RF RESONANT SKIN PATCH SENSOR FOR PERIPHERAL LIMB HEMODYNAMICS

A Thesis by

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DEDICATION

To my family, friends and Kubo
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ABSTRACT

Rapid detection and measurement of blood flow is essential in clinical care; it is one of the fundamental vital signs used to detect physiological parameters such as heart rate and blood flow and is one of the most utilized measures in assessing the health of an individual. Photoplethysmography (PPG) is a method quickly growing in popularity for point-of-care diagnostics, using light to detect blood volume shifts. However, PPG has poor penetration depth and cannot detect deep arteries, and it is susceptible to movement artifacts. The central objective of this thesis is to develop an electromagnetic sensor for the detection of blood flow for capturing hemodynamic information in the deep arteries. To accomplish this an RF resonant skin patch sensor was designed as a planar spiral, and a biological model was constructed to detect biofluid shifts due to arterial pulsatile changes in a controlled environment. This sensing technology was then further refined to optimize for body placement and penetration depth and was validated for reproducibility and accuracy in a human multisite arterial study. The sensor response was investigated via simultaneous acquisition of PPG, ECG and sensor signals for each landmark. Significant shifts in the resonant frequency were detected when the skin patch sensor was placed over important arterial landmarks, and the peak-peak intervals (PPI) were highly correlated ($R^2 > 0.97$) with corresponding changes in PPG and ECG signal.
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CHAPTER 1. INTRODUCTION

1.1 Background on Limb Blood Flow Analysis

Recent trends in healthcare technology have been focused on advancing ubiquitous remote health monitoring, where doctors can assess the health of their patients in a home setting. Monitoring a patient’s vital signs is critical for physicians to effectively screen for early warning signs of patient deterioration. Wearable cardiac monitors such as CardioNet’s Mobile Cardiac Outpatient Telemetry or Medtronic’s Insertable Cardiac Monitor [1] remotely monitors the patient’s heart activity over many days, sending the data to physicians telemetrically to monitor for abnormalities such as arrhythmias or other cardiac episodes [2]. Beyond clinical use, there are consumer targeted wearable biometric devices that are gaining significant traction for those interested in improving their health and wellness in everyday life. As we become further integrated with technology, society’s relationship with health systems will continue to evolve. Smartphones, smartwatches, and other electronic wearables are embedded with a wide array of sensors that are designed to collect meaningful biometric data and relay them to the person using them. This can be particularly important for professional athletes during conditioning, people with chronic health conditions that require continuous monitoring, and health-minded individuals that want to maintain a healthy lifestyle. There are many physiological parameters within the body that can be detected non-invasively using wearable electronics, however cardiovascular health remains one of the most significant and widely researched areas in wearable bioelectronics development.

Blood flow is one of the body’s most important vital signs used to determine the health state of an individual. It is a primary function of the cardiovascular system, used to transport oxygen and other nutrients to the all living tissues in the system. Any compromise in the
cardiovascular system could lead to hemodynamic abnormalities, affecting the quality of life and catalyzing progression of serious cardiovascular diseases in an individual, which could lead to death. Because of its clinical significance, mankind has been inventing methods for centuries to accurately detect and measure the blood flow in an individual. In doing so we now better understand cardiovascular diseases and have developed therapies to prevent or treat them, although research continues to improve this knowledge and these treatments. In the modern age, the most well-known tool for the rapid assessment of cardiovascular health is photoplethysmography (PPG). This optoelectronic sensing technology utilizes light and measures the changes in absorbance as it transmits or reflects through the tissue when placed on the body, which is altered as blood flows through the illuminated field of the sensor. The low cost and ease of use of PPG has led to a widespread adoption in wearable electronics for heart rate detection. While PPG is a useful tool for cardiovascular health, it has limitations in consumer wearables due to the technologies’ susceptibility to motion artifacts, poor penetration depth into biological tissue, and limited blood flow sites on the body the sensors are able to accurately detect.

The primary motivation for this thesis was to develop a bioelectronic system that can overcome many of the limitations of current non-invasive blood flow sensors for use as a wearable device that can detect deep arterial volumetric changes in biofluid shifts in a simple manner.

1.2 Significance

Cardiovascular disease (CVD) is currently the largest cause of death in the world, killing 17.9 million people annually [3]. CVD can be caused by many factors, most commonly due to atherosclerosis, the accumulation of fatty plaques on the arterial wall. Stress, poor diet, and
genetic predispositions can also play a large role in cardiovascular disease prevalence. Obesity, diabetes, smoking and high blood pressure are all closely linked to heart disease, and are often comorbidities of the primary disease. Because of the high associated mortality rates, it is critically important that physicians screen for CVD in the population as the earlier a condition can be diagnosed, the sooner that preventative measures can be taken to slow the progression of the disease and proper treatment can be administered. Peripheral blood flow is of particular importance when assessing cardiovascular health, as the ease of accessibility and measurement of blood flow in the limbs can serve as an important early indicator of vascular abnormalities.

In addition to health assessment on earth, peripheral limb hemodynamics are a significant area of research for long duration space flight. Astronauts spend their time living in a microgravity environment when deployed into space, where they are subjected to long periods of weightlessness. Recently, it has been discovered that long duration space flight, such as that seen in Bakelman et. al [4], can have long standing health effects on the crew members. The current mission directive for the national aeronautics and space administration (NASA) is the successful deployment of humans to mars, which will require significantly long durations of space flights of up to 7 months upon both arrival and departure to the planet. One of the prominent physiological effects observed in microgravity is a general cephalid biofluid shift, away from the peripheral limbs and into the thoracic cavity and cranium. This increases pressure in the abdomen, and subsequently increases fluid pressure along the spinal column. This pressure increase is observed in the intracranial space and is hypothesized to cause cerebrospinal fluid to travel down the optic nerve sheath, causing permanent visual impairment upon return to earth. Other effects of this biofluid shift that have been theorized are reduced bone density, peripheral limb myopathy, and hemodynamic abnormalities. Currently, astronauts would require extensive training to perform
appropriate medical procedures such as lumbar punctures or burr hole catheter insertion in a microgravity environment to further investigate the fluid shift and confirm these theories. As an alternative they use ultrasonography to assess blood flow, however this is over telecommunication with an expert on earth; the procedure is difficult to communicate and is difficult to follow and obtain inaccurate results. Furthermore, the equipment required for this testing is expensive. Thus, a lightweight simple to use blood flow sensor would be able to address the current limitations NASA has in determining the state of peripheral blood flow in astronauts.

1.2.1 Vascular health

To improve the outcomes and prevention of people susceptible to CVD, surrogate endpoints are used as preliminary screening for early warning signs of CVD and can be found by assessing the vascular health of an individual. The most clinically relevant surrogate endpoints are measures of arterial pulse wave velocity, stiffness and compliance. By evaluating the state of surrogate endpoints, physicians can assess the risk of the patient developing a cardiovascular disease in the future, thus improving risk stratification and focus on reversing the abnormalities detected and preventing disease. Arterial compliance and stiffness also correlate with blood pressure, which is important for managing hypertension. Currently there is no simple home screening method for vascular health, the clinical gold standards involve expensive equipment and requires trained personnel.

1.2.2 Endothelial function

Endothelial function is a measure of health of the layer of endothelial cells lining the intima of the main arteries and heart in the cardiovascular system. These cells regulate the artery’s vascular tone through the release of nitric oxide as a response to the arterial blood flow.
A dysfunction or abnormality of endothelial function is an indicator for increased risk of stroke and heart attack and can be used as an early screening method for these diseases. The current gold standard is an invasive test for endothelial function involving the injection of neuromodulators to determine how the vascular system reacts with changes in blood flow with a coronary angiogram. Non-invasive methods utilize ultrasonography to assess flow-mediated dilation of a large artery, but pulse amplitude tonometry and reactive hyperemia index measures are also common to assess arterial function from the microvasculature in the fingers. Current research in this area suggest this is one of the most promising early indicators of subclinical cardiovascular disease. A simple, effective screening method for endothelial health could revolutionize preventative health care and reduce mortality rates due to CVD [5].

1.2.3 Peripheral Artery Disease

Peripheral artery disease (PAD) is a condition that affects 18 million people globally [3]. It is a condition caused by atherosclerotic build-up of plaques inside the arteries providing a blood supply to the extremities, resulting in compromised blood flow to the peripheral limbs. PAD is a significant health burden globally, as it is associated with several other cardiovascular diseases as comorbidities such as coronary artery disease and stroke. Progression of PAD reduces circulation significantly and may result in limb amputation in severe cases. Currently, 120,000 amputations occur every year due to PAD.

The current gold standard for screening in PAD is the ankle brachial index (ABI) [6], a system that measures the ratio of blood pressures between the brachial artery and the vasculature in the ankle to determine the quality of blood flow to the limbs. While it has been shown to have a high accuracy and specificity for detecting arterial blockages, there are still many limitations of the ABI. ABI is an effective screening method for PAD, but it isn’t used at an early stage to
screen for the disease due to the high cost and extensive instrumentation involved; it is only employed when PAD is suspected in a patient. Better screening and monitoring techniques at an early stage for PAD could greatly improve the outcomes in individuals afflicted with the disease.

1.2.4 Wearable electronic health systems

Recently, a significant effort has been made to develop more accessible, point-of-care systems for people to use in a home setting for continuous health monitoring. These advances have sparked the genesis for heart rate monitoring integration into devices such as cell phones, smart watches, and wearable health tech. Although heart rate has been the most common physiological parameter these devices measure, there are many more biometrics that modern devices are currently being developed for, such as glucose monitoring, blood lactate, blood pressure, stroke volume, and intracranial pressure.

