CARDIAC STROKE VOLUME MEASUREMENT USING A NON-INVASIVE WEARABLE ELECTROMAGNETIC RESONATOR

A Thesis by

Fayez Hamoud Alruwaili

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CARDIAC STROKE VOLUME MEASUREMENT USING A NON-INVASIVE WEARABLE ELECTROMAGNETIC RESONATOR

The following faculty members have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirement for the degree of Master of Science with a major in Biomedical Engineering.

Kim Cluff, Committee Chair

Youngkuk Lee, Committee Member

Shunag Gu, Committee Member
I dedicate this thesis to my family, and friends.
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ABSTRACT

The measurement of cardiac output (CO) parameters is an important tool for the detection of cardio-pathologies and monitoring critically ill patients. There are various existing invasive and non-invasive medical technologies that measure CO parameters at the clinical setting including Transpulmonary thermodilution (TPTD) and echo-ultrasound. The main limitations of the existing medical technologies include the restriction to the clinical setting, intensive training, and accuracy in measurement. In this thesis project, a non-invasive wearable electromagnetic (EM) skin patch resonator was designed, tested, and developed to measure CO parameters, specifically left ventricular stroke volume (LVSV). The wearable sensor is an EM self-resonant patch that configured into a specific pattern to formulate its three passive elements (resistance, capacitance, and inductance). The EM patch has no electrical connection and is powered via an antenna embedded within the patch design. A combination of bench top models and healthy human participants were used in testing the volume sensitivity and ability of the EM skin patch in measuring LVSV. A strong linear correlation ($R^2 = 0.99$) between the volume changes and changes in the EM skin patch response was observed. Also, the EM skin patch has a detection depth capability up to 11 cm using human like tissue phantoms. Heart rate (HR), LVSV, and CO were measured with the EM patch with an average relative error of 0.209 % ($R^2 = 0.99$), 3.04 % ($R^2 = 0.96$), 3.19 % ($R^2 = 0.80$) and 3.79 % ($R^2 = 0.88$) as compared against impedance cardiography and electrocardiogram. As such, this work presents an EM skin patch that can be a unique solution for measuring CO parameters at point of care settings where access to the sophisticated medical technologies is not found.
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<td>Description</td>
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<tr>
<td>LVSV</td>
<td>Left Ventricular Stroke Volume</td>
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<td>CO</td>
<td>Cardiac Output</td>
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<td>HR</td>
<td>Heart Rate</td>
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<td>LV</td>
<td>Left Ventricle</td>
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<tr>
<td>RV</td>
<td>Right Ventricle</td>
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<tr>
<td>AO</td>
<td>Ascending Aorta</td>
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<td>PA</td>
<td>Pulmonary Artery</td>
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<td>EM</td>
<td>Electromagnetic</td>
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<tr>
<td>TPTD</td>
<td>Transpulmonary thermodilution</td>
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<td>ICG</td>
<td>Bioimpedance Cardiograph</td>
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<td>BR</td>
<td>Bioreactance</td>
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<td>PC</td>
<td>Pulse Contour</td>
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<td>RF</td>
<td>Radiofrequency</td>
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<td>LVET</td>
<td>Left Ventricular Ejection Time</td>
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LIST OF SYMBOLS

L
Inductance

C
Capacitance

R
Resistance

I
Current

Z
Impedance

PCO
Power Coefficient

S_{11}
Reflection Coefficient

J
Spatial Current Density

\mu_0
Free Space Magnetic Permeability

\mu_j
Relative Magnetic Permeability

\varepsilon_0
Free Space Electrical Permittivity

\varepsilon_r
Relative Electric Permittivity

q_0
Total Charge Density

\varepsilon_r
Relative Permittivity

\varepsilon'
Real Permittivity

\varepsilon''
Imaginary Permittivity
CHAPTER 1: INTRODUCTION

1.1 Motivation

Left ventricular stroke volume (LVSV) measurement is an important clinical parameter for the assessment of cardiac function and detection of cardio pathologies. LVSV is defined as the blood ejected by the left ventricular (LV) with each cardiac cycle with an average of \( \approx 80 \text{ mL} \) for healthy human. Measurement of LVSV at an early point of medical assessments may lead medical personnel to an accurate prediction of cardiac diseases and perform the needed medical intervention. Furthermore, measurement of LVSV, cardiac output (CO), and morphological changes in the heart may lead to the detection of LV dysfunction, aortic stenosis, atrial fibrillation, and the different stages of heart failure.

Currently, there exists various medical equipment that can measure SV and CO at the clinical setting. These technologies can be either invasive or non-invasive. The most highlighted methods include Transpulmonary thermodilution (TPTD) which stands as the golden standard for measuring LVSV and other CO parameters since it provides the most accurate measurement. Additionally, there are many other non-invasive and minimally invasive medical devices that exist for measuring LVSV and CO parameters. Echocardiography stands as golden non-invasive methods for measuring LVSV, CO, and the morphologies of cardiac chambers, valves, and wall.

Other emerging medical technologies have been developed to measure LVSV and CO parameters which include Bioimpedance Cardiograph (IC), Bioreactance (BR), and Pulse Contour (PC). All of the stated technologies have unique characteristics in their operating principles, and the information obtained. Although the major highlighted limitations of these
technologies include their accuracy, limited use to the clinical setting, intensive training, and the clinical cost.

As such, the motivation of this research was to develop an electromagnetic (EM) skin patch wearable technology that can measure SV, CO, and blood volume changes in the different chambers of the heart. The EM resonant skin patch has unique advantages over traditional wearable sensors. The EM skin patch detects blood volume shifts related in the heart – which are not detectable by traditional wearables and can only be detected with large specialized equipments found in the hospital. The proposed sensing technology can be applied in an unobtrusive nature without extensive training (similar to an adhesive bandage) and may be a valuable tool in monitoring patients with critical conditions [1-24]. Blood volume shifts in the heart induce shifts in the EM field which can be detected using the proposed technology.

This sensing system can operate as a point-of-care technology, making it applicable in limited resource environments including a microgravity, rural communities and military zones lacking access to specialized equipment found in hospitals. This sensor’s unique design results in a lightweight, wearable technology. The use of RF waves instead of mechanical waves (ultrasound) or infrared (photoplethysmography) results in increased penetration depth. Additionally, the non-invasive detection capability of this skin patch does not require invasive measures, consequently eliminating the risk of infection that can be observed in invasive measurements of cardiac function.
1.2 Objective and Specific Aims

The primary objective of this thesis is to develop a non-invasive EM skin patch resonator that can measure SV, CO, and blood volume changes of the different chambers in the heart. This objective was achieved through three specific aims:

1. Develop a bench top model to determine the volume sensitivity of the skin patch, and its ability to measure blood volume changes in the LV of a bovine heart.
2. Develop high fidelity phantom models that resample actual dielectric constant of the human chest to determine the detection depth of the EM skin patch.
3. Recruit human participants (n=4) and measure SV, heart rate (HR), and CO as compared against clinical standards ICG. Also, a repeatability study was constructed to determine the accuracy of the EM skin patch in measuring SV, HR, and CO over four different days.

1.3 Thesis Outline

1. Chapter 1 introduces the motivation, primary objective, and aims of this research.
2. Chapter 2 presents a comprehensive literature review of relevant medical technologies that measure SV, CO, and morphology of the cardiac structure. Also, the physiology and anatomy of chest and heart is presented. Lastly, design of the EM skin patch and its underlining operating principle, interaction with human tissue are discussed in this chapter.
3. Chapter 3 presents an experimental set-up to determine the volume sensitivity of the EM skin patch. Also, an animal bench top model was used to simulate fluid volume changes in LV of bovine heart and determine the skin patch ability in detecting fluid volume
shifts. Lastly, one human participant was recruited to determine the skin patch ability in measuring fluid volume shifts in the LV chamber.

4. Chamber 4 presents the developments of phantom models of the human chest and determines the detection depth of the skin patch and its ability to measure changes in fluid volume. Also, chapter 4 presents the repeatability study and the skin patch ability in measuring HR, SV, and CO in healthy human participants. Also, mathematical modeling of the AO and its relationship with electromagnetic field lines of the skin patch and fluid volume in the heart are established.

5. Chapter 5 presents the future direction of this work and conclusion.
REFERENCES


CHAPTER 2: LITERATURE REVIEW

2.1 Cardiac Anatomy and Physiology

The heart is located behind the sternum 1.5 cm to the left of the midsagittal plane in-between the lungs (Figure 2.1) [1, 2]. The heart is sheltered by the rib cage, lungs, and pericardium muscle [1, 2].

![Figure 2.1. The location of the heart in the human body. The heart is connected to the cardiovascular tree via the pulmonary artery and veins, AO, and vena cava. Courtesy of [3].](image)

The heart has four chambers which receive and eject blood into the body, and they are known as the right atrium (RA), right ventricular (RV), left atrium (LA), and left ventricle (LV) [1, 2]. Additionally, the heart has four valves that regulate the blood flow between the different chambers inside the heart, lungs, and the aorta. The heart is connected to the cardiovascular tree via the PA, PV, superior and inferior vena cava, and AO. Furthermore, the electrical activity of the heart is controlled via synchronized electrical events that is initiated at the sinoatrial node in the RA and propagate into the rest of the heart. The electrical activity of the heart is controlled via the nervous system (sympathetic and parasympathetic) with two nerves known as the accelerator and vagus nerves [1, 2]. These two nerves are highly regulated via a region in the brain known as the medulla oblongata which is sensitive to the physiological needs of the body.

