CACOM: Carotid Artery Cardiac Output Monitor Report

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Background and Introduction

An estimated 125 million American adults have been diagnosed with a form of cardiovascular disease (CD) since 2015, including thrombosis, peripheral arterial disease, and coronary heart disease [1]. Altogether, the risk factors involved with the evolution of these forms of CD into lethal conditions, more specifically acute myocardial infarction and sudden cardiac arrest, require methods of continuous maintenance to mediate such severe cases. The issue is especially prevailing for patient's afflicted with recurrent cardiovascular events or recovering from cardiac surgeries, with the mortality rate nearly doubling for patient's suffering from recurrent myocardial infarctions after the initial heart attack within a five-year recovery period [2]. Despite the existence of reliable diagnostic technology in emergency-care centers and hospitals, few options offer realistic accessibility of at-home monitoring devices for patients [3]. Portable ECG monitors provide maintenance for arrhythmia, however, regarding issues involving hemodynamics, no equivalent is available for targeting hypertension and hemodynamic instability [3].

Due to the necessity for low-cost and noninvasive cardiac output measurement devices, doppler ultrasound and arterial applanation tonometry have been an emerging research topic within the last decade. Utilizing similar technology to ultrasound equipment, doppler ultrasound technology measures the frequency shift of acoustic signals transmitted by transducers across a flowing liquid in order to estimate the liquid's velocity and flow rate. Doppler shift flowmeters have been an established industrial technology for the last 70 years of hydraulics systems; however, the device only recently was implemented for medical applications for cardiac output monitoring [4]. The concept of ultrasound technology for portable cardiac output devices has been researched and validated for the last decade as a viable future option for non-invasive monitoring but lacking the proper technology other than for clinical settings (i.e., UCOMs) [5]. With recent developments in wearable and flexible ultrasonic transducers from MIT and UC San Diego, the translation of doppler shift flowmeters into cardiac output and volumetric blood flow monitors is a more realistic opportunity [6,7]. The patch design of the new wave of ultrasonic transducers offers greater control and accuracy with measuring volumetric flow within the blood vessels, especially around active regions such as the head and neck.

Additionally, arterial applanation tonometry has been studied as a semi-occlusive method of estimating arterial blood pressure. The arterial application of the optical tonometer has offered a comparatively more precise non-invasive measurement system compared to other current options, despite contention with calibration from some [8,9]. More specifically, recent studies have proven the promises of radial artery applanation for estimating mean change in blood pressure [10]. Furthermore, metrics for estimating arterial characteristics within patients have recently developed to provide more personalized treatment systems for individuals based on lifestyle, BMI, age, etc. [11]. As such, there is strong potential for the application of applanation technology for point-of-care monitoring devices.

The feasibility of wearable cardiac monitoring devices through doppler ultrasound and blood pressure monitoring methods such as applanation tonometry has strengthened. In clinical trials, researchers have proven a strong potential for the utilization of ultrasound for estimating pulse volume waveforms from the carotid arteries within the neck, especially with point-of-care devices [5]. Additionally, other studies involving arterial applanation tonometry offer significant promise for reliable at-home blood pressure and pulse wave estimation devices [11,12]. Together, the doppler ultrasonic and arterial applanation tonometry technologies provide new methods for developing personalized monitoring of cardiac output for patients diagnosed with chronic cardiovascular disease, recovering from cardiac surgery or an acute cardiovascular event, etc.

This study focuses on developing and testing a feasible prototype design for an at-home, wearable Carotid Artery Cardiac Output Monitor (CACOM) utilizing the doppler ultrasound and applanation tonometry technology mentioned above. Designed to rest on the patient's neck, the device is intended to continuously record data recording a patient's cardiac output that is accessible through Bluetooth for doctors and medical staff to interpret. The following describes the monitoring goals, modelled designs and electrical components in the final prototype design, in addition to data confirming the feasibility of the designed interface.