1.3 Problem statement

While current methods for measuring blood flow exist, they are not without their limitations. In microgravity, astronauts are extremely limited in the equipment available to them to assess changes to blood flow in the peripheral limbs. Due to the cost of shipping heavy equipment into space, techniques such as ultrasonography are not as desirable as a lower cost, lighter weight alternative. Additionally, many of the clinically acceptable methods for measuring blood flow are either invasive or require extensive training to utilize and are not without their flaws. Photoplethysmography, the most commonly used technique both in a clinical and a home setting for early screening of cardiovascular disease, can only assess blood flow occurring at a microvascular level, very close to the surface of the skin. While clinically significant hemodynamics can be extracted from the waveforms, the sensors themselves are extremely limited in penetration depth and prone to movement artifacts [7-10], changes in contact force and
physiological changes that can affect microvascular blood flow such as limb movement or thermoregulation (e.g. vasoconstriction or vasodilation of the deep arteries).

Thus, a more robust sensing technology that addresses these shortcomings could have a significant impact across a broad spectrum: the healthcare industry, elder care, employee wellness, military use, athletics, and everyday home use would all reap the benefits of such a device. Additionally, the ability to detect deep arterial blood flow across the body with a simple to use device, in a non-invasive manner, would significantly improve early stage screening for cardiovascular diseases such as PAD, and could improve outcomes for suffering patients. RF resonators have recently become a widely researched topic for the development of environmental sensors for many industries. However, very few groups have studied the effects biological tissue have on RF resonant sensors. There is a large gap in the literature that explores this technique for in vivo biosensing, and the few articles that do exist do not elucidate the clinical significance with sufficient rigor; they are primarily concerned with the topology of the circuit and the instrumentation used to detect a response. There is a need to not only design a sensor utilizing RF resonance for physiological measurement, but to validate the measured results with clinically relevant information that could be used by a physician.

1.4 Statement of objectives

The primary motivation of this thesis is to investigate the use of RF resonance as a transducing mechanism for the detection of blood flow in the body. The proposed solution to this is a new non-invasive sensing method for blood flow that is robust against motion artifacts, offers deep penetration depth and integrated ease of use for point-of-care diagnostics and home use. The device should be inexpensive, simple to use and able to integrate into a variety of form factors, increasing the ubiquity required of a broad-scale cardiovascular screening tool. The
outcome would allow users to detect physiologically relevant parameters in a non-invasive manner, reducing trauma to patients and screening for cardiovascular diseases with a higher success rate.

The development of a non-invasive skin patch sensor for physiological measurements was comprised of the following three major milestones: 1) Design a resonant sensor capable of detecting blood flow in a phantom; 2) Validate the sensor for use in human studies; 3) Analyze and interpret the collected waveforms to determine clinical relevance and significance. The underlying rationale for these milestones is that the successful development of the above described RF resonant sensor would provide a new platform for non-invasively detecting many blood flow parameters otherwise obtained invasively, offering a new point-of-care tool to be used in home setting or in environments with low training thresholds. The central hypothesis of this research is that biofluid volumetric shifts are associated with concomitant changes in effective electromagnetic properties that can be measured using radio frequencies as a sensing mechanism. These major milestones were accomplished by achieving the following objectives:

**Objective 1:** Characterize and validate the sensor in a benchtop biological phantom model to assess detection depth, transmitted power through the tissue and feasibility of use on a human. Then, use the results to further optimize the geometry and reactance of the sensor for use in human studies and validate the optimization in a human participant pilot study.

**Objective 2:** Analyze and interpret waveforms collected at multiple arterial sites to assess optimal placement, and measurable differences in hemodynamics that normally require more invasive techniques. Lastly, investigate the extracted features of the collected waveforms and determine the skin patch sensor’s feasibility as a means of employing single site cuffless blood pressure measurement.
1.5 Thesis organization

Chapter 2 will present a literature review providing a background for devices currently used in blood flow measurement, the current state of the art in RF resonant sensors, and operational theory of the proposed RF resonant skin patch sensor. Chapter 3 will present the results from objective 1, demonstrating the feasibility of an RF resonant skin patch sensor as a non-invasive tool for detection of blood flow. Finally, chapter 4 will present results from objective 2, a multi-site comparison of blood flow in deep arteries using the proposed sensor, and the evaluation of the subsequently obtained blood volume waveforms.
CHAPTER 2. LITERATURE REVIEW

This literature review provides the prerequisite of knowledge and relevant literature for the development of a RF resonant skin patch sensor for the detection of blood flow. Section 2.1 further expands on cardiovascular health in the peripheral limbs and identifies gaps in currently employed clinical tests and point-of-care diagnostics for these diseases. Section 2.2 presents a general overview for current methodologies in blood flow sensing and compares the strengths and limitations of such technologies. Additionally, this section will discuss the current state-of-the-art technologies currently being researched to address these limitations. Section 2.3 will present a general overview of the operating theory of the proposed sensor, including the instrumentation setup and signal processing theory required to obtain the clinically relevant parameters presented in this thesis. These sections serve as a foundation for the discussion of the following chapter’s findings and interpretation of the results thereof.

2.1 Significance of Cardiovascular disease

2.1.1 Arterial stiffness and compliance

Arterial health is largely determined by assessing the stiffness and compliance of the arteries; these factors are measures of the degree of elasticity of the walls of the artery and can significantly affect the hemodynamics in the local vessel. It is a macroscopic manifestation of the hemodynamic state of the cardiovascular system and is a large contributing factor to a milieu of other cardiovascular diseases including myocardial infarction, stroke, hypertension, cardiac arrhythmia and cardiomyopathy [11]. Vascular stiffness occurs in everyone and progresses with age, but other factors such as diabetes, hypertension, and poor diet can affect the hardening of the arterial walls. As increased stiffness can cause many of these conditions, the relation acts as a positive feedback loop and accelerates disease progression in individuals.
The gold standard for determining vascular stiffness is measuring the pulse wave velocity between the carotid and the femoral artery (Cf-PWV), providing an indication of aortic stiffness. Cf-PWV is usually obtained by either a doppler ultrasonogram or tonometer. Both methods require extensive training and require expensive equipment to use; however, they are becoming common practice during screening examinations for cardiovascular health. To date, no point-of-care or home use devices measure arterial stiffness.

2.1.2 Peripheral artery disease

Peripheral artery disease (PAD) is a significant global health burden, attributing to 18 million deaths a year, and 5 million cases of comorbidity laterally induced cardiovascular events that further lead to death in the populace [12]. A condition resulting in reduced blood flow to the limb, PAD primarily manifests itself as pain in the lower limbs during rest. As the disease progresses this pain increases, and as circulation degrades localized tissue damage, gangrene and myopathy secondary to the disease occurs, eventually resulting amputation of the limb. Revascularization at this stage can be difficult, and ischemia-reperfusion damage caused by restoring flow can cause further damage, still resulting in severe muscle damage and limb amputation. As such, it is of critical importance to screen the disease at an early stage to prevent disease progression to a point of amputation or further comorbidities.

In mild to moderate occlusion of the femoral artery, patients may suffer what is known as claudication. Claudication is defined as pain during physical exertion, such as climbing stairs or walking. As many of the people afflicted with this disease are in an older demographic of 65+, many assume this symptom is a side effect of their aging and not a cardiovascular insufficiency, so screening is limited at this stage. As the blockage increases, the person suffers pain at rest. If these symptoms are presented to a physician, they then may choose to conduct an early screening.
if they suspect PAD. The current gold standard for early screening is the ankle brachial index (ABI). The ABI is a measurement of the ratios of the systolic pressure taken at the brachial artery, and the systolic pressure taken at the dorsalis pedis and posterior tibial arteries of the lower limbs. If an occlusion is present in the femoral artery this ratio is diminished, suggesting that a reduction of blood flow is present. When the ratio is between 1 and 1.4, the patient is considered healthy, but an ABI below 1 indicates disease, with ratios below 0.4 indicating critical limb ischemia. This technique has a high accuracy; however, it is not without its limitations. Although this screening method is critical to detect the disease at an early stage, many physicians do not conduct this screening early enough. As a result, many patients with PAD normally see the disease progress to further stages, and the risks associated with other cardiovascular abnormalities and muscle damage may occur. Ultrasonography is also utilized, but typically only after conducting an ABI. It is an accurate technique; however, it requires expensive equipment and technicians specialized in the instrument to operate. Once PAD is suspected, a computed tomography angiography (CTA) or magnetic resonance angiography (MRA) may be performed. These methods are the most accurate currently, however they are also the most expensive and invasive techniques. CRA also uses nephrotoxic contrast agents, so it is not as desirable to use.

There is a significant need for an early stage screening method for PAD. A point-of-care method would allow broader access to the public, and to clinicians. The ability to screen for PAD at home would greatly improve disease outcomes, and simpler screening methods may motivate physicians to regularly conduct them during routine check-up visits.
2.2 Blood flow sensing technology

Blood flow has been measured as a standard in hospitals since the 19th century, with a device called a sphygmograph. This wrist-worn device would measure mechanical deflections in the wrist, with the resulting waveforms translated to paper via pen attached to the lever. This would scribe the changes in pulse volume onto paper that would later be interpreted by a physician to assess the blood flow quality of the individual. However, developments in hemodynamic measurements have advanced significantly since then, allowing us to capture much more precise data in a more reliable manner.

2.2.1 Plethysmography

Plethysmography measures the change in fluid volume of a subject. This technique was originally developed to determine lung function and measured the amount of air expired by the body using a specialized chamber. As the user exhales, a sensor detects the amount of air volume in the chamber, thus providing a measure of lung function in an individual. However, it was found that plethysmography was also particularly useful for detecting changes in blood volume shifts in the body. Thus, the technology was adapted for physicians as a screening method for blood flow measurement in patients.