Furthermore, the main function of the heart is to maintain the physiological needs of the body by circulating oxygenated blood and nutrients [1, 2]. The heart achieves its purpose via a
highly controlled subsequent events in its four chambers, RA, LA, RV, and LV. The time period in which blood starts flowing into the RA and LA (atrial diastole) until all the blood is ejected from the LV and RV (atrial systole) is marked as a one complete cardiac cycle [1, 2]. During each cardiac cycle, five subsequent events occur in the heart which lead to the ejection of the blood into the body [1, 2]. The first event of the cardiac cycle, in which the RA and LA are filled with blood, is marked as atrial diastole. The non-oxygenated blood enters the RA via the superior and inferior vena cava (venous return) and coronary sinus [1, 2]. At the same time, the LA is being filled with oxygenated blood coming from the lungs via the PV. During atrial diastole, the atrioventricular valves are open so that blood is passively flowing into the RV and LV [1, 2]. Also, the semilunar valves, aortic and pulmonary, are closed during atrial diastole to prevent blood leakage into lung and AO [1, 2]. Passive filling of cardiac chambers occurs due to the pressure difference between the cardiac chambers and the cardiovascular tree [1, 2]. Active filling of the RV and LV occurs due to the contraction of the RA and LA (depolarization of the atriums (P peak-ECG)) which marks the second stage of the cardiac cycle, atrial systole (lasts for 100 ms) [1, 2]. The RA and LA, in a normal patient, may be filled with a maximum blood of 130 mL which marks the end diastolic volume point or preload [4].

The subsequent event of the cardiac cycle is ventricular systole, divided into two stages, which is initiated by the closing of atrioventricular valves and the isovolumetric contraction of RV and LV (depolarization of the ventricles (QRS peak-ECG)). During isovolumetric contraction, which is the first stage of ventricular systole, the pressure in the ventricles rises continuously until the pressure is above that of the PA and AO so that the semilunar are opened and marks the end of the isovolumetric contraction. The second stage of ventricular systole is the contraction of the ventricular muscle and ejection of blood into the lung and the body (QT
interval-ECG). The amount of blood ejected by the ventricles into the body and the lungs is
known as stroke volume (SV)[2]. SV ranges between 70 - 100 mL in normal healthy adults.
Body mass index (BMI) and body surface area (BSA) are correlated with the amount of SV. The
higher the BMI, the more blood is ejected by the ventricles with an increase in SV is observed.
Furthermore, the LV operates at higher pressure as compared into the RV. Pressure in the LV
ranges between 0-120 mmHg, whereas pressure in the RV ranges between 0-20 mmHg [5].

The last phase of the cardiac cycle is marked as ventricular diastole which has two
distinct phases. The first phase of ventricular diastole is known as the isovolumetric relaxation.
As the ventricular relaxes, pressure in RV and LV drops below the pressure of the PA and AO
which results in the closing of the semilunar valves to prevent back flow of blood into the heart.
At this stage the ventricles relax with no changes in the volumes. During the second stages of
ventricular diastole (late diastole), the pressure in the ventricles drops below the pressure of the
atrium which results in the opening of the atrioventricular valves and filling the ventricles with
blood.

With each cardiac cycle, the heart ejects blood (SV) into the body by the LV. Within each
minute, the average amount of blood that is ejected by the heart (CO) can be estimated as

**Equation (2.1).**

\[
CO = HR \times SV
\]

**Figure 2.2** Illustrates the cardiac cycle events for the different chambers in the heart and
AO as synchronized with ECG.
2.2 Existing Methods

2.2.1 Current Clinical Technologies

Currently, there exists various medical equipment that can measure SV and CO at the clinical setting. Transpulmonary thermodilution (TPTD) is the golden standard for measuring SV and other CO parameters since it provides the most accurate measurements [6-9]. TPTD works by injecting a cold bolus solution into the superior vena cave and a pressure tip catheter is inserted in the femoral artery (which has a thermistor that senses the changes in blood temperature [7-9]). TPTD measures CO parameters based on the Stewart-Hamilton principle where CO is a function of the thermodilution curve as a function of time and the mass of the injected indicators [7-9]. The main limitation in TPTD includes its ability to detect changes in CO parameters where the smallest detectable change was found to be 12 % [7-9]. Furthermore, pre-and-post-operative issues may rise due to bleeding, arterial puncture, and infection.
Additionally, there are many other non-invasive and minimally invasive medical devices that exists for measuring SV and CO parameters. Echocardiography stands as the golden non-invasive method for measuring SV, CO, and the morphologies of cardiac chambers, valves, and wall [10]. Different techniques and assumptions have been established for measuring SV and CO parameters using ultrasound doppler [9, 10]. Despite the many advantages of echocardiogram, limitations for its uses and operating principle exists. The major highlighted limitation for echocardiogram is the complexity during assessments of cardiac function [9, 10]. The technical expertise and training for echo personnel are confounding variables for the accurate assessments of cardiac function [9, 10].

Other emerging medical technologies have been developed to measure SV and CO parameters which include Bioimpedance Cardiograph (ICG), Bioreactance (BR), and Pulse Contour (PC). ICG is one of the earliest non-invasive methods that was developed to measure hemodynamic parameters that include SV and CO. ICG measures the electrical resistance across the thorax during the cardiac cycle and estimates cardiac parameters [11-14]. ICG is a poor instrument for measuring hemodynamic parameters due to its sensitivity to movement artifacts, certain cardiovascular diseases, and peripheral resistance [9, 14-16].

Furthermore, bioreactance (BR) is another method that is currently developed which measures reactance changes in the thoracic due to the cardiac cycle. BR uses a set of electrodes placed on the neck and the chest and injects a high oscillating current [17, 18]. The derivative of the phase shift in the reactance is used to derive SV and CO measurements [17, 18]. BR has similar limitations to ICG where it has shown to be sensitive to motion, certain cardiovascular diseases, and background noise [17, 18].
Pulse contour is another method used to estimate SV and CO parameters in the heart using the arterial pulse wave [9, 19, 20]. The pulse contour method uses certain assumptions that transform the pressure waveforms into blood flow which is critical for measuring SV, and CO parameters [9, 19, 20]. Flotrac-Vigileo and ClearSight systems are the recent developments and most investigated in the literature [20]. Flotrac-Vigileo is a minimally invasive device that requires an arterial line to obtain blood pressure waveforms. Despite the invasive nature of Flotrac, further limitations have been highlighted for its performance which include the sensitivity to certain cardiovascular diseases which may include hypothermia, decreased blood perfusion, and peripheral artery diseases [9, 19, 20]. The other newest system, “ClearSight”, is a non-invasive technique that uses the finger climb method to measure cardiac output parameters. The ClearSight has its advantages since it is a non-invasive, easy to use technique. Although, there have been many studies presented which show high error using the ClearSight system in measuring cardiac output parameters (max to 57 %) [21-23]. All of the stated technologies have unique characteristics in their operating principles, and the information obtained. The major highlighted limitation of these technologies includes limited use in the clinical setting, availability, sensitivity and the clinical cost.

2.2.2 Wearable Technology

There has been wide interest in developing wearable technologies to measure blood volume and cardiorespiratory activity based on microwave and radar biosensing. Advantages of microwave and radar biosensing include the use of non-ionizing radiation, small form factors, mobility, and high penetrating depth through biological tissue. Doppler radar radiofrequency (RF) sensors are among the earliest developed systems to measure human vital signs including HR [24-26]. Doppler radars are non-contact systems that correlate the physiological movement
to frequency changes [24-26]. Limitation for the Doppler radar include the complexity of the measurement method, the large form factor, and the presence of noise in the system [25, 27].

More recent biosensing radar technologies have been developed to measure arterial pulsation which uses Ultra-wideband radar systems. A group from London [28] was able to develop a single-chip Ultra-wideband to measure arterial pulse wave velocity from six different locations on the body including the heart [28]. Their experimental set-up utilizes two body coupled antenna ($S_{21}$) and radar-based analyses to measure arterial pulsation. As compared to our skin patch, their technology does not estimate ventricular volume or any other physiological parameters. Their obtained physiological waveforms are described as the pulse wave velocity, but they are unitless and as such have no physical meaning [28].

Furthermore, a group from Stanford has developed a biodegradable antenna to monitor blood flow in an artery [29]. The biodegradable antenna is fixated on the artery and energized via an external loop antenna via inductive coupling [29]. As the blood volume is changing within the artery, the reflection coefficient ($S_{11}$) within their antenna is changing. As compared to our skin patch, their antenna is similar, however, it is invasively placed [29]. Highlighted limitation of their work is the noise inherited in their collected signal in the in vivo experiment. The signal is poor and altered significantly by the surrounding tissue and blood vessels.

Other groups from China, Norway, and Northland have developed variant EM resonators to measure blood flow in the artery and the heart [28, 30-32]. A non-contact flexible radiofrequency (RF) resonator was developed to measure HR during sleep [30]. The developed sensor measured HR from the radial artery with 95% accuracy. However, the developed RF
resonator was only used to detect pulsations in the superficial radial artery and not deep arterial pulsations such as those found in the ascending aorta or heart ventricles.

Additionally, a digital-IF Doppler radar system was developed to measure the motion of cardiac muscle [33]. In this system, a high frequency signal was used (>15 GHz) which can limit the detection depth to superficial organs and not blood volume changes inside the heart [33]. This may present a major limitation for females and overweight patients due to the large amount of adipose tissue that may obstruct and attenuate the signal. In a different study, a complimentary split-ring resonator was developed to collect cardiac signals from the heart [34]. In the developed system, changes in the resonance frequency of the S21 transmission coefficient due to movement in the chest was measured. The signal obtained was well suited for HR measurements, however, the signal lacked critical information about the cardiac cycle events to derive cardiac output (CO) parameters such as SV.