Methods

Ultrasound is a critical method of non-invasive imaging and monitoring, however, is limited to clinical devices in modern medicine. With significant medium-density changes experienced at the boundary of air and soft tissue, ultrasound requires professional monitoring under precise conditions in order to remain effective[13]. The feasibility of a wearable cardiac output monitor is primarily due to recent developments in ultrasonic patches in the Zhao Lab at MIT and the Xu Lab at UC San Diego. The creation of an adhesive patch for topical application significantly reduces the risk of ultrasonic refraction experienced by conventional, non-adhesive devices without the proper coupling medium. As such, the ultrasound patch design is a realistic component for the creation of a continuous, wearable ultrasonic device.

With the ultrasound patch, the cardiac output prototype estimates arterial blood velocity through Doppler shift ultrasound. In the device, the ultrasound patch sensor operates as a set of transducers that emit a frequency-constant ultrasonic pulse wave and receive the signal reflecting from the particles flowing in the blood vessels (i.e., red blood cells). The following is achieved with a coded microprocessor that receives the reflected waves, analyzes the frequency shift, and computes the blood velocity through the following Doppler shift formula: $Blood\ Velocity = \frac{c*(f_t - f_r)}{2*f_t*cos\theta}$. The speed of sound in ultrasound in tissue (1540 m/s [4]), transmitted signal frequency, insonation angle, and signal amplitude are all preset values monitored through the microprocessor. Different transmitted frequencies are set per experiment based on the specific transducer type. In prototype testing, singular ultrasound transducers are set at 40 kHz for measuring purposes, however, ultrasound patch recommendations for deep tissue signaling are about 2 MHz[6].

Arterial Applanation is another recent development in monitoring cardiac output, specifically targeting stiffness and blood pressure. A semi-occlusion method of blood pressure estimation is preferable in the given circumstance considering the continuous application of the device and location of the sensor, and as such arterial applanation is the preferable method[14]. In this circumstance, by adapting Imbert-Fick's Law ($Pressure = \frac{Applanation\ Force}{Applanated\ Area}$), arterial pressure is estimated by flattening a set area of an artery with a "force-resistive sensor"[8,10]. For these probes, force is calculated by measuring the resistive change and converting with the sensor's specific resistance-force regression. For the following prototype, testing is conducted with an Ezweiji Film Pressure Sensor with the following resistance-force graphs:

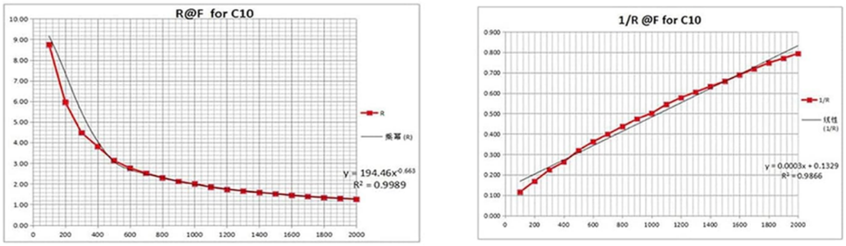


Figure 1: The above diagrams were provided by the Ezweiji Film Pressure Sensor manufacturer, describing the relationship between measured resistance and force.

However, considering conventional "force-resistive sensors" are dependent on the force applied over the sensor area, the above graphs require the complete engagement of the sensor to apply. As such, for the prototype, a spring-loaded pressure sensor design is designed to increase the applanation area and standardize the area the force is measured over on the sensor. In experimentation, the Ezweiji Film Pressure Sensor is fitted with a spring-loaded testing apparatus to maintain load uniformity on the sensor. After mapping resistive change to applied pressure, the applied force is measured through the equation

$F = P * 50.27$ mm^2. Blood pressure is then derived by dividing the applied force by the experimental applanation area. Future iterations of the design have the potential for measuring other indicators of cardiovascular condition such as arterial stiffness.