2.2.1.1 Photoplethysmography

PPG is one of the most widely used sensing technologies for measuring blood volume shifts [13]. It consists of either transmitting or reflecting photoelectric diodes (LEDs) that emit light at specific frequencies that penetrate into the surrounding tissue. As blood perfuses through the capillary beds near the surface of the skin, the region that is illuminated by the light will absorb some of the light following beer’s law, which is observed by a photodetector measuring the intensity of the light that was transmitted/reflected to it. This technique is extremely easy to
use, non-invasive, and cheap lending itself to a wide adoption rate by many people in wearable form factors, and with physicians for health monitoring.

Unfortunately, PPG has several flaws limiting it from being more clinically diagnostic than it currently is. Currently, PPG can measure the heart rate in an individual, and if two different wavelengths of light are used, pulse oximetry can also be employed to measure tissue oxygenation. However, PPG is extremely susceptible to motion artifacts, drastically reducing its accuracy and in many cases preventing its use during rapid motions such as those observed in exercise. This is not a problem in a hospital setting, but severely limits the efficacy of PPG at home or in public settings. Additionally, it is sensitive to changes in the local degree of blood perfusion to superficial tissues, which can change significantly in short intervals due to autonomic regulation, thermoregulation, or blood pooling caused by centrifugal force of limb motion. Changes in contact force can also affect the sensor response and is difficult to standardize between patients. Additionally, light pollution can interfere with the signal if it is not properly adhered. The sensors are also limited in placement on the body, and is normally only used for finger, toe, or earlobe applications. Thus, PPG cannot easily detect deep arterial blood flow, simply microvascular blood flow in the capillary beds of the epidermis.

2.2.2  **Doppler ultrasound**

Ultrasound uses the wave properties of sound by propagating mechanical acoustic waves at high frequencies on the scale of MHz into a substrate, which in medicine is typically biological tissue [14]. While most commonly used as an imaging modality, ultrasound is also capable of measuring fluid flow rates in the body and is one of the most widely used instruments in clinical practice when blood flow rates of a patient are desired. There are both invasive and
non-invasive methods for ultrasound, the latter being used when extremely precise flow rates are required for a particular vessel.

2.2.3 Magnetic flow meters

Another method for accurate blood flow detection is the application of magnetic flow meters [15]. These instruments are attached on the outside of an artery of interest and detects perturbances in the magnetic field to determine the flow rate in the artery. Because of the underlying physics that is used to sense the flow rates, this method is considered the most precise, and can measure flow rates in a wider dynamic range than doppler blood flow measurements can. However, this is another invasive technique however and is typically only conducted during surgery.

2.2.4 Ballistocardiography

Ballistocardiography is a measure of the mechanical forces acting on the body due to the physical pumping of blood through the heart itself and is capable of measuring blood flow and blood pressure in the body [16]. It is currently being researched as a method for non-contact monitoring via camera. However, this type of sensing is extremely sensitive to movement artifacts and currently has limited applications.

2.3 State-of-the-art wearable electronics

Because of the current limitations in blood flow measurement techniques, a large focus of research is dedicated to inventing new methods for blood flow detection, or improving existing techniques so they can be employed in a wearable fashion.

Rogers et. al. pioneered the development of tattoos as a blood flow sensing form factor [17]. This tattoo exploits heat transfer at the surface of the skin as blood passes by multiple
discrete points on the tattoo and correlates the corresponding change in current to measure blood flow. It addresses some of the issues that PPG has such as contact force and light pollution, however it is still susceptible to motion artifacts. Since the sensor only measures blood flow at the surface of the skin like PPG, it is also susceptible to artifacts due to local thermoregulation, and blood pooling in the peripheral limbs.

Wang et al. have developed an ultrasound skin patch sensor to non-invasively measure blood pressure in the carotid artery in a point-of-care setting [18]. This technology is capable of detecting blood pressure similar to an ultrasound, but just like the original technique it is limited in that it cannot penetrate through bone very easily, making areas like the skull or ribcage difficult areas to assess vascular health in. The technology also requires an extensive readout system to detect a response.

Kim et al developed microwave sensors that can detect blood flow by measuring the change in air gap between the sensor and the surface of the wrist by using an array of inverted f antennas [19]. While this work is promising, it only evaluates blood flow at a single frequency, and the quality of its signal is quite poor. Additionally, measuring changes in blood flow due to air gap can cause sensor instability, as the change in air gap is hard to control and is extremely sensitive, resulting in errors in the response signal.

Teichmann et al elucidated mechanisms for inductive and capacitive sensing and demonstrated the theory with non-contact monitoring using a simple inductive sensing ring and capacitive sensing parallel plates adhered to the back of a chair [20]. These sensors detected the displacement current and eddy current due to changes in the space in the thoracic cavity and were able to obtain respiration and pulsatile blood flow information. However, the clinical significance was not particularly rigorous and did not investigate the relevance of the obtained
signals to the participants being measured. Additionally, the pulsatile waveform appeared to lack any detail containing vascular health, rather the waveform appeared to be a simple peak that could determine a binary response and estimate the average heart rate. The data was not compared to a clinically standard measurement for validation, so the legitimacy was not able to be determined. These sensors were also wired and hooked up to a large readout system that would be required to be installed in the furniture or a room where the measurement was taking place.

2.3.1 RF resonant sensors

Spiral resonators were first invented in 1897 by Nikola Tesla, as a proposed means of wireless power transfer using radio frequencies. Since then planar spiral resonators have been largely adopted in fabricating microwave circuits, as they are effective bandpass/bandstop filters. They have also been used extensively in very-large-scale integration (VLSI) as planar inductors and are useful in microfabricating integrated circuits. In recent years, resonant circuits have seen an explosion of research growth in implementing them as passive sensors for several applications.

Our group has been investigating the feasibility of utilizing RF resonance to measure blood flow in the body. This type of sensing has been proven to have a high degree of accuracy, simple to implement and often low cost to fabricate, which all fit criteria defined for the proposed blood flow device. Cluff et al demonstrated the use of such technology in an arm phantom, where pulsatile flow was detected and correlated with clinically relevant ultrasound data [21]. Griffith et al further demonstrated an RF resonant sensor’s ability to measure blood flow by detecting intracranial fluid volume shifts, a feat that ultrasound is very limited by [22]. Furthermore, there are no known non-invasive intracranial pressure sensors currently on the
market. Alruwaili et al demonstrated the use of this sensor for monitoring blood flow in the heart, which could have significant applications for heart failure patients [23].

In electrical AC circuits, resonance is observed when inductive energy being dissipated is equivalent to the capacitive energy being absorbed, and vice versa. This feature is primarily observed in RLC tank circuits. Originally, RF resonators exploited this phenomenon and used resonance as a bandpass filter in microwave circuits. Recently, they have become a large topic of interest for sensor development due to the low fabrication cost and robust degree of applications for the technology. Originally, many instances of RF resonators were as a sensing mechanism created for harsh or extreme environmental sensing, such as those seen in high temperature or corrosive chemical environments. As RF resonators are typically passive components, they are less prone to damage in extreme heat, and because of the sensing mechanism they can be placed on the outside of a chemical tank, thus avoiding damage.

2.4 Operating theory

2.4.1 Dielectric theory of biological tissues

Electrical permittivity is one of the fundamental properties of a material that describes a substrates state when perturbed by an electromagnetic field. Specifically, permittivity represents the resistance to forming an electric field when one is applied in a material. As the electric field is produced, polar molecules in the dielectric will polarize, and form an opposing electric field to the one that is being applied. This degree of polarization and subsequent reduction of electric field is defined as the permittivity, or dielectric constant k. Dielectrics play an important role when describing capacitance, as the dielectric material between the plates of a capacitor dictate the energy that is stored between the plates, which is what is formally defined as the capacitance of a circuit.
Capacitive sensors have exploited this relationship between permittivity and capacitance as a means for transducing measurands of interest, thus establishing a class of sensors that can transform a broad array of measures of interest into electrical signals. In the simplest case, a simple parallel capacitor is a function of charge and voltage, which is determined as a function of the permittivity of the dielectric material between the plates, and the area distance between the two plates. Changing the gap between the plates or the permittivity of the dielectric material used in the capacitor will induce an electrically measurable change in capacitance. If one holds the permittivity constant, changes in the gap between the plates due to deformation, strain, pressure, or some other externally applied force may be measured. Alternatively, holding the gap distance constant one can measure changes in the effective electromagnetic properties of dielectric materials that are placed between the parallel plates.

Electric fields that are present in a capacitor, however, are not strictly directed between the two plates. Fringing electric fields are present that originate between the two plates at every point, even outside of the plate gap. Because of this phenomenon, the electric fields formed by a capacitor will penetrate surrounding substrates. This feature of capacitors is used for capacitive touch screens and for dielectric probes to directly measure the permittivity of a material. Some other common measurands for this class of sensors include fluid level sensing, proximity, and material analysis.

The electromagnetic properties of biological tissues are a large area of research, primarily in radio frequency radiation dosimetry; determining the specific absorption rate (SAR) of electromagnetic waves, such as those produced by a cell phone or a magnetic resonance imaging machine (MRI), into the surrounding tissues of the bodies is a critical safety requirement when designing microwave circuits that interact with biological tissue. However, the dielectric
properties of tissues are also of great interest to the author as changes to the effective properties of biological tissues can be correlated with physiologically relevant information. For example, changes in fluid volume such as those associated with pulsatile blood flow, can cause an increase in the effective permittivity of the biological tissue. If one interprets the biological tissue as a multilayer composite material that an electromagnetic field surrounds, then one can assign weighted values of permittivities for each tissue layer present in the interrogated region of interest. On a relatively short time scale, one can observe a temporal increase in blood volume in an artery at each point of the cardiac cycle. During peak systole, the pressure of the ejected blood is at a maximum, which results in arterial distention and a subsequent increase in the volume of blood present in the region of interest. Similarly, as the left ventricle relaxes and the pressure of the blood traveling through the body reaches a minimum at peak diastole, the total blood volume being interrogated will concomitantly decrease. These changes in volume are typically measured with plethysmographic sensors that utilize photoelectric LEDs, impedance electrodes, or strain gauges.