2.3 Electromagnetic Skin Patch

2.3.1 Skin Patch Theory Design and Operating Principles

The EM skin patch sensor is designed from a single baseline component (copper) configured into a square planner spiral. When the sensor is energized via an external RF waves, it produces a current flowing in the trace and a resonant frequency response with oscillating magnetic and electric fields that surround the sensor. The EM skin patch has specific design parameters that define its electrical component, namely, the resistance (R), inductance (L), and capacitance (C). The inductance of the EM skin patch is the sum of self and mutual inductance. The magnetic field is generated around the trace width with a self-inductance value calculated according to Equation (2.2) [35, 36].
\[
L = \frac{\mu_0}{4\pi I^2} \iint \left[ \frac{J(r_i)\mu_i \ast J(r_j)\mu_j}{r_i - r_j} \right] d^3r_id^3r_j \quad (2.2)
\]

Where, \(L\) is the total self-inductance, \(J(r_i)\) is the spatial current density as a function of the conductive traces, \(\mu_0\) is the free space magnetic permeability \((\mu_0 = 4\pi \times 10^{-7} \text{ N} \cdot \text{A}^{-2})\), \(I\) is the total current in the circuit, \(\mu_i\) and \(\mu_j\) are the relative magnetic permeability of the material near the sensor at locations \(r_i\) and \(r_j\) respectively.

Furthermore, the gap width between the parallel traces provides an inherent parasitic capacitance when the sensor is impinged upon by an RF wave. The oscillating magnetic and electric fields are stored alternatively in order for the sensor resonance [36, 37]. The capacitance value of the sensor can be calculated as **Equation (2.3)** [35, 36, 38].

\[
C^{-1} = \frac{1}{4\pi \varepsilon_r \varepsilon_0 |q_0|^2} \iint \left[ \frac{\rho(r)\rho(r')}{|r - r'|} \right] drdr' \quad (2.3)
\]

Where, \(C\) is the capacitance, \(r\) is the length of the sensor trace, \(\varepsilon_0\) is the free space electrical permittivity \((\varepsilon_0 = 8.85 \times 10^{-12} \text{ F} \cdot \text{m}^{-1})\), \(\varepsilon_r\) is the relative electric permittivity, and \(q_0\) is the total charge density.

The resistance of the EM skin patch is based on the overall trace dimensions that include the length of the trace and the gap width. The total resistance of the skin patch is a combination of the parallel and series resistance. The series resistance is both dependent and independent on the frequency. The total length of the EM skin patch accounts for the DC independent frequency series resistance. The eddy current accounts for the dependent frequency series resistance. Furthermore, the parallel resistance is the result of the finite resistance between the sensor and the human body.
Once a sinusoidal AC current is delivered to the loop antenna, the EM skin patch is inductively coupled and develops its own electromagnetic field. At resonance, the EM patch sensor develops a resonant frequency peaks that are calculated according to \textbf{Equation (2.4)}.

\[
f = \frac{1}{2\pi \sqrt{CL}} \quad (2.4)
\]

Where \( L \) is the inductance value inherited from the sensor design (trace width length), and \( C \) is the capacitance value of the sensor design inherited from the geometric design and fluid volume changes. Furthermore, changes in the resonant frequency is inversely proportional to changes in the capacitance (Fluid volume changes) \textbf{Equation (2.5)}. As the capacitance increases (increase in the volume which due to the increase in the overall effective permittivity), a decrease in the resonant frequency is observed.

\[
C = \frac{1}{4\pi^2 f^2 * L} \quad (2.5)
\]

At resonance, the ratio of the reflected to the transmitted power from the skin patch is known as the \( S_{11} \) reflection coefficient \textbf{Equation (2.6)}.

\[
S_{11} = \frac{\text{Reflected power}}{\text{Forward power}} \quad (2.6)
\]

Where the forward power is the maximum amount of power transmitted from the skin patch to medium, and the reflected power is the power received from medium to the skin patch, after interaction. Additionally, the impedance (\( Z \)), which is defined as the resistance to the EM field lines, is modulated by the changes in the \( S_{11} \) reflection coefficient \textbf{Equation (2.7)}.

\[
Z = \frac{1 + S_{11}}{1 - S_{11}} * Z_0 \quad (2.7)
\]
Where $Z_0$ is the base impedance 50 Ω, and $Z_L$ is expressed as a rectangular value, and $Z_L = R + jX$ with R being the real impedance, and X is the imaginary impedance. During an ideal condition and a full power transfer from the skin patch to the medium, the $Z_L$ and R is at 50 Ω and X is 0. The EM skin patch in the project was efficiently designed to resonate between -15 to -50 dB when placed on the chest. **Table 2.1** provides the different design parameters that used to optimize the performance of the EM skin patch.

Tables 2.1 Sensor design parameters and operations [39].

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Design/Alteration</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Size</td>
<td>Larger vs Smaller</td>
<td>The resonate frequency of the skin patch depends upon the length of the trace wire. The longer the trace (larger skin patch), the lower the resonate frequency and higher self-inductance. Also, the shorter the trace length, the higher the resonate frequency and self-inductance.</td>
</tr>
<tr>
<td>Number of Turns</td>
<td>High vs Low</td>
<td>The overall length of the skin patch is related to the number of turns. The higher the number of turns results in a longer trace length and lower resonate frequency. The self-inductance and capacitance of the skin of the patch is proportionally related to the length of the trace and number of turns</td>
</tr>
<tr>
<td>Gab Width</td>
<td>Larger vs Smaller</td>
<td>Decreasing the gab width increases the speed of the current and the induced electromotive force. This results in maximizing the strength of the EM field. Decreasing the gab width increases the parasitic capacitance along the length of the pattern.</td>
</tr>
<tr>
<td>Trace Width</td>
<td>Larger vs Smaller</td>
<td>The induced current in the skin patch travels along the trace. The inductance is inversely proportional to the width of the trace.</td>
</tr>
</tbody>
</table>

The design of the skin patch was optimized to have high sensitivity to fluid volume changes and maximum power transfer. **Figure 2.3** presents Smith chart which analyzes the impedance of the skin patch sensor while placed on the chest (On top of the AO). Impedance analysis in **Figure 2.3** demonstrates that the skin patch was impedance matched (50 Ω) with the load (the
chest of participant). This illustrates the efficiency of the skin patch in measuring cardiac information.

![Smith Chart](image)

**Figure 2.3.** Smith chart: the normalized real (R) and imaginary (X) impedance of the skin patch sensor while placed on top of the AO. The middle point in the graph indicates a full match between the source (EM skin patch) and the load (participant chest). This indicates that there was a full power transfer from the skin patch to the participant’s chest during measurement of cardiac information.

2.3.2 Skin Patch Interaction with Biological Tissue

The electromagnetic field of the skin patch response is dependent on the material’s relative permittivity, relative permeability, and electric conductivity. Once the skin patch is energized via an external RF wave, the skin patch develops an alternating EM field that propagates along different tissue layers and gets reflected, absorbed, and transmitted at the boundary of tissues due the changes in the relative permittivity \( \varepsilon_r \)[40, 41]. The magnitude of the reflected signal at the boundary is dependent upon the resistance of the electric field (EF) that
is experienced at each tissue layer which is a function of the relative permittivity. The relative permittivity is a complex number having a real and imaginary component **equation (2.8)** [40, 42, 43].

\[ \varepsilon_r = \varepsilon' + j \varepsilon'' \quad (2.8) \]

Where \( \varepsilon_r \) is the relative permittivity, \( \varepsilon' \) is the real component of permittivity and \( \varepsilon'' \) is the imaginary component of permittivity. \( \varepsilon' \) is known as the measure of the EF storage in a tissue layer and \( \varepsilon'' \) is the measure of how dissipative the tissue is to the external EF [42, 43]. Human tissues with high relative permittivity absorb the EF in a greater extent as compared to human tissue with a low relative permittivity.

At a frequency <300 MHz, human tissues have very large relative permittivity value which can be attributed to the polarization time of the cells [40, 42, 44]. The longer the polarization time, the more charged the cells become and the more EF gets absorbed. Whereas, at the ultra-high frequency >300 MHz, the EF alternates rapidly which decreases the polarization time of cells and subsequently the EF travels to a deeper organ in the body (ex. The heart). However, this phenomenon is not true at all operating frequencies. Once the alternating EF becomes extremely fast (> 10 GHz), the EF is dissipated as heat due to the internal friction of polarization in the cell [42]. In this study, the frequency bandwidth was chosen to be between 1000 -1200 MHz in which the optimal response from the heart was obtained.

Blood volume changes are collected using the EM skin patch are as a result of changes in the reflection coefficient (\( S_{11} \)) which was modulated by the interaction between the EM field of the skin patch and the change in fluid volume in nearby substrate. As such, changes in the
resistive impedance due to fluid volume changes directly influence the current strength which can be describe by equation (2.9) [45].

\[ Z = \rho \frac{L}{A} \quad (2.9) \]

Where, \( Z \) is the impedance (\( \Omega \)), \( \rho \) is the resistivity (\( \Omega \cdot cm \)), and \( L \) and \( A \) are the length (cm) and cross-sectional area (cm\(^2\)), respectively. To determine the volume, the nearby substrate is assumed to be a cylinder having a constant length and varying cross-section-area, which varies with fluid volume that is inversely proportional to the impedance. Upon multiplying the numerator and denominator of equation (2.9) by \( L \), equation (2.10) is obtained [13, 46].

\[ Z = \rho \frac{L}{A} \cdot \frac{L}{L} = \rho \frac{L^2}{V} \quad (2.10) \]

Where, \( A \times L = \) volume (V) and then simplified to equation (2.11) to calculate for volume in mL [13, 46].

\[ V = \rho \frac{L^2}{Z} \quad (2.11) \]
REFERENCES


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CHAPTER 3: PASSIVE SELF RESONANT SKIN PATCH SENSOR TO MONITOR CARDIAC INTRAVENTRICULAR STROKE VOLUME USING ELECTROMAGNETIC PROPERTIES OF BLOOD


