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TOWARDS A UNIVERSAL DEVICE FOR POINT-OF-CARE MEDICINE: A CUSTOM TRANSDUCER FOR LONG-TERM MONITORING OF LOCAL VASCULAR FLOW VIA ULTRASOUND IMAGING

Haley Abramson
Johns Hopkins University
Baltimore, MD

Eli Curry
Johns Hopkins University
Baltimore, MD

Kaushik Sampath
ARTPARK
Bangalore, India

James Wissman
Syntonics, LLC
Columbia, MD

Griffin Mess
Johns Hopkins University
Baltimore, MD

Rasika Thombre
Johns Hopkins University
Baltimore, MD

Smruti Mahapatra
Blackrock Microsystems
Salt Lake City, UT

Fariba Aghabaglou
Johns Hopkins University
Baltimore, MD

Nicholas Theodore
Johns Hopkins Hospital
Baltimore, MD

Aliaksei Pustavoitau
Johns Hopkins Hospital
Baltimore, MD

Amir Manbachi
Johns Hopkins University
Baltimore, MD

ABSTRACT

Universalized point-of-care medicine demands long-term, automated, and ubiquitous solutions to monitoring patients. Ultrasound imaging can be found in nearly all fields of healthcare. Therefore, developing a platform for continuous ultrasound acquisition could transform the point-of-care arena. However, long-term monitoring using ultrasound imaging requires both the simplification of large quantities of data and a hands-free, flexible device. Here, we reduce data-heavy spectral Doppler imaging by tracking local vascular flow in vitro *and* in vivo *as a single, clinically interpretable value over time. Imaging is performed using a novel probe designed specifically for continuous monitoring with ultrasound. This semi-conformal specialty probe was fabricated by removing the plastic casing of a commercially available probe, bending the tip of the piezoelectric transducer head at a nearly ninety-degree angle, then casting the electronic components in silicone rubber, which allowed the probe to rest comfortably on any surface. No statistically significant difference existed when comparing the Doppler fluid velocity detected by the specialty probe with two commercial probes, where velocity directly leads to calculation of vascular flow. Additionally, continuously tracked velocity over the period of an hour and during periods of fluctuating flow rates demonstrated the potential for accurate, long-term monitoring using this ultrasound device. Thus, translating this technology from bench to bedside could provide a universal solution to point-of-care medicine.*

Keywords: continuous monitoring, ultrasound, probe, spectral Doppler imaging, cardiac output, vascular flow

NOMENCLATURE

3-D	Three Dimensional
PSV	Peak Systolic Velocity
SV	Stroke Volume
CSA	Cross-sectional Area
VTI	Velocity Time Integral
HR	Heart Rate
CO	Cardiac Output
EMI	Electromagnetic Interference

1. INTRODUCTION

Point-of-care medical management demands constant monitoring of a patient's overall health status and could be applied to more patients through the development of an automated device for universal care. Ultrasound has been used ubiquitously as a medical imaging tool and therefore could enable noninvasive, long-term patient surveillance and immediate clinician response via the design and development of a hands-free, continuously operable ultrasound transducer. Local vascular "output," the amount of blood pumped through a given vessel every minute, is an example of a hemodynamic parameter

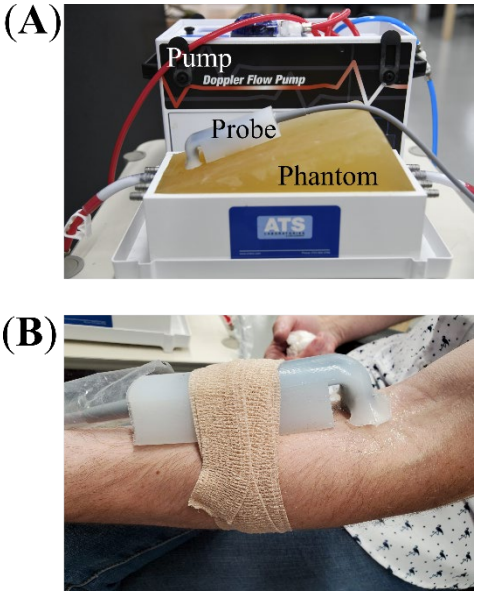

FIGURE 1: EXPERIMENTAL SETUP. (**A**) CUSTOM FLEXIBLE PROBE RESTING ON THE TISSUE PHANTOM ATTACHED TO THE CARDIAC DOPPLER PUMP (LABELED). (**B**) CUSTOM FLEXIBLE PROBE RESTING ON A VOLUNTEER'S ARM AND REINFORCED WITH SELF-ADHERENT ELASTIC WRAP.

that can be measured using ultrasound imaging and inform clinicians about a patient's cardiac output (CO) and, importantly, variability in blood flow. There is an unmet need for a clinically available ultrasound probe capable of noninvasively capturing vital signs such as long-term vascular flow without the need for constant manual guidance.