The utility of measuring the permittivity of biological tissues is broader than blood volume measurements. For example, it has been demonstrated that tumors exhibit a measurable difference in permittivity value for a given tissue than the normal phenotype for that tissue. Changes in bone density can alter permittivity of the bone as well, which could be a significant marker for osteopathic diseases such as osteoporosis. Additionally, biological tissues have been shown to exhibit unique dielectric relaxation dispersion regions that are a function of the frequency of the interrogating electromagnetic field. It has been shown that the lower frequency alpha region dispersion is primarily due to the ionic flux of molecules through permeable cell membranes or through interstitial tissues. Permittivity changes in this frequency range have been
shown to detect changes in the DNA of cells, specific changes in protein content, and electrolyte content in biological tissues. Sensing changes in alpha dispersion could be utilized in future studies to detect specific chemical concentrations in the body in a non-invasive manner, such as blood oxygen levels. Beta dispersion is primarily attributed to changes in bulk fluid concentrations in the body. This range of dispersion would be more useful in applications such as the blood volume shifts proposed in this thesis. Additionally, this range would be more applicable towards detecting changes in air volume to assess lung function, and cerebrospinal fluid in the spine or cranial cavity, thus providing a more robust foundation for intracranial pressure measurement.

The proposed planar spiral resonator used in the studies were composed of a single baseline component: a thin trace of copper wound in a spiral pattern, laminated by a dielectric isolating layer (Kapton) on both sides. This yielded a completely wireless, passive, and battery-less architecture that forms the basis of all our sensing form factors. As outlined by Maleeva et al, spiral resonators are considered a type of metamaterial [24]. A metamaterial is a material that displays properties that are not found in naturally occurring materials. Specifically, these materials tend to exhibit negative refractive indices, permeabilities, permittivities, and can manipulate electromagnetic waves in unique ways. These materials have led to a new frontier in materials research; some of the outcomes range from next generation remote sensors to medical devices, and even invisibility cloaks. One of the first discovered metamaterials were split ring resonators, which demonstrate great utility in both wireless sensing and wireless power transfer. However, many scientists have recently been proposing the use of planar spiral resonators in place of SRRs, as they have been known to reduce the size required for an operating wavelength,
are multi-resonant (SRRs only resonate at a single frequency) and have demonstrated excellent inductive coupling to interrogating loop antennas.

The core fundamental concepts that provide the foundation for the theory of operation of spiral resonant sensors are all derived from Maxwell’s four equations of electromagnetism. Specifically, the Maxwell-Faraday law is the most crucial in describing the RF resonant skin patch sensor’s ability to function in a wireless, passive manner. This law states that a time varying magnetic field produces an electric field. When taking into consideration Ampere’s law, that a changing electric field produces a magnetic field, these laws uphold some of the primary axioms of electromagnetic physics and is the foundation for which a large body of work on electromagnetic circuits have been derived. These laws can be used to show how electromagnetic waves can travel in free space. In the context of the proposed skin patch sensor, these laws provide a basis for wirelessly power transfer with a separate interrogating loop antenna. As the loop is injected with an alternating current, an electromagnetic field forms around the loop. This loop couples with the skin patch sensor, and invoking Maxwell’s laws, the sensor’s changing magnetic field induces a current within the planar spiral. The spiral then produces its own electromagnetic field that can couple with both the interrogating antenna and any substrate that is within its penetrating region. Any changes in the electromagnetic properties of the substrate will cause a change that is reflected in the interrogating antenna, which can be measured with an appropriate instrument or readout circuit.

To detect the effective permittivity changes due to blood volume biofluid shifts in the body, a vector network analyzer (VNA) was employed. This instrument measures the impedance and scattering parameters of any device under test (DUT) that is connected to the instrument’s ports. Impedance constitutes the real, purely resistive portion of any circuit combined with the
imaginary, reactive components of the circuit, thus it is a complex value. Scattering parameters are a standardized, structured system for analyzing reflections and transmissions of energy to RF and microwave circuitry to quantitatively analyze their behaviors. Notation is defined by the port number (e.g. $S_{11}$ is the reflection coefficient, or the ratio of power that was transmitted out of port one to the power reflected back to port one, and $S_{21}$ would be the ratio of the power transmitted from port 1 to the power reflected to port 2.) The VNA works by injecting a fixed AC voltage into a port with the DUT connected to it. In this context, we define our DUT as a system comprised of the interrogating loop antenna, the planar spiral resonator, and the material under test (MUT), which is the biological tissue placed within the vicinity of the sensor. Once energized, power transfer occurs at a maximum at the resonant frequency, and a large degree of loss is observed in the $S_{11}$ signal; at resonance there is very little of the power reflected into port 1. Similarly, at the same frequency a large degree of transmission is observed in the $S_{21}$ signal, indicating that power has indeed been coupled and transmitted through the biological tissue. Any changes in effective permittivity then change the capacitance in the system, which in turn changes the resonant frequencies of the skin patch sensor. These values can then be used to determine the sensor response to physiological conditions in the body, acting as an effective biosensor. VNAs are powerful instruments, and can measure the vector information, which includes both amplitude and phase information in the circuit system. This means the variables are conveniently interchangeable through simple algebraic relations that have been widely established. By collecting scattering parameters, one also has access to the impedance, phase, and voltage standing wave ratio (VSWR) responses.
REFERENCES


CHAPTER 3. SKIN PATCH RF RESONATOR FOR DETECTION OF PULSATILE BLOOD VOLUME SHIFTS

3.1 Abstract

*Objective:* Measuring vital signs such as heart rate and blood flow is one of the most important functions in assessing the health of an individual. While photoplethysmography (PPG) is commonly used, there are limitations in its execution due to poor penetration depth and movement artifacts. In this study we propose a new method for detecting blood flow using an RF resonant skin patch sensor. *Methods:* The detection depth of the sensor was assessed using a biomimetic tissue phantom consisting of bovine muscle tissue. The phantom was embedded with an artificial artery connected to a heart pump system to measure the sensor’s frequency shift due to fluid volume changes in the artery. To investigate the feasibility of this method for use in a clinical setting, a human study was conducted using a sensor developed based on the results from the tissue phantom. *Results:* Paired t-test results showed significant shifts (p<0.0001) in resonant frequency in muscle thicknesses up to 3 inches due to fluid volume changes in the artery. The time-varying waveform of the radial artery pulse exhibited similarities to classical PPG waveform features, suggesting its use in measuring blood flow. *Conclusion:* A skin patch sensor was developed in this study that detected changes in arterial blood volume, generated clinically relevant plethysmography data, and accurately detected heart rate in an individual. *Significance:* Passive RF resonant sensing was demonstrated as a non-invasive technique for detecting biofluid shifts in the body and has the potential to become a point-of-care diagnostic wearable device.
3.2 Introduction

Blood flow is one of the most fundamental vital signs in the human body and is the most widely known physiological measurements used for rapid assessment of the health of an individual. It can provide information on the health of the heart, including heart rate, cardiac output, blood pressure, overall circulation, and indication of cardiovascular disease. Because of this, clinical settings critically rely on the ability to accurately and quickly assess the quality of blood flow in an individual. Currently, there are several methods for measuring blood flow in the body both invasively and non-invasively that are employed by physicians [1]. If high accurate flowrates or fluid pressure information is needed in vivo, magnetic flowmeters or catheterized ultrasound doppler are used in the region of interest in the patient [2]. Non-invasive methods are more commonly used and typically consist of ultrasonography or photoplethysmography (PPG) measurements [3].

While these techniques are considered gold standards in obtaining clinically accurate blood flow data from the patient, they are not without their limitations. Ultrasound machines are very expensive, require extensive training to be able to use, and are limited to the clinical setting. PPG sensors are more widely used in point-of-care settings, however they can only measure peripheral blood flow at the surface of the body, as near infrared light can only penetrate a couple of millimeters into the skin [4]. Furthermore, they are susceptible to erroneous measurements due to motion artifacts, poor contact force of the optical sensor to the skin and reduced peripheral circulation [5-7]. Thus, there is a need to develop accurate, non-invasive sensors for measuring blood flow in a cost effective, point-of-care manner.
In this study, a radio frequency (RF) resonant sensor is proposed as a new method to investigate the feasibility of its use as a blood flow sensor. In the field of RF engineering, resonant sensors are a class of resistive-inductive-capacitive (RLC) circuits that can be used to detect changes in electromagnetic fields that surround them by measuring shifts in the resonant frequency of the sensor when energized [8, 9]. The operating principle of the RF resonant sensor used in this study, outlined in our prior in vitro study, exploits the underlying physics of resonant circuit phenomena to detect and measure physiological changes inside the body [10]. Very little research has been conducted to understand the interactions between the electromagnetic fields of RF resonant circuits and changes in biological tissue, but the preliminary evidence is promising. Early stage research has been performed by our group showing the capability of RF resonant sensors for measuring changes in intracranial pressure and blood flow in the heart [10-13]. However, to better optimize resonant sensor design for physiological measurement, it is necessary to understand the effects that biological tissue have on the sensor response. As physiological variability from person to person will reflect different compositions of biological tissue composition and can cause subsequent changes in the detection depth of the measurable signal from the sensor. The objective of this study was to 1) develop an electromagnetic RF resonant sensor for detection of blood flow in a biomimetic blood flow phantom model 2) characterize the sensor response in terms of resonant frequency shift and detection depth and 3) develop a flexible skin patch sensor based on these results to obtain blood flow measurements in a human pilot study.
3.3 Materials & Methods