3.1 Abstract

This study focuses on the development of a passive, lightweight skin patch sensor that can measure fluid volume changes in the heart in a non-invasive, point-of-care setting. The wearable sensor is an electromagnetic, self-resonant sensor configured into a specific pattern to formulate its three passive elements (resistance, capacitance, and inductance). In an animal model, a bladder was inserted into the left ventricle (LV) of a Bovine heart and fluid was injected using a syringe to simulate stoke volume (SV). In a human study, to assess the dynamic fluid volume changes of the heart in real time, the sensor frequency response was obtained from a participant in a 30° head-up tilt (HUT), 10° HUT, supine and 10° head-down tilt (HDT) positions over time. In the animal model, an 80 mL fluid volume change in the LV resulted in a downward frequency shift of 80.16 kHz. In the human study, there was a patterned frequency shift over time which correlated with ventricular volume changes in the heart during the cardiac cycle. Statistical analysis showed a linear correlation $R^2 = 0.98$ and $0.87$ between the frequency shifts and fluid volume changes in the left ventricle of the bovine heart and human participant, respectively. Additionally, the patch sensor detected heart rate (HR) in a continuous manner with a $0.179 \%$ relative error compared to electrocardiography (ECG). These results provide promising data regarding the ability of the patch sensor to be a potential technology for SV monitoring in a non-invasive, continuous, non-clinical setting.
3.2 Introduction

Stroke volume (SV) is a critical cardiac output parameter that can offer critical assessments of cardiac function [1, 2]. SV is defined as the volume of blood ejected from the left ventricle with each cardiac cycle. Utilization of SV measurements can be a valuable tool for early detection of cardio-pathologies and monitoring pharmacological stimuli in ill patients [3, 4]. Medical applications utilizing SV measurements for detection and diagnosis include an investigation of left ventricular dysfunction, assessing fluid responsiveness, and heart failure [1, 5, 6]. Recent studies have demonstrated that point-of-care technologies can have beneficial results in detecting critical ischemic events and monitoring patient health in a non-clinical setting [7, 8].

Pulmonary artery catheterization with blood flow thermodilution has been highlighted as the standard method for measuring SV [2, 6]. However, various complications are encountered with this procedure due to insertion of a pulmonary artery catheter which include increased mortality, dysrhythmias, arterial puncture, and the high clinical cost [9-11]. Additionally, echocardiography is another common clinical method for measuring SV based on viewing the anatomy of the left ventricle (LV) chamber and the hemodynamic flow [2]. However, this method poses several limitations which include the requirements of specialized equipment, extensive training, and non-continuous measurements [6, 12].

Furthermore, there are a wide variety of devices that are used in the medical field that measure Cardiac Output (CO) parameters point by point, including SV. These devices include finger cuff technologies and impedance cardiography [3, 13]. Despite the efficiency of the stated devices, the requirement of a clinical setting, extensive training, and reliability of measurements are the highlighted limitation for these devices [3, 6]. Additionally, other implantable devices
have been developed to provide a real time assessment of cardiac function [14, 15]. However, the main limitation for these devices is that they are invasive and require implantation for monitoring cardiac events.

The development of a non-invasive, continuous, point-of-care technology may overcome current challenges faced in providing reliable health care for patients who live in areas that lack hospitals and certified physicians [16, 17]. Utilization of a non-invasive, point of care technology for screening cardiac performance may significantly benefit both patients and health care facilities [7, 17]. In an emergency setting, this benefit can be seen through reduced time between arrival and discharge, for the patient, and reduction of inpatient bed turnover for the health care facility [7].

In the past few decades, Doppler radar radiofrequency (RF) sensors have been investigated to monitor heart rate (HR) through correlating the physiological movement to frequency changes [18, 19]. The main limitation for the Doppler radar is the complexity of the measurement method and the presence of noise in the system [19, 20]. Furthermore, other RF sensors have been developed to monitor human HR. However, these sensors lack the ability to measure blood volume in the heart [21, 22]. Recently, RF sensors have been developed to detect human vital-signs, whereas, in this study we seek to further the capabilities of RF resonators to measure ventricular volume changes, which may be used as a cardiac parameter to assess the function of the heart.

In summary, this study presents a foundation for the development of a passive skin patch sensor, powered externally by radiofrequency (RF) waves via an antenna, to measure cardiac fluid volume changes. In our previous work, we were able to demonstrate the ability of an RF
skin patch sensor to detect intracranial fluid-volume shifts, detect pulsatile blood flow in a human arm phantom, identify hemodynamic waveform features, and measure heart rate [23-26]. The patch sensor was designed from a single baseline component comprised of a trace of silver configured into a square planar spiral patch. The conductive material in the sensor was designed in a specific pattern which makes up three passive elements of an open circuit resonant sensor, namely, the resistance (R), capacitance (C), and inductance (L) [27, 28]. The patch sensor does not have any electrical connection and can be applied as a simple adhesive bandage or woven into a garment.

The hypothesis guiding this study was that changes in the dielectric properties in the heart of the animal model and human heart due to fluid volume changes can be registered as shifts in the resonant frequency response of the sensor. The hypothesis was evaluated by pursuing the following specific objectives 1) develop an electromagnetic skin patch sensor, 2) investigate the volumetric sensitivity of the electromagnetic skin patch, 3) quantify the sensor performance using a biological-animal model, and 4) investigate the sensor frequency response in a human participant.

3.3. Material and Methods

3.3.1 Sensor Design

An electromagnetic skin patch sensor was built using a trace of conductive material configured into a square planar spiral comprising of inherited inductance (number of turns) with a gap width and trace width (Figure 3.1 A & B).
Figure 3.1. A) Microscopic snapshot of the original design for the spiral patch sensor (10.16 cm x 10.16 cm x 0.48 mm). The skin patch sensor was built from a conductive trace of copper, with spiral turns which contributed to the inductance, gap separation between the adjacent turns which contributed to the inherent capacitance, and the trace width. A loop antenna (10.30 cm x 10.30 cm) built around the sensor to energize the sensor with an oscillating radio frequency wave. B) Snapshot of the human skin patch resonant sensor (22.0 mm x 22.0 mm x 0.40 mm). A loop antenna (30.5 mm x 30.5 mm) was built around the sensor to energize the sensor with an oscillating radio frequency wave.

**Figure 3.1 A** shows the first sensor that was used for data collection for the volumetric sensitivity study and the biological model. The first sensor was designed as an original model to investigate the resonant frequency response to volumetric fluid change in beakers and non-active biological tissue. However, for active human studies, the skin patch sensor was designed accordingly for an optimal volumetric sensitivity detection and placement on the chest of the participant (**Figure 3.1 B**). The patch sensor is a self-resonant, open circuit sensor built on a flexible polyimide substrate to make its three passive elements. The open circuit sensor is governed by Maxwell’s equations for the electric and magnetic field and the right-hand rule [28].

A loop antenna made of copper was aligned around the skin patch to radiate RF waves and collect the frequency signals and the $S_{11}$ reflection coefficient. A SubMiniature Version A (SMA) connector was soldered to the antenna, and then it was connected to a Vector Network.
Analyzer (VNA) via a 50-ohm coaxial cable. For this study, a VNA was utilized for the purpose of inductively energizing the patch sensor with RF waves and recording the return loss $S_{11}$ parameter. The return loss parameter, $S_{11}$, describes the relationship between the reflected waves to the incident waves energizing the sensor. The primary factor affecting the return loss $S_{11}$ parameter in this study is the substrate through which the sensor’s electromagnetic field travels. Changes in the effective permittivity of the substrate, caused by an increase in blood volume in the heart, affect the ratio between the reflected and incident waves. These changes in the ratio are the key parameters being utilized to detect changes in fluid volume [29-31].

### 3.3.2 Fluid Volume Sensitivity Measurements and Frequency Relationship

The quantification of fluid volume sensitivity of the sensor was tested using a model to analyze the relationship between the fluid volume changes and the frequency shifts of the patch sensor. The model system consisted of an empty 100 mL beaker placed next to the sensor, antenna, and VNA (SDR-Kits DG8SAQ). Water ($\varepsilon_r \approx 78.3$) was added to an empty 100 mL beaker in increments of 0.5 mL, 1 mL, 10 mL, and 20 mL. As the volume of water in the beaker was increased from 0 mL to 100.5 mL, changes in the effective permittivity of the sensor’s electric field was induced and subsequently frequency shifts in the sensor response were detected. Measurements of $S_{11}$ parameters were recorded within a frequency range of 1-3 MHz using 1000 data points after every volume increment. Four sweeps were taken at each increment for noise characterization. A statistical correlation analysis was performed to determine the correlation between fluid volume and shifts in the sensor’s peak resonant frequency response.

### 3.3.3 Pre-Clinical Bovine Heart Measurement

Stroke volume (SV) measurement was simulated by developing a biological model. The system consisted of the VNA (SDR-Kits DG8SAQ), the patch sensor, and a non-active bovine
heart (relative permittivity myocardium tissue, $\varepsilon_r \approx 300$) [32]. The Bovine heart was utilized to assess the capability of the patch sensor to measures fluid volume shifts through myocardium tissue. A plastic bladder, attached to a plastic tube, was inserted into the left ventricle of the Bovine heart through the aorta (Figure 3.2A).

Starting with a baseline of 20 mL of water, increments of 20 mL of fluid volume were added to the bladder using a plastic syringe. Once the baseline was established in the sensor frequency response, any additional increments of water introduce a change in the effective permittivity of the myocardium tissue and water layers. This change to the effective permittivity is measured as frequency shift. The sensor was placed within 1 cm of the external layer of the LV and the shifts in the sensor’s resonant frequency were registered as fluid was pumped into the LV chamber, wall thickness $\approx 2$-3 cm (Figure 3.2B).

The VNA was calibrated to take measurements of the $S_{11}$ parameter in a frequency range of 1-5 MHz using 1000 data points. Multiple sweeps were collected (from 1-5 MHz) at each
increment of fluid volume for noise characterization. Statistical correlation analysis was performed to determine the relationship between the frequency shifts and fluid volume changes in the Bovine heart model.