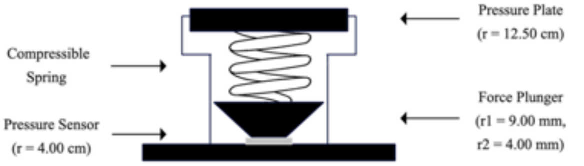


Figure 2*: A diagram of the pressure sensor apparatus design for the monitor with dimensions from the testing apparatus*

Data collection, analysis, and storage for both the ultrasound patch and force-resistive sensor are controlled by a coded microprocessor. More specifically, an Arduino Nano is implemented as the major microprocessor of the cardiac output prototype, operating as the central processing unit. For the ultrasonic patch, the Arduino Nano controls the signal pulse rate, instantaneous Fast Fourier Transformation (FFT) of the received signal, blood volumetric flow rate calculations, and data storage. The Arduino sends a pulsed sine wave every 0.5 seconds to the ultrasound patch to limit the set of blood velocity values and reduce the data storage necessity. A coded sine wave generator on the Arduino creates a signal with controllable amplitude and frequency that is emitted through the ultrasonic patch. After amplification and filtering, the Arduino additionally executes a program from the "ArduinoFFT" library, computing an FFT with the received signal and calculating the instantaneous blood velocity. For the force sensor, the Arduino is responsible for measuring the resistive change due to the sensor, computing the resistance-force regression, and calculating instantaneous blood pressure.

Supplementary equipment is included, including the HC-05 Bluetooth, TP4056 Micro-USB Charging, and SD Card Storage Modules, to improve the usability of the point-of-care device in real-world applications. The HC-05 Bluetooth and SD Card Storage Module both interface with the Arduino Nano, more specifically to store the blood flow rate and pressure values within a ".txt" file and communicate the data to external computers through Bluetooth. Currently, data text files are sent to the Arduino IDE; however, to improve interactivity for patients and medical professionals, an app should be designed in the future to receive and visually represent data. Finally, the Micro-USB charging port, with the appropriate lithium-ion batteries, provides rechargeable capabilities for the device to increase longevity and usability for the user.

Prototype components are tested in two parts: isolated and integrated trials. Efficacy is primarily analyzed in the isolated trials to confirm both the precision and accuracy of the sensors in ideal experimentation. However, considering each of the sensors are designed on an individual basis, the integrated trials are additionally conducted to ensure no interference with the functionality of each part in patient trials. For the isolated trials, pipe flow is simulated with a roller pump feed with distilled water, creating the idea circumstances for measuring blood velocity and blood vessel pressure, etc., and are compared against theoretical prediction. For blood velocity, results are compared against the model for blood velocity demonstrated with the Principles of Doppler Shift ($Blood\ Velocity = \frac{c*(f_t - f_r)}{2*f_t*cos\theta}$). For the blood vessel pressure, an analysis of the apparatus utilizing Bernoulli's Principles was conducted to derive the ideal fluid velocity at the measure location of the pipe, which is multiplied by applanated area for predicted blood pressure:

$$Force = \left(\frac{1}{2}\left(0.001\ \frac{kg}{cm^3}\right)\left(Flow\ Rate\ \frac{L}{\min}\right)\left(0.012\ \frac{kg}{s}\right)^2\left(\frac{1}{\left(\frac{(0.476250\ cm)}{2}\right)^2} - \frac{1}{\left(\frac{(0.793750\ cm)}{2}\right)^2}\right) + \left(\left(980.665\ \frac{cm}{s^2}\right)\left(.001\ \frac{kg}{cm^2}\right)(Height\ cm) + 10.1325\ \frac{N}{cm^2}\right)\right)\left(Area\ Applanated\ cm^2\right)$$