3.3.1 Sensor Design

The RF resonant sensor (4 x 4 inches) was designed as a planar square spiral open circuit, fabricated on FR-4 (Figure 3.1). The sensor design geometry consisted of a 0.1 mm trace width, 0.1 mm gap width spiral with 4 sides and 250 turns. Higher turns and smaller gaps contribute to the frequency response by increasing the overall capacitance and inductance in the spiral, which in turn reduces the resonant frequency [8, 9]. Equation 1 is the governing equation for calculating the first principal resonant frequency where \( f \) is the resonant frequency, \( L \) is the inductance and \( C \) is the capacitance of the sensor. This effect drives the criteria for the sensor design; when the number of turns is increased in the geometry overall inductance will increase, and when gaps between the traces become smaller the parallel plate capacitance between the traces increase. Thus, the working frequency of the RF resonant sensor can be tuned by making appropriate changes to the geometry. When wirelessly interrogated with a loop antenna, the self-resonating spiral is energized and forms an electromagnetic (EM) field that penetrates into surrounding substrates such as biological tissue. Any changes in the effective permittivity such as those induced by changes in blood volume will produce measurable corresponding perturbations in the EM field, identified as detectable shifts in resonant frequency or amplitude in the RF spectra.

\[
f = \frac{1}{2\pi \sqrt{LC}}
\]  

(1)
Figure 3.1. (A) Resonant sensor design micrograph. (B) As the conductive traces in the sensor are impinged upon by an external RF wave, an electromagnetic field forms around the sensor and penetrates into surrounding substrates, which allows it to measure the electromagnetic properties within that field.

3.3.2 Vector Network Analysis

A 2-port vector network analyzer (SDR-Kits) was used to investigate the transmission characteristics and the frequency shift response of the sensor when placed on biological tissues.

A vector network analyzer (VNA) measures the scattering parameters of a device under test (DUT) by means of a frequency bandwidth sweep. The energy transmitted to the DUT can either be reflected back into the VNA or transmitted through the surrounding substrates. Scattering parameters were collected to obtain reflection ($S_{11}$) and transmission ($S_{21}$) coefficients of the sensor when energized, which are measured ratios of reflected to incident and transmitted to incident waves, respectively (2-3), where $Pr$ is the reflected power, $Pi$ is the incident power, and $Pt$ is the transmitted power of the waves. In this study, the transmission coefficient represents the amount of power transmitted from the energized sensor to a receiving antenna placed on the opposite side of the DUT, which represents the amount of signal transmitted through the biological tissue. The reflection coefficient represents the signal that is reflected back into the port of the VNA when the radiating electromagnetic waves reach different permittivity
boundaries in the tissue. For each study, RF spectra were generated for the resonant frequency bandwidth of the sensor to study the corresponding changes.

\[ S_{11} = \frac{E_r}{E_i} \]  

\[ S_{21} = \frac{E_r}{E_i} \]  

3.3.3 RF Opacity Study

To characterize the detection depth of the RF resonant sensor, a RF opacity study was performed to measure the amount of RF waves that were transmitted through biological tissue at increasing thicknesses to determine the detection depth. The detection depth is a critical aspect for design, as it can influence the sensor’s ability to measure volumetric changes present in deep tissue, such as arterial blood flow. It is related to the penetration depth, which is defined as the depth at which the intensity of the electromagnetic field is reduced by 37% of its original intensity, or 1/e, due to the decay of the electromagnetic waves as they propagate through a medium [8]. For highly conductive materials such as biological tissue, the penetration depth can be numerically characterized by (4), where \( f \) is the operating frequency, \( \mu \) is the magnetic permeability and \( \sigma \) is the conductivity of the substrate, respectively. This occurs because the absorption of the electromagnetic waves in a lossy medium such as biological tissue induces a significant degree of signal loss [14, 15]. It should be noted that with decreasing frequency, the penetration depth of the fields into a substrate is higher. However, the detection depth is distinctly different from the penetration depth of an electromagnetic wave. While the RF resonant sensor may exhibit a certain penetration depth of electromagnetic fields into the tissue, a detectable signal response due to fluid volume changes or other disturbances may occur much
deeper than the penetration depth. For example, at 1.5δ or 2δ the signal intensity in the substrate may be below 63%, but detectable shifts in the $S_{11}$ resonant frequency may still occur.

Bovine round meat was used to simulate human muscle tissue. To collect transmission information, $S_{21}$ measurement was set up by placing the muscle on top of a receiving loop antenna connected to port 2 of the VNA (Figure 3.2). To collect reflection information, $S_{11}$ measurement was set up by connecting the sensor complexed with a 4 x 4 inch loop antenna connected to port 1 of the VNA. Both antennas were connected to the VNA coaxial cables via sub-miniature version A (SMA) adapters, which were calibrated and fixed in position prior to the study. Polystyrene foam was used as a stage due to its low dielectric permittivity, approximating an open air environment [16]. Data was collected for 5 trials at 3 increasing muscle thicknesses: 0.5 inch, 1.5 inch and 3.5 inch muscle samples.

$$
\delta = \frac{1}{\sqrt{f \pi \mu \sigma}}
$$  \hspace{1cm} (4)

**Figure 3.2.** RF opacity model setup: Muscle tissue of increasing thicknesses (d) were placed on a polystyrene foam stage, with a transmitting antenna sensor complex (top) and receiving antenna (bottom) connected to port 1 and port 2 of the VNA, respectively.

### 3.3.4 Biomimetic Blood Flow Phantom Model – Detection Depth

To simulate volumetric changes observed in arterial blood during pulsatile flow, a biomimetic blood flow phantom model was constructed. This model was designed as a system
containing an artificial artery, a heart pump, an inline stop valve, and a fluid reservoir to simulate a circulatory vascular system (Figure 3.3). The artificial artery was embedded through bovine round meat to test the sensor response to fluid volume changes in biological tissue. As the stop valve was closed, the fluid pressure in the system increased and caused the artery to expand. To simulate systole, where arterial blood volume is at a maximum, the stop valve was half closed to constrict the fluid flow in the system and expand the artery diameter simulating pulse volume changes in arterial blood flow [17, 18]. Similarly, when the stop valve was completely open the fluid pressure would decrease, causing the artificial artery to regress back to its normal diameter, simulating diastole.

$S_{11}$ values were collected for both diastole and systole fluid volume states by placing the sensor complexed with a coplanar interrogating loop antenna on top of the muscle tissue being studied and connecting the complex to port 1 of the VNA. Reflection coefficient data was collected for 5 trials at 3 increasing muscle thicknesses: 0.5 inch, 1.5 inch and 3 inch muscle samples. Each trial was carried out on the same muscle sample for a total of 5 separate times per thickness.
3.3.5 Human Pilot Study – Wrist Blood Flow Trial

The human pilot study was reviewed and approved by the Wichita State University Institutional Review Board (IRB) and informed consent of the participant was obtained prior to the study. To investigate the resonant frequency response in the presence of radial artery blood flow, a flexible RF skin patch sensor was placed on the wrist above the radial artery and reflection coefficient data was collected. The radial artery was located on the participant via palpation and the aperture of the sensor was placed in the center of the radial artery. Double sided tape was attached to the bottom of the sensor to assure proper adhesion and conformability to the wrist. $S_{11}$ data was collected from the VNA at the first principal resonance of the sensor for 60 seconds with a sweep time of 43.837 ms. Each sweep contained 501 data points and was taken from 25 MHz to 35 MHz to collect data in the bandwidth of the first principal resonant peak in the spectra. To compare the heart rate with the sensor response, the participant’s heart rate was obtained using a heart rate monitor on the participant just prior to data collection. The
frequency shift was transformed to the time domain, by plotting the time-varying amplitude of the resonant frequency at the inflection point on the inductive side of the resonant frequency peak. This data was collected at 28.11 MHz for 60 seconds, with a sampling rate of 100 data points/second. The resulting signal was processed to filter out noise using a 4th order bandpass Butterworth filter with a low pass corner frequency of 0.5 Hz and a high pass corner frequency of 10 Hz. To compare the heart rate obtained from the heart rate monitor with the pulse waveform measured with the RF skin patch sensor, systolic peaks were detected in the signal and the total was compared to the heart rate monitor value.

The detection depth of the skin patch sensor was investigated by conducting a circulation study. After 15 minutes of acclimation to a temperature controlled 73-degree Fahrenheit environment, the participant was subjected to localized tissue cooling and heating to induce vasoconstriction and vasodilation, respectively. A temperature-controlled clay pack was used to heat and cool the skin directly over the left radial artery and index finger to induce the changes for each treatment. For both the cooling and heating tests, the clay pack was placed on the skin for 5 minutes, and the temperature was recorded using a thermocouple sensor (National Instruments). Baseline pulsatile data was collected for 15 seconds using the skin patch sensor. Subsequent sensor data was collected after each round of cooling and heating the tissue. Pulse amplitudes were extracted from the signal and compared to identify any changes.

3.4 Results

3.4.1 RF Opacity Study

An RF opacity study was performed to characterize the sensor response when placed on increasing thicknesses of muscle. An initial baseline in air was collected to determine the frequency spectra of the sensor without the presence of any biological tissues. Figure 3.4
presents the spectra, with a first principal resonant peak at 1.913 MHz and periodic resonances with increasing frequencies roughly 2-3 MHz apart.