### 3.3.4 Human Blood Volume Measurements

After obtaining Institutional Review Board (IRB) approval, a healthy male participant was selected to investigate the sensor frequency response in an active human tissue. The blood volume changes in the heart of the human participant were measured throughout the cardiac cycle during 30° head-up tilt (HUT), 10° HUT, supine, and 10° head-down tilt (HDT). The experimental method was chosen to investigate the ability of the sensor to detect various volumetric amounts in the heart due to different tilting positions [33-35]. The VNA (Rohde & Schwarz, ZNC3. Vector Network Analyzer 9 kHz – 3 GHz) was calibrated with a frequency range of 880-930 MHz for the collection of the $S_{11}$ reflection coefficients. Sweep time of 43.6 ms and 501 equidistant data points were used to optimize the signal for an optimal sampling rate.

The participant was placed on an inversion table in a supine position and the patch sensor was adhered onto the patient’s chest above the 5th intercostal space lateral to the sternum (~3 cm) (Figure 3.3). The sensor was placed so that its electromagnetic filed is detecting changes in fluid volume in the LV.
Figure 3.3. Human participant placed on an inversion table for data collection. The patch sensor was adhered to the top of participant chest in 5th intercostal space lateral to the sternum (~3 cm).

To establish a steady-state prior to data collection, the participant was placed in a supine position for 5 min [36]. After establishing steady-state, the participant was subjected to a 30° HUT for 5 min, inducing a shift in ventricular volume. Two sets of continuous data were collected using a continuous sweep for 10 seconds while the participant was holding his breath. The participant was asked to hold his breath in order to eliminate the changes in the effective permittivity due to air lung volume [37]. So, changes in the effective permittivity due to blood volume changes during the cardiac cycle were detected by the sensor. After collection of measurements for 30° HUT position, the participant was subjected to a 10° HUT for 5 min to induce another change in ventricular volume due to change in the hydrostatic pressure [36]. Continuous data was collected during the 10° HUT for 10 seconds while the participant again held his breath. Using the same procedure above, data was collected during supine, and 10° HDT.
Furthermore, to validate the ability of the sensor to measure heart rate, ECG was simultaneously recorded during sensor data collection. The electrical signals of the heart are a precursor to the fluid volume changes occurring. Therefore, each QRS complex is associated with ventricular contraction and subsequent volume change. Diastolic and systolic pressure were collected using a blood pressure cuff device. Additionally, for validation of the sensor’s volume detection capabilities, ultrasound echocardiogram (Model: Mindray M7, National Ultrasound, Duluth, GA) was utilized to quantify volumetric changes in the heart while the participant was subjected to various HUT and HDT postures. An apical four chamber view was obtained and the end diastolic and end systolic volumes were determined by finding the volume of LV chamber [38].

3.3.5 Signal Processing

Signal processing of data collection was performed to identify the relationship between the sensor signal response and volumetric changes in the heart. The signal was processed in two ways: 1) analyzing the sensor resonant frequency response over time utilizing a frequency tracking algorithm and 2) analyzing the time varying $S_{11}$ reflection coefficient within the resonant frequency over time. In the first case, the frequency response over time was tracked by selecting a $S_{11}$ reflection coefficient amplitude on the resonant peak and indexing the corresponding frequency as it shifted over time. In the second method, fluctuations in the $S_{11}$ amplitude at a selected frequency were plotted over time. Additionally, after the collection of the sensor frequency response, a zero-phase digital filtering was used to smooth the signal without altering the phase of the signal.
3.4 Result

3.4.1 Volumetric Sensitivity Measurements

A volumetric sensitivity study was conducted to investigate the sensor performance due to different fluid volume increments and to determine the relationship between the fluid volume changes and frequency shifts. Figure 3.4 shows the correlation between increases in fluid volume and first resonance frequency peaks ($R^2 = 0.96$). An analysis of variance (ANOVA) followed by a Bonferroni adjusted multiple comparison test indicated that there was significant difference between the frequency shifts with each volume increment.

![Figure 3.4 Statistical correlation analyses between the fluid volume increments and frequency shifts illustrate a strong relationship ($R^2 = 0.96$).](image)

3.4.2 SV Animal Model Measurements

Data collection of the $S_{11}$ reflection coefficient was obtained and a graph was plotted to illustrate frequency shifts due to fluid volume additions (Figure 3.5 A). The graph shows a frequency shift of 80.16 kHz which corresponds to the total increments of water to the bladder (80 mL). Also, an average shift of 20.04 kHz was detected due to each increment of 20 mL of water. Changes in fluid volume in the left ventricle can be correlated in a linear relationship to the frequency shifts (Figure 3.5 B). The correlation plot illustrated a strong relationship between
the fluid volume changes and the frequency shifts \( (R^2 = 0.98) \). The significance difference between frequency shifts with the fluid volume changes can be seen as the result of changes in the effective permittivity of the layered system. A downward frequency shift was obtained with increased fluid volume content in the LV.

Figure. 3.5 A) Shifts in the resonant frequency were recorded as fluid volume increased in the Bovine heart by increments of 20 mL. B) A statistical correlation analysis of fluid volume shifts in the LV chamber and the principal resonant frequency response illustrate a strong relationship \( (R^2 = 0.98) \).
3.4.3 Participant Blood Volume Measurement

Table 3.1 presents HR, diastolic, systolic blood pressure, and end diastolic, systolic blood volume measurements. HR decreased by 11 BPM from 30° HUT to 10° HDT.

<table>
<thead>
<tr>
<th>Physiological Measurements</th>
<th>30° HUT</th>
<th>10° HUT</th>
<th>Supine</th>
<th>10° HDT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (BPM)</td>
<td>57</td>
<td>63</td>
<td>50</td>
<td>46</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>109</td>
<td>118</td>
<td>117</td>
<td>116</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>73</td>
<td>74</td>
<td>73</td>
<td>67</td>
</tr>
<tr>
<td>End Diastolic Volume (mL)</td>
<td>108.5</td>
<td>122.2</td>
<td>131.6</td>
<td>138.8</td>
</tr>
<tr>
<td>End Systolic Volume (mL)</td>
<td>57.6</td>
<td>65.7</td>
<td>58.8</td>
<td>61.9</td>
</tr>
</tbody>
</table>

An increase in blood volume in the EDV and ESV was observed going from HUT to HDT. EDV and ESV were obtained using the ultrasounds from four apical chamber views (Figure 3.6).

Figure 3.6 A) End systolic volume calculation by finding the volume of the LV chamber during peak systole. B) End diastolic volume calculation by the finding the LV chamber during peak diastole.

Figure 3.7 presents the $S_{11}$ reflection coefficient pulsing over time due to the changes in the effective permittivity of the heart and blood during the cardiac cycle.
Figure 3.7. Pulsing fluctuation of the sensor frequency response during cardiac cycle.

Frequency values for the end diastolic volume during 30° HUT, 10° HUT, supine and 10° HDT in the sensor’s resonant frequency response are presented in Figure 3.8. During 30° HUT the LV chamber had an EDV of 108.5 mL and the sensor resonated at frequency of 900.08 MHz. During 10° HDT, the LV chamber had an EDV of 138.8 mL and the sensor resonated at frequency of 800.985 MHz. So, an increase in EDV in the LV chamber corresponded to a frequency decrease in the sensor resonant frequency response.
Figure 3.8 Shifts in the resonant frequency response due to fluid volume increase in LV chamber during 30° HUT, 10° HUT, supine, and 10° HDT.

Furthermore, changes in the $S_{11}$ reflection coefficient and frequency pulsation over time showed characteristics typical of a waveform of blood volume changes in the LV. The waveform in Figure 3.9 showed an end diastolic volume peak (EDV), end systolic volume (ESV) peak, an extended period of time for the filling of blood into the left ventricle and a faster period of time for the ejection of blood into the body. Continuous HR measurements, acquired from the peak to peak frequency waveform, showed a relative percent error of 0.179% compared with the ECG reference device. Additionally, with an increase in volume in the heart (EDV), a smaller frequency was observed and an increase in frequency until reaching the ESV.
Figure 3.9. A) Volume changes detected as rhythmic shifts in the sensor frequency response over time. B) Simultaneous ECG recording during sensor data collection. C) Volume changes detected as rhythmic shifts in the S11 reflection coefficient over time. The waveform resembles a volumetric waveform including, end diastolic volume (EDV) mark, end systolic volume (ESV) mark and heart rate (HR).

3.5 Discussion

Stroke volume measurement is a powerful tool for the assessment of cardio-pathologies. In this study, we have demonstrated the ability of an electromagnetic skin patch sensor to detect shifts in fluid volume of less than 20 mL in a beaker and fluid volume changes through cardiac muscle in a bovine heart and human participant. Detecting fluid volume shifts through cardiac muscle with a skin patch sensor is a robust first step to non-invasive point of care SV measurement. Also, the patch sensor has demonstrated its capabilities of measuring HR with a 0.179 % relative error compared to the standard method, ECG. Currently, research regarding RF resonators and the heart focus primarily on HR measurements, however, the focus of this study, in regard to quantification of SV, addresses an area that has not been extensively investigated. Additionally, the electromagnetic skin patch sensor addresses the primary limitation of invasiveness in the standard method, pulmonary artery catheterization, and complexity of ultrasounds.
3.5.1 Sensor Detection Principles

This study demonstrates the ability of the RF skin patch sensor to detect fluid volume changes in multiple environments such as in a beaker, left ventricle of a Bovine heart, and in a human participant. Changes in the sensor’s resonant frequency correspond with fluid volume fluctuations in each system. These results can be explained through the analysis of near RF field at which the patch sensor operate. In the near RF field, electric and magnetic fields are decoupled [39]. So, changes in the magnetic field are not subsequently affecting changes in the electric filed and vice versa. Additionally, at a low magnetic field, at which our sensor operates (-10 dbm), human tissues are not magnetizable [23, 40]. Changes in the magnetic field is constant with a total inductance value inherited from the sensor’s geometric design and changes in the electric field is only detected.