Here we present a custom, hands-free, flexible probe that can be constructed rapidly from a commercially available probe. The probe has a similar production cost to other ultrasound transducers and operates seamlessly with the Verasonics Vantage research ultrasound system. It should be noted this fabrication process is not dependent on this specific choice of probe and system. While other research groups have shown the potential for developing a wireless ultrasound patch [1-3], these are a long way from production and clinical implementation. By using the electronic components of a probe constructed by TransducerWorks (TransducerWorks, Pennsylvania, USA), the custom probe described here demonstrates 2-D visualization via B-mode ultrasound and flow detection via pulsed wave (spectral) Doppler imaging that have already been approved for commercial use. A novel silicone rubber mold was designed to provide a semi-conformal outer casing to lay on any surface and operate without further handling after placement. Experiments *in vitro* and *in vivo* demonstrate the probe's ability to operate long-term, detect sudden changes in local vascular "output," and capture human-level blood velocities. This study serves as a first step towards a wireless ultrasound patch capable of monitoring patients on the timespan of hours to days, automatically alerting clinicians of sudden changes in patient health status, and thus transforming point-of-care medicine.

2. MATERIALS AND METHODS

The probe was designed to enable hands-free operation (Fig. 1) and has been analyzed *in vitro* and *in vivo* for accuracy and patient safety. A cardiac Doppler phantom (Model: 523A, CIRS) and Doppler flow pump (Model: 769, CIRS) enabled *in vitro* investigation and provided set tube diameters for Doppler fluid (Model: 769DF, CIRS) flow, which mimics blood flow. The brachial artery of a human volunteer served as our *in vivo* model.

2.1 Probe Design

Piezoelectric components and all electronics for the custom probe were extracted from a commercially available ultrasound transducer (TransducerWorks, Pennsylvania, USA). After removing the hard-plastic external cover of the probe, the stiff copper foil surrounding the electronics was also removed and

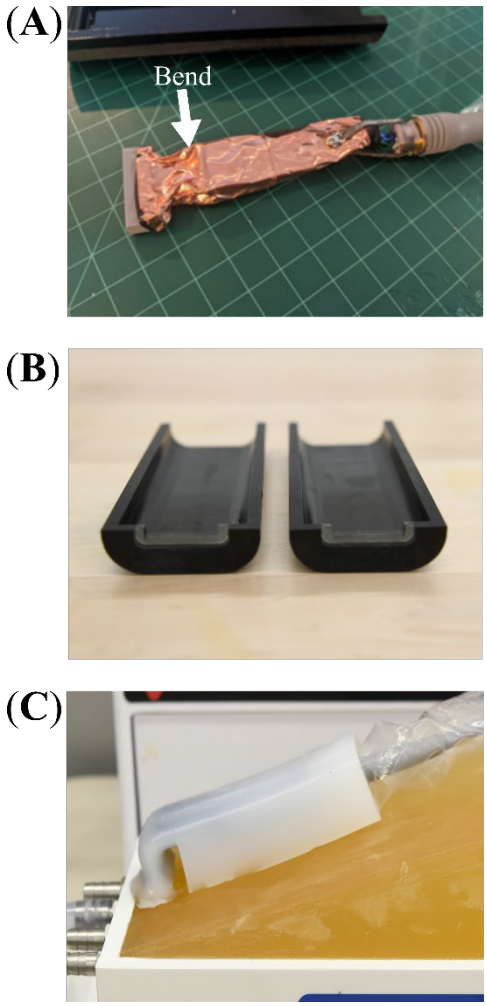

FIGURE 2: PROBE DESIGN PROCESS. (**A**) THE STIFF COPPER CASING SURROUNDING THE ELECTRONICS OF THE COMMERCIAL PROBE (SHOWN HERE) WAS REMOVED AND REPLACED WITH ELECTRICALLY CONDUCTIVE ACRYLIC PADS. (**B**) 3-D PRINTED MOLD WITH CAST OF PLATINUM CURE SILICONE RUBBER. (**C**) CUSTOM PROBE RESTING ON A CARDIAC DOPPLER PHANTOM.

replaced with carbon-containing electrically conductive acrylic pads (eCAP, 3M, part 7850). The flexibility provided by this material allowed the head of the probe, which sends and receives ultrasound signals, to bend nearly perpendicularly to the rest of the components. A mold to fabricate the new housing for the bent ultrasound transducer was designed using SolidWorks (Massachusetts, USA), 3-D printed on a PolyJet printer (Stratasys J750, Israel), and then cleaned using a waterjet. Platinum cure silicone rubber (Ecoflex 00-30 Parts A and B) (Fig. 2) was then cast into the mold to fabricate the flexible transducer housing. The cast probe has a total mass of 214.6 grams, length of 5 inches, height of 1.25 inches, and width of 2.25 inches (the aperture length is 1 inch). The design sits flat on a phantom or patient (Fig. 1), using friction from the silicone rubber to keep it in place.

