i)}{r_o^2 - r_i^2} \frac{1}{r^2}
\]

\[
\sigma_\theta = \frac{p_ir_i^2 - p_or_o^2}{r_o^2 - r_i^2} - \frac{r_o^2r_i^2(p_o - p_i)}{r_o^2 - r_i^2} \frac{1}{r^2}
\]

the estimation of radial stress is 2.07 kPa and circumferential stress is 40.00 kPa.

The equations used in this thesis, model an estimate that uses a combination of radial and circumferential stress, yet as shown by this example, the majority of the stress is circumferential.
APPENDIX B

Changes in vessel between systole and diastole:

Cross-sectional area of vessel:

\[
\text{Area} = \pi (r_o^2 - r_i^2)
\]

\(\text{Diastole:}\)

Assuming a \(r_o \) of 5 mm and a \(r_i \) of 4 mm, cross-sectional area of this artery is 28.3 mm\(^2\).

\(\text{Systole:}\)

Assuming an incompressible material, cross-sectional area remains at 28.3 mm\(^2\) during systole. Assuming a 10% expansion in vessel diameter (outer) during systole, the outer diameter is 11 mm, therefore the outer radius is 5.5 mm. To find the change in wall thickness (x):

\[
\text{Area} = 28.3 = \pi * (5.5^2 - (4+x)^2), \text{ therefore } x = 0.6 \text{ mm. which is the change in vessel wall thickness from systole to diastole.}
\]

\(\text{Strain in this estimation is:}\)

\[
\text{Strain} = \frac{\Delta L}{L} = \frac{(4.6-4.0)}{4.0} = 0.15
\]
APPENDIX C

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federal wide Assurance with the Office for Human Research Protections (OHRP). The Assurance number is FWA00005960 and it expires on September 29, 2013. The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56.

Principal Investigator: HOYT, KENNETH L.
Co-Investigator(s): SORACE, ANNA
Protocol Number: X110316007
Protocol Title: Ultrasound Mapping of Normal Brachial Artery for Tracking Vessel Wall Movement (R11-013)

The IRB reviewed and approved the above named project on 4/22/11. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.

IRB Approval Date: 4-22-11
Date IRB Approval Issued: 4-22-11

Marilyn Doss, M.A.
Vice Chair of the Institutional Review Board for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.
Informed Consent Document

TITLE OF RESEARCH: Ultrasound mapping of normal brachial artery for tracking vessel wall movement (R11-013)

IRB PROTOCOL: X110316007

INVESTIGATOR: Kenneth Hoyt, PhD

SPONSOR: University of Alabama at Birmingham
Department of Radiology

This consent form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

Explanation of Procedures

You are being asked to participate in a research study designed to test and validate a computer program that tracks brachial artery (blood vessel in your arm) wall motion in healthy subjects. The brachial artery is the main blood supply to the arm, and easily seen with ultrasound. It is hoped that a database of normal values for vessel wall movement in healthy subjects will help to better understand the elasticity of the brachial artery, to compare to patients with severe health problems such as chronic kidney disease.

If you participate you will have a vascular ultrasound image of your upper arm. Ultrasound uses sound waves to generate images. ECG leads will be placed on your upper chest, back and hip before scanning begins. An electrocardiogram (ECG) measures the electrical activity of your heart. During the ultrasound, you will be seated. A sonographer (person performing the ultrasound) will scan your upper arm. The ultrasound will take approximately 10 minutes. Afterwards, a blood pressure measurement will be completed. There are no significant side effects associated with vascular ultrasound scans. You may experience boredom during the duration of the test and may feel uncomfortable sitting still during the collection of ultrasound images.

This study will enroll 50 participants over the course of 6 months.

Risks and Discomforts

There are no significant side effects associated with ultrasound scans of blood vessels. You may become uncomfortable sitting still during the collection of ultrasound images.
Any findings in the ultrasound images will be discussed with a radiologist and if needed, you will be advised to see your personal doctor. Blood pressure measurements will be taken in order to standardize the results. If an abnormally high blood pressure is measured, the measurement will be repeated after twenty minutes. If it is still abnormal, you will be advised to see your personal doctor.

Benefits

You will not benefit directly from taking part in this study. However, this study may help us better understand brachial artery elasticity in patients with severe medical conditions such as chronic kidney disease.

Alternatives

This study is only being done to gather information. Your alternative is not to take part in this study.

Confidentiality

Information obtained about you for this study will be kept confidential to the extent allowed by law. You will be assigned an ID code and data collected from study evaluations will be identified by codes only. However, research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of the Office for Human Research Protections (OHRP). The results of the research may be published for scientific purposes; however, your identity will not be given out.

Refusal or Withdrawal without Penalty

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed. You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Cost of Participation

There will be no cost to you for taking part in this study. There will be no charge for the ultrasound images required by the study.

Payment for Participation in Research

You will not receive payment for participating in this research study.
Questions

If you have any questions, concerns, or complaints about the research, please contact Kenneth Hoyt, PhD. He will be glad to answer any of your questions. Dr. Hoyt’s number is 205-975-6465.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact Ms. Sheila Moore. Ms. Moore is the Director of the Office of the Institutional Review Board for Human Use (OIRB) at the University of Alabama at Birmingham. Ms. Moore may be reached at (205) 934-3789 or 1-800-822-8816. If calling the toll-free number, press the option for “all other calls” or for an operator/attendant and ask for extension 4-3789. Regular hours for the Office of the IRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

Legal Rights

You are not waiving any of your legal rights by signing this informed consent document.

Signatures

Your signature below indicates that you agree to participate in this study. You will receive a copy of this signed document.

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University of Alabama at Birmingham

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION
FOR RESEARCH

What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your health information may be used for the research.

Participant Name: ___________________________  UAB IRB Protocol Number: X110316007
Research Protocol: Ultrasound mapping of normal branchial artery for tracking vessel wall movement (R11.013)
Principal Investigator: Kenneth Hoyt, PhD
Sponsor: University of Alabama at Birmingham
Department of Radiology

What health information do the researchers want to use? All medical information and personal identifiers including past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind related to or collected for use in the research protocol.

Why do the researchers want my health information? The researchers want to use your health information as part of the research protocol listed above and described to you in the Informed Consent document.

Who will disclose, use and/or receive my health information? The physicians, nurses and staff working on the research protocol (whether at UAB or elsewhere); other operating units of UAB, HSF, UAB Highlands, The Children's Hospital of Alabama, Callahan Eye Foundation Hospital and the Jefferson County Department of Public Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees; and outside regulatory agencies, such as the Food and Drug Administration.

How will my health information be protected once it is given to others? Your health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

How long will this Authorization last? Your authorization for the uses and disclosures described in this Authorization does not have an expiration date.

Can I cancel the Authorization? You may cancel this Authorization at any time by notifying the Director of the IRB, in writing, referencing the Research Protocol and IRB Protocol Number. If you cancel this Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the health information that was provided before you cancelled your authorization.

Can I see my health information? You have a right to request to see your health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: ____________________________ Date: ____________
or participant's legally authorized representative: ____________________________ Date: ____________
Printed Name of participant's representative: ____________________________
Relationship to the participant: ____________________________