Increases in the volume surrounding the area of the sensor’s electromagnetic field induce a change in the effective permittivity and result in subsequent changes in the capacitance value [23]. Increases in the capacitance value results in a decrease in the sensor frequency response. The result of our previous publication and the current study reinforce the stated concept in which increase in volume of the surrounding object induce a decrease in the sensor frequency response [23]. Maximizing the capacitance value in the sensor design resulted in better volume detection values and resonant frequency response.

3.5.2 Measurement to Guide the Assessments of Cardiac Function

Sensors that can be applied in an intuitive nature without extensive training (similar to an adhesive bandage) may be a valuable tool in monitoring patients with critical conditions. Due to the simplicity of the skin patch operation and the usage of non-ionizing radiation, the risks and limitations associated with current methods for measuring SV could be significantly reduced.
Furthermore, it has been established in the clinical field that a parameter such as SV can guide the assessments for acute cardiovascular conditions such as myocardial infarction (MI) and the response to pharmaceutical stimuli [41-43]. This technology may be used as a diagnostic tool to identify abnormal heart function accompanying morbidity by assessing the fluid dynamics of the LV chamber. One potential application is by monitoring the effect of ischemic heart disease on hemodynamic flow in the LV chamber [44, 45]. Utilization of factors affecting SV such as preload, afterload, and contractility can be significant for assisting cardiac dysfunction [46]. Thus, our sensor may possess advantages for providing a simple to use, point-of-care, and cost-effective pre-clinical assessment for patients with heart health related issues.

3.5.3 Limitation and Future Work

Despite the strong correlations, this study possesses several limitations. These limitations include simplification of the biological model, utilization of a Bovine heart, and absence of other biological tissues present in the body layers (skin, adipose, muscle, and bone). However, including a human participant in this study assessed in quantifying the sensor ability in detecting volumetric changes in the human heart. The main limitation in the human study is sensor placement and penetration depth of the sensor’s field.

Sensor placement is an important factor as well. Despite our efforts to ensure that the sensor was placed above the LV, there is a chance that the sensor was detecting ventricular volume changes in both RV and LV. However, results of the paper validate the ability of the sensor to detect fluid volume changes in the human heart and serve as a preliminary validation of the sensor’s working principle. To address this limitation in future studies, an array of multi-resonant sensors may be used to reveal the relative frequency shifts between the different chambers and may help to establish blood volume changes in the different chambers of the heart.
Additionally, the penetration depth of the sensor’s electromagnetic field is an important factor. We have conducted some preliminary studies with varying thickness of muscle tissue and bone and have been able to detect usable signals in depths of up to 26 cm [26, 47]. Due to the operating principles of the sensor, the penetration depth is substrate specific. Thus, the penetration depth will vary slightly between participants based upon the variance in adipose tissue, muscle, and other tissue in the chest.

Furthermore, to ensure the sensor signal response was not from changes in the skin and sternum due to blood pulsations, an examination between the sensor’s signal response on the right side of the chest (~ 3 cm to right side of the midline of sternum) and the left side was performed. The results of this investigation show that the sensor’s signal response on the right side had no pulsations compared to the response seen on the left (heart side).

Further limitations of this study include practical issues such as signal noise due to motion artifacts. To address this issue, further signal processing techniques will be explored to filter out noise due to motion. Other limitations include, the need for a vector network analyzer, which is not suitable for use in a wearable form factor. However, we are currently working on developing new bioinstrumentation which can wirelessly energize and interrogate the RF resonant skin patch, such that it could be worn in a wearable form factor. Future work will validate the sensor performance in measuring ventricular volume and compare it with other clinical standard measurement devices.

### 3.5.4 Conclusion

In summary, this work presents a foundation for the development of a skin patch sensor that may be used as a non-invasive, point of care diagnostic to identify abnormal heart function
by assessing the fluid dynamic of the LV chamber. The patch sensor is suited to measure volumetric changes which is directly related to the changes in the electric permittivity of the surrounding material. Thus, this patch sensor may be able to measure fluid volume changes in the LV chamber as frequency shifts in the sensor resonant frequency response with each cardiac cycle. Due to the simple nature, ease of operation, and point of care utilization, this patch sensor may be utilized in populations that lack hospitals, certified physician, medical field, and it would not be restricted to the clinical setting.
REFERENCES


CHAPTER 4: CARDIAC OUTPUT MEASUREMENTS USING A NON-INVASIVE ELECTROMAGNETIC WEARABLE SKIN PATCH RESONATOR

“This chapter has been submitted to a peer reviewed Journal and is under review”

4.1 Abstract

Cardiac output (CO) parameters are clinically important for the assessment of cardiac performance. The focus of this study was to develop a wearable electromagnetic (EM) skin patch that could be applied like an adhesive bandage to measure ventricular stroke volume (SV). An EM skin patch was designed from a trace of a copper configured into a square planar spiral. The EM skin patch self-resonates when impinged upon by a specific range of radio frequency (RF) waves. Human participants (n = 4) were recruited to measure CO parameters and determine the repeatability of the EM skin patch as compared against impedance cardiography (ICG). Changes in the S\textsubscript{11} coefficient due to changes in the ascending aorta (AO) blood volume were directly correlated to the measurements of SV. Heart rate (HR), SV, and CO were measured with the EM patch with an average relative error of 0.209 \% (R\textsuperscript{2} = 0.99), 3.04 \% (R\textsuperscript{2} = 0.96), 3.19 \% (R\textsuperscript{2} = 0.80) and 3.79 \% (R\textsuperscript{2} = 0.88) for HR-ECG, HR-ICG, SV, and CO, respectively. As such, this work demonstrates an EM skin patch that can be a unique solution for measuring CO parameters at point of care settings.
4.2 Introduction

Wearable technology is an emerging field of research with potentials to make significant impacts in communities that lack affordable health care or medical access [1-4]. Measurement of vital signs using wearable technology, in an emergency setting, has the potential to benefit patients by reducing time between arrival and discharge, health monitoring, and reduction of inpatient bed turnover for the health care facility [5]. The use of non-ionizing electromagnetic (EM) wearable technologies is a valuable emerging field in the health system for diagnostic and treatment purposes.

Wearable technologies utilizing EM radiation have been developed to measure vital signs and blood flow in the human body. For example, a non-contact flexible radiofrequency (RF) resonator was developed to measure heart rate (HR) during sleep [6]. The developed sensor measured HR from the radial artery with 95% accuracy. However, the developed RF resonator was only used to detect pulsations in the superficial radial artery and not deep arterial pulsations such as those found in the ascending aorta or heart ventricles.

Additionally, a digital-IF Doppler radar system was developed to measure the motion of cardiac muscle [7]. In the developed system, a high frequency signal was used (>15 GHz) which can limit the detection depth to superficial organs and not blood volume changes inside the heart [7]. This may present a major limitation for females and overweight patients due to the large amount of adipose tissue that may obstruct and or attenuate the signal. In a different study, a complimentary split-ring resonator was developed to collect cardiac signals from the heart [8]. In the developed system, changes in the resonance frequency of the S21 transmission coefficient due to movement in the chest was measured. The signal obtained was well suited for HR
measurements, however, the signal lacked critical information about the cardiac cycle events to derive cardiac output (CO) parameters such as stroke volume (SV).

EM wearable technologies are accurate and repeatable for the measurements of HR, and movement of cardiac muscle [9-11], however, there has not been an EM wearable developed to measure CO parameters specifically, ventricular SV. The presented work is a study to validate the ability of a wearable EM resonator to measure blood volume changes in the heart. In our previous work, we were able to establish the operating principle of a self-resonating EM skin patch for measuring blood volume changes in an arm phantom, and the heart of a human subject [12-19]. Limitations of our previous work are investigated in this study which include the detection depth, repeatability, and CO parameter measurements using our EM skin patch [12-19].

The objectives of this study were 1) to determine the EM skin patch sensor’s ability to measure SV, HR, and CO as compared against clinical standard impedance cardiography (ICG), and 2) to determine the detection depth of the EM skin patch. The objectives of the study were evaluated by 1) recruiting healthy human participants (n = 4) on 4 different days to determine the performance of the EM patch sensor in measuring SV, HR, and CO, 2) developing tissue phantom models that resemble equivalent dielectric properties of human tissue, and 3) detection depth analysis and signal processing.

4.3 Material and Methods

4.3.1 Human Cardiac Measurements (Multiple Locations and Repeatability)

An Institutional Review Board (IRB) was obtained, and 4 healthy male participants were recruited to determine an optimal location for the EM skin patch placements to detect cardiac
information, measure SV, HR, and CO and investigate the repeatability of the skin patch resonator. The skin patch was placed at four different locations on the chest while participants were lying in a supine position; 1) 0.5 cm inferior to the sternal angle (on top of the ascending aorta, (AO)); 2) 0.5 cm lateral left to the sternum at the 5\textsuperscript{th} intercostal space (on top of the right ventricle (RV)); 3) 3.5 cm lateral left to the sternum at the 5\textsuperscript{th} intercostal space (on top of the left ventricle (LV)); and 4) 1.5 cm lateral left to sternum at the 3\textsuperscript{th} intercostal space (on top of the pulmonary artery (PA)). For repeatability assessments in measuring SV, human participants were recruited for 4 extra days and the EM skin patch was placed on location 1 only, top of the AO.

Furthermore, to validate the skin patch signal response, ECG was simultaneously recorded during data collection. The electrical signals of the heart are a precursor to the fluid volume changes occurring. Therefore, each QRS complex is associated with ventricular contraction and subsequent volume change in the heart. Also, a clinical standard BioZ Impedance Cardiography system was used to collect physiological data that include, HR, SV, and CO. Statistical correlation analysis was performed to analyze the relationship between the predicted and measured CO parameters. Additionally, percent relative error between the actual and measured CO parameters were analyzed to examine error in the predicted values. Participant demographic and physiological information were recorded which include, age, race, smoking, history of previous cardiac diseases, and body mass index (BMI).