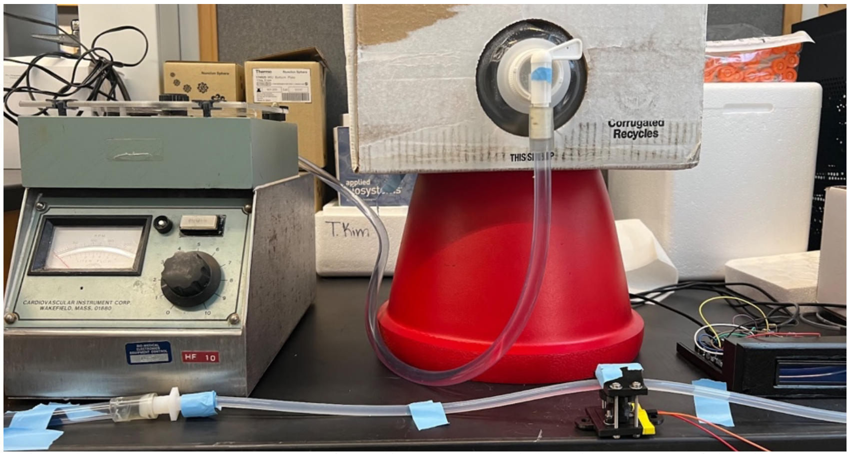
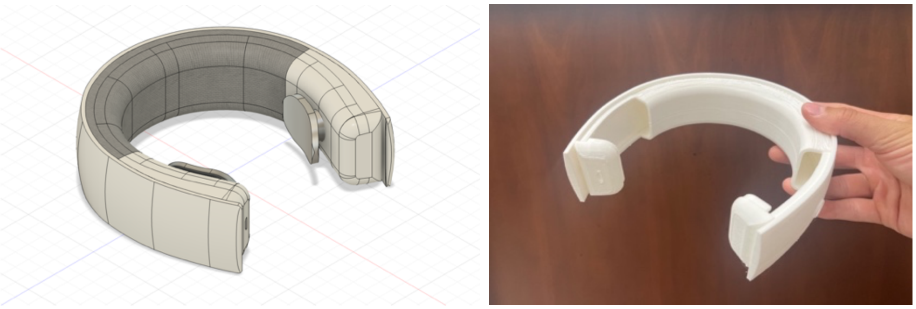


Figure 3*: The isolated trial apparatus is comprised of a roller pump (right) and reservoir of distilled water (center), and vinyl pipe (bottom). The figure specifically illustrates the isolated trial for the pressure sensor, which demonstrates the utilization of additional resources (such as a clamp) to test efficacy.*

The microprocessor, electronics for the sensors, data storage, and charging boards are housed in a prototype device frame. The model shape is inspired by the geometry of a neck massager, creating a structure well-fitting to the average neck dimensions. The rigidity of the PLA plastic secures the internal hardware while additionally providing support for the sensors against excessive movements. Joints are added to improve the efficacy of support parts with permeant adhesives. Beyond the 3D printed components, the design describes the implementation of LSR Silicone and PVC Vinyl Foam on the device. These components primarily act as additional padding for the sensors and neck rest respectively and create a more comfortable patient experience. In trial, components are housed externally for easy of adjustments, however, the finalized product possesses the necessary space for electronics.



Figures 4 and 5: A full 3D rendering was generated to visualize the concept and construct the exterior shell, neck supports, and base caps of the prototype (printed to scale with PLA).

Finally, an analysis on predicted return-on-sale and the prototypes observable strengths regarding current market trends to briefly evaluate the product viability after the prototype's completion. More specifically, materials and manufacturing costs are estimated utilizing the current design choices and the observable strength and weaknesses are contextualized with immediate opportunities and threats for the products in target markets. Overall, emphasis is specifically weighed towards confirming the isolated efficacy of each sensor for targeted cardiac output data, confirming the ability to cooperatively integrate the sensors into a realistic design, and evaluating market viability of the design given the overall productiveness of the device.

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