![Graph showing spectra with resonant peaks](image)

*Figure 3.4. Baseline reflection coefficient data of RF resonant sensor in air.*

Figure 3.5A illustrates the concomitant changes of the first principal resonant frequency and the return loss of the signal in the $S_{11}$ reflection coefficient with varying thicknesses of muscle tissue. The signal exhibited a leftward resonant frequency downshift of 390 kHz, and an amplitude increase of 7.16 dB as the muscle thickness was increased from 0.5 inches to 3 inches. Figure 3.5B shows the changes in the $S_{21}$ transmission coefficient of the sensor. The $S_{21}$ amplitude represented the transmitted signal that was received by the loop antenna placed underneath the muscle tissue. The transmission response of the sensor showed a similar 390 kHz downshift in resonant frequency of that observed in the $S_{11}$ response, and a 43.4 dB decrease in amplitude, as muscle thickness increased from 0.5 inches to 3.5 inches. This demonstrated that the RF wave, generated by the resonant sensor, can be transmitted through muscle up to 3.5 inch thick, as evidenced by the transmitted signal being detected by the receiving $S_{21}$ antenna. This suggests the RF wave can penetrate in depths of up to 3.5 inches of muscle tissue.
**Figure 3.5.** (A) $S_{11}$ reflection coefficient and (B) $S_{21}$ transmission coefficient for increasing thicknesses of muscle tissue. The $S_{11}$ and $S_{21}$ represent the signal being transmitted through the muscle, which is observed in the attenuation of the amplitudes of the resonant peaks in both plots with increasing muscle thickness. Low, negative amplitudes seen in the $S_{11}$ signal represent higher levels of power lost, or transmitted out of the sensor complex. Similarly, higher amplitudes in the $S_{21}$ signal represent the energy received by the second loop antenna after it has transmitted through the muscle.

### 3.4.2 Biomimetic Blood Flow Phantom Model – Detection Depth

To investigate the sensor response for detecting changes in arterial blood volume in biological tissue, a fluid flow study was performed using a biomimetic blood flow phantom. Ultrasonography was used to validate the phantom and to confirm pulse volume changes during systole and diastole. Figure 3.6 displays a transverse view of the artificial artery embedded in the phantom.

**Figure 3.6.** Ultrasonogram of the biomimetic tissue phantom. (A) Demonstrates the artificial artery during diastole, when the fluid volume is at a minimum. (B) Illustrates the artery at peak systole, where the fluid volume is at a maximum.

Figure 3.7 shows the sensor resonant frequency response for the (A) 0.5 inch, (B) 1.5 inch, and (C) 3 inch muscle layers at diastole and systole states. In the 0.5 inch muscle sample, the first principal resonant frequency shifted from 1.473 MHz at diastole to 1.447 MHz at
systole, resulting in a 26 kHz downshift in frequency. For the 1.5 inch muscle sample, the first principal resonant frequency shifted from 1.3 MHz at diastole to 1.272 MHz at systole, resulting in a 28 kHz frequency downshift. Lastly, the 3 inch muscle sample exhibited a resonant frequency spectra of 1.04 MHz at diastole, and a spectra of 1.04 MHz at systole, resulting in a negligible frequency shift. This data suggests a limit to the detection depth through muscle of approximately 3 inches in this frequency range and using this RF resonant sensor design geometry.

![Graphs showing frequency shift with different muscle thicknesses](image)

Figure 3.7. Detection depth of resonant frequency shift during systole and diastole in the biomimetic blood flow phantom model. (A) Frequency shift with 0.5 inch thick muscle, (B) frequency shift with 1.5 inch, and (C) frequency shift with 3 inch thick muscle tissue.

A statistical analysis of the blood volume induced frequency shifts at each thickness of muscle was conducted to determine if there was a significant shift in frequency, using a paired t-test. Significant p-values (p < 0.0001) were obtained for the resonant frequency shift in the 0.5 and 1.5 inch muscle thicknesses, however the 3 inch muscle sample showed a non-significant shift (p > 0.05). This further suggests that the ability to detect pulse volume changes is limited to
a detection depth between 1.5 inches and 3 inches in muscle tissue, for this frequency range and for this resonant sensor design.

### 3.4.3 Human Pilot Study – Wrist Blood Flow Trial

Figure 3.8A presents the sensor baseline response when placed on the skin of the participant, with a first principal resonance at 28.7 MHz. As the blood volume in the radial artery changed, a simultaneous downshift of the resonant frequency occurred. Figure 3.8B shows a resonant frequency shift occurring due to pulse volume changes during systole and diastole at two different time intervals. The resonant frequency shifted from 28.7 MHz to 28.68 MHz, a 20 kHz downshift. Fig. 3.8C-D presents the frequency shift as a time-varying waveform by plotting the amplitude, at the inflection point of the inductive side of the resonant frequency peak, over time.

![Figure 3.8. (A) Baseline response of the sensor when placed on skin. (B) Illustrates the frequency shift at the first principal resonant frequency present in the baseline. (C) Time varying waveform of the frequency shift due to pulse volume changes during systole and diastole in the radial artery. (D) The time varying waveform displays many similarities to traditional PPG signals and appears to contain similar features, such as the systolic and diastolic peaks, a dicrotic notch and a peak signifying venous return.](image-url)
During vasoconstriction, the average pulse amplitude from the time-varying waveform was decreased by 50% when compared to the baseline. In contrast, the signal amplitude was increased by 50% when compared to the baseline during vasodilation.

3.5 Discussion

In the biomimetic blood flow phantom model, the frequency downshifts that occurred during peak systole were attributed to measurable increases in the effective permittivity of the biological tissue, artificial artery, and water that were contained as a multi-layered substrate in the detection field of the sensor. When the valve was partially closed, the fluid volume contained in the artery increased, simulating an increased blood volume state such as that observed at systole. This increase in fluid volume increased the overall effective permittivity of the system, as larger proportions of materials with high permittivity values within the composite substrate would result in higher effective permittivity values of the total composite substrate. Biological tissues are a weakly diamagnetic material - at low magnetic field strengths the inductance of the tissue does not change, and the magnetic permeability is typically modeled as that of free space [19-22]. Since inductance does not change, increases in capacitance caused by increases in effective permittivity was the primary contribution to inducing frequency shifts in the $S_{11}$ reflection signal captured with the VNA.

Because biological tissue is a high lossy material, it was critical that the detection depth of the electromagnetic field was investigated to optimize design considerations for the sensor being developed. Previous studies have suggested that the inductive coupling of RF resonators to the biological tissue will induce eddy currents that penetrate into a substrate at a specific depth [23]. By utilizing both $S_{11}$ to investigate the energy reflected back into port 1 of the VNA at the surface of the muscle, and $S_{21}$ to investigate the energy transmitted through the whole composite
biological sample, a more comprehensive understanding of the detection depth of the sensor was able to be obtained. For the RF resonant sensor designed in this study, 3 inches of detection depth was deemed sufficient for measuring arterial blood volume shifts in healthy individuals. Arteries beyond that depth would result in negligible shifts in frequency and fail to detect any pulsatile blood flow unless the detection depth of the sensor was increased.

Similar resonant frequency shifts were observed when placed on the wrist. The sensor was re-designed as a more flexible, smaller skin patch sensor to better conform to the body. The first principal resonant frequency was higher than the frequency range of the RF resonant sensor used in the biomimetic blood flow phantom model, which demonstrates the sensor’s ability to measure blood volume changes within a broad frequency range. It is interesting to note that at different frequency ranges, different mechanisms for permittivity relaxation/dispersion states exist [24]. Teichmann et al. also reported an increased sensitivity to capacitive sensing of blood as the frequency increases. These findings suggest that the mechanism for detecting changes in fluid volume may be different depending on the frequency range being used. At lower frequencies, the change in ion flow may be the dominant measurand, which would be attributed to the increased ion content present with an increased fluid volume whereas at higher frequencies, changes in bulk fluid volume may be the primary measurand for the sensor [25]. This distinction is important, as depending on how the skin patch sensor is designed, it may be possible to detect chemical changes in the biological tissues separately from the fluid volume changes, which could be the basis for future studies.

Figure 3.8B demonstrates the shift in resonant frequency due to the pulsatile effect of arterial flow. At systole when the blood volume is at its highest, the resonant peak is lower. Subsequently when the arteries relax, and the blood volume decreases during diastole, there is a
resonant frequency upshift of 20 kHz. This shift is smaller than the frequency shift observed in the biomimetic blood flow phantom model, however, this was anticipated as the radial artery has a smaller change in blood volume as it pulses. The final number of systolic peaks detected in the time domain was 71 over the course of 60 seconds, which matched the heart rate measured in the study.

The time-varying waveform represented the change in frequency shift at a single point. This waveform was plotted by showing how the value on the inductive, rightmost side of the resonant peak at the inflection point changes over the course of time in the data that was collected. It is interesting to note that the waveform closely resembled that obtained by traditional PPG sensors, including classical features such as a systolic peak, a diastolic peak, and a dicrotic notch [26]. This data suggests that the skin patch sensor response may be measuring the change in fluid volume in the human participant and warrants a larger scale study to further determine the validity in using RF resonant technology for measuring blood flow in an individual.

Altering the skin temperature to induce vasoconstriction and vasodilation changed the pulse amplitude of the signal. It is interesting to note that the amplitude changes in the skin patch sensor signal captured from the radial artery is similar to that of the PPG sensor signal captured on the index finger, however the PPG was not able to capture a usable signal from the radial artery. While PPG has been demonstrated to obtain signals from the radial artery, the technique requires increased contact force for the sensor to displace more tissue, and thus decrease the distance between the artery and the sensor to within normal PPG penetration depths. In this study however, as penetration depth was the main parameter being investigated, care was taken not to deform the tissue when placing PPG on the skin as to observe the results solely due to
penetration depth of the light for the PPG sensor and RF waves for the skin patch sensor, respectively. Thus, we can conclude that the skin patch sensor does indeed illustrate a deeper penetration depth as it detects arterial pulse changes in the radial artery with no deformation in the skin.