Frequency sweeps were obtained using a VNA (Rohde & Schwarz, ZNC3 Vector Network Analyzer 9 kHz – 3 GHz). The VNA was calibrated at a frequency range of 1000-1200 MHz for the collection of the $S_{11}$ reflection coefficients at power level of 10 dBm. During frequency sweeping, participants were asked to hold breath and stay still for the course of data collection (10 seconds) to eliminate noise due to lung air volume.
4.3.2 Phantom Models

Phantom models were designed to mimic the behavior of the actual human torso. Skin, muscle, fats, bones, lung, heart muscle, and effective tissue layers were made with relative permittivity values that resembled actual human tissues [20, 21]. Table 4.1 lists the materials type and their amounts which were used to model chest tissue layer phantom. The working frequency for phantoms were 500-2500 MHz [22].

Table 4.1. Chemical agents used for the developments of human tissue phantoms. Amount of chemical agent makes a volume of \( \approx 1000 \text{ mL} \) for each tissue layer.

<table>
<thead>
<tr>
<th>Material/Tissue type</th>
<th>Skin</th>
<th>Muscle</th>
<th>Fat</th>
<th>Bone</th>
<th>Lung</th>
<th>Heart-Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(_2)O (DI) (mL)</td>
<td>964.3</td>
<td>964.3</td>
<td>964.3</td>
<td>964.3</td>
<td>964.3</td>
<td>964.3</td>
</tr>
<tr>
<td>Polyethylene (g)</td>
<td>72.3</td>
<td>48.1</td>
<td>257.1</td>
<td>240.9</td>
<td>192.9</td>
<td>42.8</td>
</tr>
<tr>
<td>Sodium Azide (g)</td>
<td>0.57</td>
<td>0.57</td>
<td>0.57</td>
<td>0.57</td>
<td>0.57</td>
<td>0.57</td>
</tr>
<tr>
<td>Agar (g)</td>
<td>29.9</td>
<td>29.9</td>
<td>29.9</td>
<td>29.9</td>
<td>29.9</td>
<td>29.9</td>
</tr>
<tr>
<td>TX-151 (g)</td>
<td>27.5</td>
<td>31.6</td>
<td>9.5</td>
<td>10.1</td>
<td>13.0</td>
<td>32.6</td>
</tr>
<tr>
<td>Sodium Chloride (g)</td>
<td>2.9</td>
<td>5.8</td>
<td>1.4</td>
<td>1.0</td>
<td>1.9</td>
<td>8.6</td>
</tr>
</tbody>
</table>

The phantoms were made by heating ager with the required water content to 80°C. After heating agar, TX-151 was added to the mixture and stirred with caution to eliminate any formation of water bubbles in the mixture. Polyethylene (PE) powder was added to the mixture and mixed well to create a homogenous mixture. Lastly, sodium chloride was added into the mixture to adjust the conductivity values. It has been noticed and reported previously that changes in the amount of polyethylene powder and water are the key components in adjusting the permittivity values of the phantoms [22]. Increasing the water level, increases the permittivity values, whereas, increasing the PE powder, decrease the permittivity values. Also, adjusting the amount of TX-151 is used to increase the viscosity of the medium and help mix
polyethylene powder with agar. Lastly, sodium azide was used as a preservative agent for the longevity of the phantoms.

Different phantom blocks were used to determine the detection depth of EM skin patch: heterogeneous blocks (different body tissue layers), and a homogenous block (an effective layer of the different tissue in the chest). The different body tissue phantoms were made with relative permittivity values that correspond to an actual human tissue layer [21]. For the homogenous block, the phantoms were made with a permittivity value specified IEEE standards for partial body parts ($\varepsilon_r=41.5$) [23].

An experimental set-up was adapted to determine the detection depth of the EM patch. The adapted experimental set-up had different tissue phantoms (skin, fat, muscle, etc.) blocks placed in front of a 500 mL beaker and volume was increased in the beaker from 0 mL to 500 mL. The tissue phantom blocks were placed in front of the beaker at seven different stages and the $S_{11}$ reflection coefficient data was collected; skin-to-lung (6.0 cm), skin-to-heart (7.5 cm), and then increased by 1 cm using the effective layers until the $S_{11}$ reflection coefficient signal was lost. Data was obtained using the VNA (Rohde & Schwarz, ZNC3 Vector Network Analyzer 9 kHz – 3 GHz) and was calibrated with a frequency range of 950-1300 MHz for the collection of the $S_{11}$ reflection coefficients at a power level of 10 dBm.

4.4 Results

4.4.1 Cardiac Output Measurements

Wichita State University Institutional Review Board (IRB) approval was obtained prior to starting this study and human participants gave informed consent. Participants ($n=4$) were recruited from different demographics having no previous history of cardiovascular diseases.
Multiple Location Cardiac Measurements

The EM skin patch sensor was placed at four different locations on the chest guided by ultrasound echo, namely, above ascending aorta (AO), right ventricle (RV), left ventricle (LV), and pulmonary artery (PA) for all participants (Figure 4.1). Table 4.2 presents demographic information, including, age, race, smoking, history of previous cardiac diseases, and body mass index (BMI) of the recruited participant.

Figure 4.1. A wearable EM patch sensor was used to measure cardiac waveform from human participants. The patch sensor is designed with a 0.130 mm gap width, and 2.13 mm trace width. The EM patch sensor was placed at each location on the chest: ascending aorta (AO), right ventricle (RV), left ventricle (LV), and pulmonary artery (PA) for all participants.
Table 4.2. Participant demographic and physiological information including, age, race, smoking, previous cardiac diseases, and body mass index (BMI).

<table>
<thead>
<tr>
<th>Demographic and physiological info</th>
<th>Age</th>
<th>Race</th>
<th>Smoking</th>
<th>Previous cardiac diseases</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participant 1</td>
<td>21</td>
<td>Asian</td>
<td>No</td>
<td>No</td>
<td>21.6</td>
</tr>
<tr>
<td>Participant 2</td>
<td>21</td>
<td>Caucasian</td>
<td>No</td>
<td>No</td>
<td>19</td>
</tr>
<tr>
<td>Participant 3</td>
<td>24</td>
<td>Hispanic</td>
<td>No</td>
<td>No</td>
<td>21.5</td>
</tr>
<tr>
<td>Participant 4</td>
<td>20</td>
<td>African American</td>
<td>No</td>
<td>No</td>
<td>23.7</td>
</tr>
</tbody>
</table>

The EM skin patch was placed on the specified locations and synchronized with electrocardiogram (ECG) for 10 seconds. Placement of the EM skin patch at different chest locations produced unique localized cardiac information which may contain clinically relevant information regarding the hemodynamics at different chamber of the heart (Figure 4.2). For example, when the EM skin patch was placed on top of the sternum, at the level of the third intercostal space, waveform contained information of the blood volume changes in the ascending aorta. Whereas, when the EM skin patch was placed on top of the LV, waveform contained information regarding blood volume changes in the LV. Additionally, the individual waveforms may contain unique diagnostic information which is specific to the location it was collected from and may be used to diagnose specific heart disease.
Figure 4.2. EM skin patch cardiac waveforms obtained from four different locations on the chest. The waveforms contain information associated with rhythmic volume shifts in the heart which were measured as changes in the skin patch impedance response over time. ECG recordings were collected simultaneously as a reference to the cardiac cycle events.

SV Measurements and Repeatability

To determine the ability of the EM skin patch in measuring cardiac output (CO) parameters, a repeatability study was performed. Participants were recruited on four different days and measurements using the EM skin patch, ECG, and Impedance Cardiography (ICG) were synchronized. Measurement using the EM skin patch was taken from one location only, on top of the ascending aorta (AO) (Figure 4.3, 4.4, 4.5, and 4.6).
Figure 4.3. Cardiac waveform collected from the AO for human participant (1) on four different days. The waveforms illustrate the fluid volume changes in the AO.

Figure 4.4. Cardiac waveform collected from the AO for human participant (2) on four different days. The waveforms illustrate the fluid volume changes in the AO.
Figure 4.5. Cardiac waveform collected from the AO for human participant (3) on four different days. The waveforms illustrate the fluid volume changes in the AO.

Figure 4.6. Cardiac waveform collected from the AO for human participant (4) on four different days. The waveforms illustrate the fluid volume changes in the AO.
Cardiac waveforms collected from the AO were used to calculate HR (beat per minute (bpm), SV (mL), and CO (L/Min). HR, SV, and CO measured values using the skin patch were compared against values obtained from ICG for HR, SV, and CO and ECG for HR. **Figure 4.7 a and b** illustrate strong correlation for HR measurements using the EM skin patch (predicted) with an $R^2$ of 0.99 and 0.96 as compared against ECG (actual) and ICG (actual), respectively for each participant for each day. **Figure 4.7 c and d** presents strong correlation for SV and CO measurements using the skin patch (predicted) with an $R^2$ of 0.80 and 0.88 as compared against ICG (actual) for SV and CO, respectively for each participant for each day.

**Figure 4.7.** HR, SV, and CO measurements using the EM skin patch, for each participant on each day, compared against ICG and ECG to determine the statistical correlation between the actual and predicted values. Statistical correlation shows a high correlation in measuring HR, SV, and CO as compared to the ICG and ECG for each participant for each day.

To further examine the ability of the skin patch in predicting SV, percent relative error was calculated for each trial and for each participant. The skin patch measured SV with a maximum error of 12.2% and minimum error of 0.52%. Average relative error was 0.209%, 3.04%, 3.19% and 3.79% for HR-ECG, HR-ICG, SV, and CO, respectively. Furthermore, the Bland-Altman plot presents the bias of the skin patch in measuring HR, SV, and CO (Figure
4.8). The mean difference (bias) between the skin patch and BioZ was -1.87 (mL) and 0.0212 (L/min) for SV and CO measurements, respectively. Additionally, measurement’s differences were within the 95 % confidence band except for one outlier. As such, the EM skin patch has acceptable repeatability and accuracy in measuring HR, SV, and CO.