Furthermore, this technique bears many similarities to impedance plethysmography, without the use of multi-site circumferential electrodes on a peripheral limb. Research on the topic has demonstrated that impedance plethysmography is capable of estimating cardiac output by analysis of the captured signals based on changes in impedance, thus providing a measure of blood flow. It may be possible to follow a similar method using the proposed skin patch sensor to measure blood flow, as S11 can be used to calculate impedance maybe insert equation here. Impedance based analysis using the RF skin patch sensor may be further investigated in a larger scale human.

To better optimize the sensor in vitro, it will be necessary in future work to utilize multilayer phantoms that more accurately represent the human body. While muscle and blood are among the most conductive materials in the body, it is important that the effects of fat and skin layers have on the detection depth of the sensor. Fat has been shown to be an excellent transmitter for electromagnetic waves, and skin conductivity could play a role in the overall attenuation of the waves [14]. While this early stage human pilot study suggests that the current detection depth is sufficient, a multilayer skin phantom may be necessary to design a sensor that can penetrate further into the body for deep arteries. Additionally, such a phantom could be used to optimize the sensor geometry when embedded in different substrates, increasing the potential to be integrated into several wearable form factors, such as clothing or a watch (Figure 3.9).
Figure 3.9. A prototype wearable form factor for an RF resonant biosensor. The technology could be embedded into a wrist bracelet or existing smart watches.

3.6 Conclusions

This study demonstrated the use of RF resonators as a feasible technology for detecting biofluid volume changes occurring in biological tissue. The results from the human pilot study are promising and suggest that this class of sensors can be used as a non-invasive method in a low-cost, point-of-care manner. Furthermore, the underlying mechanism of operation for the sensor establishes a framework for measuring multiple physiological conditions in the body and could potentially be used as a diagnostic device in the future.

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CHAPTER 4. MICROWAVE ARCHIMEDEAN SPIRAL RESONATOR DETECTION OF PERIPHERAL LIMB DEEP ARTERIAL HEMODYNAMICS: A MULTI-SITE VALIDATION STUDY

4.1 Abstract:

Objective: Peripheral blood flow is one of the most important vital signs that physicians use as an early screening indicator of subclinical cardiovascular disease. In a previous study it was shown that RF resonators can detect biofluid shifts that occur in the body in a non-invasive manner as a flexible, conformable smart skin patch form factor. The purpose of this study was to validate the feasibility of an electromagnetic skin patch sensor as a clinically relevant method for assessing peripheral blood flow in deep arteries. Methods: After ultrasound directed location of each landmark, arterial pulse waveforms from common upper body and lower body arterial pulse sites. Synchronized ECG, index finger PPG, and sensor data was collected for each arterial site. Multiple and single linear regression was performed on the corresponding peak-peak intervals for each hemodynamic biosignal to determine correlations between methods. Additionally, Bland-Altman plots were produced to assess the validity and repeatability of the study. Results: Carotid and dorsalis pedis pulsatile waveforms yielded coefficients of variability (CV) and reproducibility coefficients (RPC) above 5%, suggesting a lower repeatability than the rest of the arterial sites investigated, while the other arterial landmark exhibited high degrees of CV and RPC. All waveforms showed high degrees of correlation with $R^2 > 0.95$. Conclusion: An RF resonant skin patch sensor was used to detect deep arterial blood flow in a first of its kind human pilot validation study and demonstrated high degrees of repeatability, showing promise as a an early stage cardiovascular disease screening device.
4.2 Introduction:

Cardiovascular disease is one of the most prevalent causes of mortality in the world, responsible for a whole suite of health problems such as cerebrovascular events, heart attack, heart failure and peripheral artery disease. To reduce the incidence of cardiovascular disease new interventions, therapies and screening methods need to be developed to address limitations in the currently adopted techniques. Early screening for subclinical cardiovascular disease has shown to be an effective way to prevent serious disease, and in some cases diagnose CVD at an early stage to improve the outcome of the individual.

One of the most commonly adopted measures of vascular health is blood flow. In order to deliver oxygen and nutrients to tissues distributed throughout the body, blood is pumped in a pulsatile manner by the heart through the arterial tree. The quality of blood flow in these arteries directly affects the blood supply to the end organs they deliver the nutrients to, so the health state of the artery can directly affect the health of the end organ. Impairment or abnormal blood flow in arteries can be indicative of a more serious condition and can harm the affected tissues. For example, macrovascular impairment via atherosclerotic blockages can induce myocardial infarction or peripheral artery disease depending on the location of the blockage, and deep vein thromboses have a significantly high mortality rate. It has also been shown that microvascular dysfunction can cause myopathy secondary to CVD [1, 2]. Early stage screening for pathophysiological changes in blood flow is typically conducted using ultrasonography, an imaging technique using mechanical sound waves to measure blood flow velocity via the doppler effect [3]. Ultrasonography has revolutionized health care as it is a non-ionizing form of medical imaging, presents little to no harm to the patient, and can be used to obtain important cardiovascular information to investigate presence of plaques, valve stenosis, or overall heart
function [4]. However, the instrumentation required to obtain clinically relevant images is still quite expensive and requires a trained technician to obtain and interpret the data. Photoplethysmography has been gaining popularity in recent years as a tool for screening at earlier stages, by measuring the changes in microvascular blood flow and correlating those changes to the vascular health of the individual. Plethysmography, the measure of changes in fluid volume has been widely employed to measure several conditions in the body. Some common uses are for lung function using an air volume displacement chamber and limb volume changes using strain gauges [5, 6]. However, to measure changes in blood volume, the most commonly used method uses photoplethysmography (PPG) sensors. PPG uses light emitting diodes (LEDs) in combination with photodetectors to measure the amount of light absorbed by blood after it has transmitted through or reflected from the tissue. While PPG has been widely adopted by wearable manufacturers to use in their devices for measuring heart rate, the method is still limited in penetration depths no further than 5 mm and vulnerable to motion artifacts [7, 8]. While a significant research effort is currently underway for developing better algorithms for reducing motion artifacts and to better interpret the data, there is still a fundamental limitation in tissue penetration depth by using light. Though this method is still valuable for obtaining biometric data, it can only detect changes in the microvasculature of a human and small arteries only in the extreme peripheries of the body. Unfortunately, PPG is not able to detect blood flow present in deep arteries, which is an important aspect when screening for CVD. In fact, there are currently no point-of-care screening devices that are commonly used in the market today.

In a prior study our group designed and developed a next generation electromagnetic skin patch sensor for detecting biofluid volume shifts in the body and demonstrated its feasibility using a hemodynamic biological tissue phantom and a human in a pilot study [9]. The skin patch
sensor is a RF resonant circuit that is flexible and skin conformable, with the ability to detect biofluid shifts in a non-invasive manner by simply adhering the sensor to the body. The purpose of the proposed work was to further investigate and validate detected arterial waveforms acquired by the skin patch sensor and investigate their correlations with clinically relevant hemodynamic parameters.

A novel multisite blood flow study was conducted to determine the skin patch sensor’s response from different localized arterial sites. The arterial sites selected for the study ranged from superficial arteries to deeper arteries to assess the efficacy of the skin patch sensor in obtaining blood flow information at different detection depths in the body.

4.3 Methods:

4.3.1 Sensor fabrication:

A single arm Archimedean spiral RF resonator was designed to non-invasively detect deep arterial blood flow as a conformal skin patch sensor (Figure 4.1). To achieve sufficient conformity, a copper clad laminate (Dupont Pyralux LF9120R) was used to fabricate the resonator. The spiral was designed using an equation driven spiral custom written function in MATLAB and exported as a scalable vector graphics file (SVG). The design was applied as a positive mask directly to the copper clad laminate using a modified wax-based printer (Xerox Colorqube 8580). The laminate was introduced into the printer and the mask was printed directly to the substrate. The final skin patch sensor was formed via wet etching in ferric chloride.
4.3.2 Multisite Arterial Pulse Study:

Two subjects were selected to participate for data collection. This study was approved prior by the Internal Review Board of Wichita State University, and each participant consented to the study. For blood flow comparison, six sites were chosen based on their significance in the cardiovascular system, location, and tissue depth. Specifically, the femoral artery, dorsalis pedis artery, and posterior tibial artery were selected to assess lower body hemodynamics while the brachial artery, radial artery, and carotid artery were selected to assess upper body hemodynamics (Figure 4.2). The study was unilateral; the left side of the body was used to obtain arterial blood flow waveforms. Each participant laid supine on a patient table in a controlled, heated environment at 74 degrees Fahrenheit (Figure 4.3). After 15 minutes of acclimation, ultrasound (M7 Mindray) was used at each of the arterial sites to be investigated; pulse wave doppler, arterial depth, TAMEAN and TAMAX were collected at each site, and the skin superficial to the arteries were marked to establish the skin patch sensor placement.
Figure 4.2. Arterial pulse site locations used to collect data in the study. All locations were measured on the participants left side, and ranged from superficial arteries such as the radial, dorsalis pedis, and posterior tibial artery to deeper arteries such as the femoral, brachial and carotid arteries.
Scattering parameters from the skin patch sensor were collected using a vector network analyzer (VNA, Rhode & Schwarz), synchronized to a data acquisition system used to collect simultaneous PPG and electrocardiogram (ECG) signals (Biopac MP35). Each signal was collected at a sampling rate of 200 Hz for a duration of 15 seconds. To obtain the $S_{11}$ response, the change in amplitude was measured at the half power amplitude of the inductive side (rightmost side) of the first fundamental resonant peak. Baseline blood pressure and heart rate data was collected before each acquisition. The obtained physiological waveforms were preprocessed in Matlab to remove noise and lower frequency components using a filter, and analytically compared. Each waveform was manually inspected to remove incomplete cardiac cycles, defined as the onset of the P-wave of the ECG waveform to the onset of the P-wave of
the subsequent ECG waveform in the next cardiac cycle. To calculate the heart rate the peak to peak index (PPI) of the S₁₁ and PPG waveform was determined from the data and compared with the R-R interval of the ECG waveform during the same cardiac cycle. PTT was also calculated from the resulting waveforms, defined in this study as the difference between the R peak of the ECG waveform and the maximum systolic peaks of the MPG and PPG waveforms.

4.3.3 Repeatability/Correlation study:

The hemodynamic parameters obtained with the skin patch sensor were compared to both ECG and PPG to determine its performance as a blood flow screening device, and for reproducibility, repeatability, and precision. To accomplish this, first a multiple linear regression was conducted to qualitatively identify any trends in the PPI/RRI between all 3 measurement methods. The PPI/RRI used in the multiple linear regression was conducted on a compiled set of all PPI obtained for each participant in the study at every arterial site investigated (n=146). Additionally, simple linear regression was conducted to determine any correlations between the 3 measurement methods. Regression was carried out for the PPI/RRI of total compiled data (n=146) for S₁₁ vs. ECG, S₁₁ vs. PPG, and PPG vs. ECG instantaneous heart rate intervals. Linear regression was also carried out on compiled data sets for individual localized sites S₁₁-ECG and S₁₁-PPG signals as well to determine how sensor placement and arterial location affected the accuracy of the obtained data. Coefficient of determination (R²) and root mean squared error (RMSE) was calculated for each regression.

4.3.4 Similarity Analysis:

To determine the repeatability, reproducibility and precision of the measurement techniques, Bland-Altman plots were created to produce a mean difference plot. Similar to the regression analysis, Bland-Altman plots were produced for both the whole data set (n=146) and
individual arterial site locations comparing $S_{11}$-ECG, $S_{11}$-PPG, and PPG-ECG. The coefficient of reproducibility/repeatability (RPC) and coefficient of variation (CV) were calculated for each data set to determine the reproducibility and precision of each measurement technique, respectively.

4.4 Results:

4.4.1 Multisite Arterial Study:

Figure 4.4 shows the ultrasonograms collected used to determine the hemodynamic parameters and establish sensor placement for each participant. The collected pulsatile flow response from the PPG and skin patch sensors is presented in figure 4.5 and shows an observable delay between R-wave onset and the systolic peaks of the biofluid volume shifts. PAT was calculated for both PPG and skin patch responses to observe physiological relevance.

Figure 4.4. Ultrasonograms collected for blood flow analysis. Each image illustrates an arterial site selected to be tested for skin patch sensor pulse detection, from top to bottom, left column: A) Carotid artery, B) Brachial artery, C) Radial artery; right column: D) Femoral artery, E) Posterior Tibial artery, and F) Dorsalis Pedis artery.
Figure 4.5 Pulsatile waveforms collected from each arterial landmark. The orange waveform illustrates the $S_{11}$ response from the skin patch sensor, the blue dotted line indicates the PPG signal collected from the index finger of the participant, and the blue solid line illustrates the ECG collected for each participant. For each pulse site, each sensor was time-synchronized to compare the hemodynamic response collected from each method. Top column, left-right: Carotid artery, brachial artery, and radial artery waveforms comprise the upper body blood flow signals collected. Bottom row, left-right: Femoral artery, posterior tibial artery and dorsalis pedis artery waveforms comprise the lower body blood flow signals collected.

The physiological data collected using the PPG and the skin patch sensor was filtered using a Butterworth bandpass filter from 0.5 Hz-8 Hz. The high-pass frequency of 0.5 Hz was used to eliminate the lower frequency physiological effects on the signal, while the low-pass frequency of 8 Hz was used to eliminate higher frequency noise.

### 4.4.2 Repeatability/Correlation Study:

Figure 4.6 shows the multiple linear regression for all 3 measurement methods. The $S_{11}$ and PPG signal are modeled as two independent variables, and the ECG signal is modeled as the predictor variable; correlations between all 3 classes of sensors can be observed by qualitative trends apparent in the multiple regression plot. A trend in the plot was observed that appears to be positive towards ECG and slightly skewed towards the $S_{11}$ signal from the skin patch sensor. Figure 4.7 presents the linear regression and Bland-Altman analytical results between each of the measurement methods for the total compiled PPI data at every location, and figure 4.8 presents
the linear regression and Bland-Altman analytical results of the measurement methods of the S11 vs. ECG PPI data for each individual location.

Figure 4.6. Multiple regression plot illustrating predictive relationships between the 3 proposed measurement methods. A Clear positive trend is observed between S11 vs. ECG, and S11 vs. PPG, while there is a slightly positive trend for PPG vs. S11, which can be observed in the trend plane skew in the plot.

Figure 4.7. Statistical analysis of individual arterial site comparing the skin patch sensor PPI with the corresponding ECG RR interval; for each panel, 2D linear regression plots (left) and Bland-Altman plots (right) are presented. A) presents the corresponding statistical analysis for the S11 PPI vs. the ECG RR interval, while B) and C) present the statistical analyses for the PPG PPI vs ECG RR interval and S11 PPI vs. ECG RR interval, respectively.
4.4.3 Discussion:

The filtered temporal waveforms that were obtained with the skin patch sensor indicated a pulsatile detection of blood volume shifts in the localized arterial sites that were studied. Each waveform contains a systolic upstroke, incisura (dicrotic notch), and a diastolic downslope. Each pulse in the cardiac cycle had PAT that were consistent with common literature, however it is important to note that these values may differ significantly depending on the individual, their physiological condition, mental state, or several other health related or environmental factors.
Nevertheless, this suggests that the PAT derived from the waveforms are in good agreement with the blood flow measured in the participants. The PPG derived PAT was consistent as it was only taken at the index finger of everyone, however it was useful to compare against the PAT of the skin patch sensor response. The skin patch sensor pulsatile peaks occur after the ECG t-wave but briefly before the finger PPG signal in the upper body waveforms collected in the carotid, brachial, and radial arteries. This was expected as the pulse of blood ejected from the heart would travel to those regions before reaching the fingertip of the individual. PTT calculated between the systolic peak of the skin patch sensor waveform and the systolic peak of the PPG waveform also demonstrate that distance between each pulse is approximately the same physical distance that the sensors are placed away from each other. Conversely, the skin patch sensor waveforms in the lower body were shown to occur after the fingertip PPG signal, which was also expected as the signal would propagate through the upper body before the lower body would experience pulsatile flow.

Regression analysis clearly demonstrates that the PPI detected in the skin patch sensor waveform is an accurate predictor for instantaneous heart rate and is very strongly correlated with both ECG and PPG peak-to-peak intervals. This suggests that this sensing method is viable for obtaining clinically accurate measurements for heart rate. Additionally, Bland-Altman analysis produced low RPC and CV values, suggesting that the method is highly reproducible with high precision. However, upon investigation of regression and Bland-Altman analysis of the individual arterial pulse sites, it was found that the skin patch sensor detection of the Dorsalis Pedis artery and Carotid artery yielded lower RPC, CV, and R² values. While CV values were still under 5%, RPC values were higher than 5%. This would suggest that these arterial sites are not as reproducible as the peripheral arteries investigated for detection of hemodynamic
parameters. Nonetheless, the $R^2$ values still show very strong correlation to the ECG and PPG intervals. Overall these decreases in reproducibility and correlation can be attributed to outliers due to natural physiological variation in the participants. An alternate hypothesis would be that the Dorsalis Pedis artery is known for large variations in blood flow in different individuals and is sometimes advised against using as measurement in clinical diagnostics such as an ABI. The higher elasticity present in a central artery such as the Carotid artery may also alter the sensor response due to blood flow, as the biofluid volumetric shift may be altered when compared to the other arterial sites investigated in this study.

The skin patch sensor was able to successfully detect pulsatile blood flow in each of the arterial sites studied in this experiment. The highest average depth of arteries investigated was 2.5 cm in the femoral artery. Successful detection of arterial blood flow from these regions demonstrate the skin patch sensor as a new sensing method for non-invasive detection of arterial blood flow in deep arteries, which to the author’s knowledge is the first of its kind. However, the technology is not without its limitations; the sensor readout instrumentation is currently comprised of a desktop VNA, which is very bulky and expensive. While spiral resonant antennas such as that present in the skin patch sensor can communicate wirelessly, this has yet to be optimized so it is currently interrogated coplanar to a loop antenna, which introduces motion artifacts into the signal if the cable attached to the loop antenna moves.

### 4.4.4 Conclusions:

Electromagnetic RF resonant circuits have only recently gained interest in its use in biosensing, however the field has significant potential to impact the medical field. The wearable skin patch sensor proposed in this study is low cost and has the potential to be interfaced with current day internet of things (IoT) or other smart devices. By providing an accessible platform
for people to continuously monitor their health, this skin patch sensor could serve as a useful point-of-care device for early stage screening of cardiovascular diseases. Additionally, we have demonstrated the sensor’s ability to obtain clinically accurate, reproducible results for cardiovascular parameters, thus the device could be used in a clinical setting as well as a simpler, earlier stage approach to obtaining blood flow parameters from deeper arteries in the body. This would allow clinicians to better assess the presence of blockages in these deeper arteries, allowing them to make better informed decisions on whether further testing or imaging is required to determine if disease is present or an intervention is required.
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