Figure 4.8. The Bland-Altman plots the measurements difference between the skin patch and ICG vs the mean of the two measurements, left SV (mL) and right CO (L/Min).

4.4.2 Tissue Phantoms

Further characterization of our EM skin patch detection depth was performed with tissue phantom layers. The tissue phantom layers were made with relative permittivity values as shown in Figure 4.9. The relative permittivity values of tissue phantoms were measured using a dielectric probe (DAK-12 probe, P/N: SM DAK 020 BA). Tissue phantom’s relative permittivity were compared against actual human tissue relative permittivity values at 1.1 GHz, and had a percent relative error as follows; skin (17.9 %), fat (18.0 %), muscle (12.0 %), bone (9.0 %), lung (7.9 %), and heart muscle (9.0 %) [21].
4.4.3 Detection Depth

The detection depth of our EM skin patch was characterized by utilizing tissue phantom blocks. Tissue phantom blocks with various thicknesses were placed in front of a 500 mL simulated heart chamber and the $S_{11}$ reflection coefficient data was collected; skin-to-lung (6.0 cm), skin-to-heart (7.5 cm), and then incrementally increased by 1 cm using an effective layer ($\varepsilon_r = 42.5$) until the EM skin patch signal response was not detected (Figure 4.10).

Figure 4.10. Experimental setup used to determine the detection depth of the skin patch. The phantoms were placed in an incremental set-up and the fluid volume was added continuously (0-500 mL).
The EM skin patch was able to detect a volume change in the simulated heart chamber up to a phantom thickness of 10.5 cm. **Figure 4.11 a, b, c, and d** present the skin patch response corresponding to increase in the volume from 0 mL – 500 mL in the simulated heart chamber for each skin-to-heart phantom thickness at 8.5 cm, 9.5 cm, 10.5 cm, and 11.5 cm, respectively.

![Image of graphs showing impedance vs. volume for different phantom thicknesses](image)

Figure 4.11. Impedance was measured as volume increased inside the simulated heart chamber (glass beaker) with various phantom depths. Phantoms were placed in front of the 500 mL simulated chamber and water ($\varepsilon_r = 80$) increased from 0 to 500 mL. A) An $R^2 = 0.95$ at 8.5 cm, B) $R^2 = 0.96$ at 9.5 cm, C) $R^2 = 0.90$ at 10.5 cm, and D) an $R^2 = 0.45$ at 11.5 cm were obtained.

### 4.5 Discussion

In this study, characterization of the detection depth of an EM skin patch, repeatability, and its ability to measure HR, SV, and CO were performed. The EM resonant skin patch used in this study has unique advantages over traditional wearable sensors. The EM skin patch was able to detect fluid volume shifts related in the heart – which are not detectable by traditional wearables and can only be detected with large specialized equipment’s found in the hospital. The proposed sensing technology can be applied in an unobtrusive nature without extensive training (similar to an adhesive bandage) and may be a valuable tool in monitoring patients with critical...
conditions. Blood volume shifts in the heart induce shifts in the EM field of the system which can be detected using the proposed technology [12-17].

This sensing system can operate as a point-of-care technology, making it applicable in limited resource environments including a microgravity, rural communities and military zones lacking access to specialized equipment found in hospitals. This sensor’s unique design results in a lightweight, wearable technology. The use of RF waves instead of mechanical waves (ultrasound) or infrared (photoplethysmography) results in increased penetration depth. Additionally, the non-invasive detection capabilities of this method does not require invasive measures, consequently eliminating the risk of infection that can be observed in invasive measurements of cardiac function.

Cardiac waveforms collected using the EM skin patch were as a result of changes in the reflection coefficient ($S_{11}$) which was modulated by the interaction between the EM field of the skin patch and the change in blood volume in the AO and different chambers of the heart. As such, changes in the resistive impedance due to blood volume changes in the AO and different chambers of the heart directly influence the current strength which can be described by equation (4.1) [24].

$$Z = \rho \frac{L}{A} \quad (4.1)$$

Where, $Z$ is the impedance ($\Omega$), $\rho$ is the resistivity($\Omega \ast cm$), and $L$ and $A$ are the length (cm) and cross-sectional area (cm$^2$), respectively. Current conventional methods measure the impedance of the thoracic region using a combination of gel electrodes [25, 26], whereas, the EM skin patch is able to measure the localized impedance in the AO and different chambers of the heart. As such, using the skin patch, changes in the localized AO impedance is directly harvested to calculate HR, SV, and CO. The AO impedance waveforms are unique and were
used to determine volume skin patch ($V_{\text{skin\ patch}}$). To determine $V_{\text{skin\ patch}}$, the AO was assumed to be a cylinder having a constant length and varying cross-section-area, which varies with pulsatile blood volume that is inversely proportional to the impedance. Upon multiplying the numerator and denominator of equation (4.1) by L, equation (4.2) is obtained [25, 26].

$$Z = \rho \frac{L}{A} \frac{L}{L} = \rho \frac{L^2}{V} \quad (4.2)$$

Where, $A \times L =$ volume (V) and then simplified to equation (4.3) to calculate for volume in mL [25, 26].

$$V = \rho \frac{L^2}{Z} \quad (4.3)$$

Using the EM skin patch, volume change in the AO ($V_{\text{skin\ patch}}$) was calculated using equation (4.4).

$$V_{\text{skin\ patch}} = \rho \frac{L^2}{\int_{t_0}^{t} Z(t)dt} * \text{LVET} \quad (4.4)$$

Where $\rho$ ($\Omega \ast \text{cm}$) is the resistivity of blood at the resonating frequency (at $\approx 50 \, \Omega$), and L (cm) is $L_{\text{field}} \times \text{power coefficient (PCO)}$. $L_{\text{field}}$ is the maximum length of the developed EM field around the skin patch which was $\approx 5.7$ cm. The length of the field depends on the power transferred to the skin patch which can be scaled by the PCO. PCO is a function of the ($S_{11}$) reflection coefficient and calculated as shown in equation (4.5). The skin patch resonates between -10 to -50 dB when placed on top of the AO which can be translated to a PCO of 0.8 - 1. A PCO of 1 indicate an ideal scenario (impedance match and full power transfer to the skin patch) whereas 0 as full mismatch between the source (skin patch) and human participant.

$$\text{PCO} = \text{abs} \left( \frac{1 + S_{11}}{1 - S_{11}} \right) \quad (4.5)$$
Also, \( \int_t^{t_0} z(t) \, dt \) (\( \Omega \)) is the total impedance due to volume change in the AO. Figure 4.12 illustrates a single cardiac cycle of the AO waveform which was used to estimate the total impedance. The impedance was estimated using the trapezoidal rule and was averaged over 10 seconds of data collection. Lastly, left ventricular ejection time (LVET) is the ejection period of blood from the heart into the body, and it’s estimated as the time interval during systole.

![AO impedance changes due to blood volume changes in the AO. The waveform resembles the cardiac cycle volumetric events. The total area under the curve corresponds to the ejection period of the cardiac cycle.](image)

Additionally, SV in the heart was predicted by formulating a partial least square regression (PLS) model with leave-one-out cross validation. The PLS model account for the variant combination of different tissue layers in the human torso which appears unique for each participant. The PLS model consisted of variable collected form each participant’s that include \( V_{skin\,Patch} \), age, and percent body fat as expressed in equation 4.6.

\[
SV_{predicted} = -12.0510 \times Age + 7.0443 \times %Fat + 8.2284 \times V_{skin\,Patch} + 105.8125, \tag{4.6}
\]

The variables, Age, %Fat, and \( V_{skin\,Patch} \) were normalized using the means and standard deviations.
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CHAPTER 5: CONCLUSION AND FUTURE WORK

In our previous and current work, we have been able to establish the EM skin patch operating principles, detection depth, and its ability to measure cardiac output parameters as compared against the clinical standard impedance cardiography [1-8]. Despite that, our work still contains limitations which include noise due to breathing artifacts and the sample size (n = 4). Noise due to breathing, air ($\varepsilon_r=1$), presents as an artifact to the propagation of EM waves. EM waves are reflected, transmitted, and absorbed at the boundary between different tissue layers [9, 10]. EM waves reflection are dependent upon the ratio of the dielectric constant in-between two preceding tissue layers [9, 11]. As such, the larger the difference of the dielectric constant between two preceding tissue layers, the higher the reflection of EM waves. Since the air dielectric constant is significantly different than other human tissue layers, higher reflection of EM waves occur. As such, participants were asked to exhale and hold breath during data collection. This process maximized transmission of EM waves into the AO and produced accurate waveforms to derive cardiac output parameters.

Another limitation of the current work is the sample size (n = 4). The population used in the study consisted of healthy male participants, which is not representative of the general population. Future studies will consider a larger population with varying age, BMI, race and gender. Also, the EM skin patch will be validated against ultrasound as a third validation device to measure CO parameters. Machine learning algorithms will be integrated into future studies to utilize quantitative data obtained by the skin patch to provide easy-to-interpret feedback and help guide medical decisions and administration of countermeasures.
The primary focus of this thesis was to design these “smart” processes to leverage evidence-based indicators of health such as SV, HR, and CO parameters. As cardiovascular deconditioning occurs, changes in SV, HR, and CO can be used to provide useful information regarding myocardial infarction, atrial fibrillation, and vascular stiffening [12, 13]. Additionally, the cardiac volume waveforms measured from each cardiac chamber provide another dataset for analysis. Certain situations exist in which obtaining values for SV, HR, and CO are insufficient for diagnosis [14-19]. Therefore, quantitative analysis of key markers in the obtained waveform can be used to detect flow abnormalities that are indicative of varies cardiac pathologies.
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