2.2 Device Analysis

The goal of this study is to continuously and non-invasively monitor vascular "output" and local flow in large vessels using the custom probe. Spectral Doppler imaging captures the velocity of Doppler fluid *in vitro* and blood *in vivo* (see Eq. 1).

$$v = \frac{c\Delta f}{2\sqrt{2} f_0 \cos\theta} \quad (1)$$

Here, f_0 represents the programmed frequency of the transmitted wave, Δf is the Doppler shift detected by the transducer, and c is the speed of sound in tissue. The velocity is additionally divided by $\sqrt{2}$ to account for Poiseuille's law for parabolic flow [4]. The angle between the transducer and the direction of the traveling fluid is represented by θ. Placing the transducer at exactly 90 degrees is therefore ineffective at measuring velocity because $\cos(90) = 0$. Here, θ is determined by the angle of the tissue phantom *in vitro* and determined using a goniometer *in vivo*. In this study, θ was determined to be 73 degrees *in vitro* and 81.5 degrees *in vivo*.

Locally measured stroke volume (SV), the amount of blood pushed through a vessel per heartbeat, can be found by taking the integral of the velocity versus time curve (velocity time integral, VTI) displayed during spectral Doppler imaging and scaling it by the cross-sectional area (CSA) of the vessel (Fig. 3, Eq. 2).

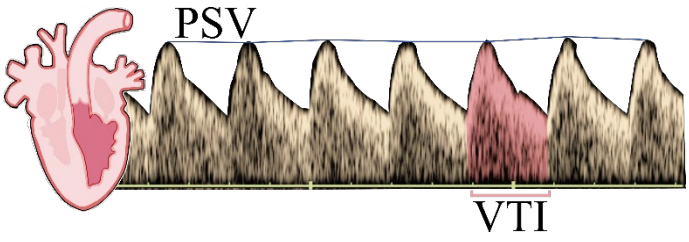

FIGURE 3: SPECTRAL DOPPLER IMAGING SHOWS VELOCITY OVER TIME AS DISPLAYED HERE IN PEACH AND BLACK WAVEFORMS. PEAK SYSTOLIC VELOCITY (PSV) TRACKS THE HIGHEST VELOCITY THAT OCCURS DURING A HEARTBEAT (TYPICALLY SYSTOLE, ALSO KNOWN AS EJECTION). THE VELOCITY TIME INTEGRAL (VTI) LEADS DIRECTLY TO CALCULATION OF CARDIAC OUTPUT.

CSA is found using 2-D ultrasound imaging prior to initializing the spectral Doppler mode.

$$SV = VTI * CSA \quad (2)$$

CO is the volume of blood pushed out by the heart every minute, and therefore is found by scaling the overall SV from the left ventricle by the heart rate (HR, see Eq. 3).

$$CO = SV * HR \quad (3)$$

In this study, locally measured SV was analyzed as a precursor to local vascular "output," which parallels the CO calculation (Eq. 3).

2.2.1 *In vitro* Analysis

The *in vitro* analysis took on three forms: (1) comparing the velocity values captured by three different transducers, (2) observing long-term (one hour) monitoring using the custom probe, and (3) ensuring the probe's ability to capture changing values more representative of human blood flow.

The custom probe, a TransducerWorks probe with the original hard plastic housing, and the eL18-4 probe on the Philips Epiq 7 were each used to capture peak systolic velocities (PSV) when the cardiac Doppler flow pump output three different volumes (2, 5, 7.5 mL) at seven different flow rates (1, 2, 3, 4, 5, 6, 7 mL/sec). The data were then analyzed using a two-tailed T-test to investigate potentially significant differences in measurements.

The custom probe was also used to track Doppler imaging over the course of one hour when the flow pump was programmed to pump 2mL of Doppler fluid at a flow rate of 3mL/sec.

An experiment was also performed to track the PSV and SV in comparison to ground truth values by changing the volume and flow rate incrementally throughout a roughly thirty-minute data collection. The cardiac Doppler flow pump was initially programmed to dispense 2mL at a flow rate of 3 mL/sec. The flow rate was then varied to 5 mL/sec, and then down to 2 mL/sec. The programmed output volume was then increased to 4mL, and the flowrate was initially set to 3 mL/sec before being varied to5 mL/sec, and then down to 2 mL/sec. The pump was then re-programmed to have an output volume of 2mL at a flowrate 3mL/sec. Each set of variables was run for approximately 5 minutes before reprogramming the phantom.

Additionally, this study looked at heat dissipation by the custom transducer when operating the pump at a constant volume and flow rate. A thermal camera (FLIR ONE Gen 3 - iOS) connected to an iPad (Model A2197) captured heatmap images approximately every 30 seconds for 25 minutes. These images showed the temperature at the hottest part of the probe, which was located at the tip of the transducer head (Fig 5**B**).

2.2.1 *In vivo* Analysis

The flexible, semi-conformal transducer was placed on the brachial artery of a volunteer. Spectral Doppler imaging captured the velocity of blood through the vessel for one minute. PSV and local vascular SV were calculated from these values.

3. RESULTS AND DISCUSSION

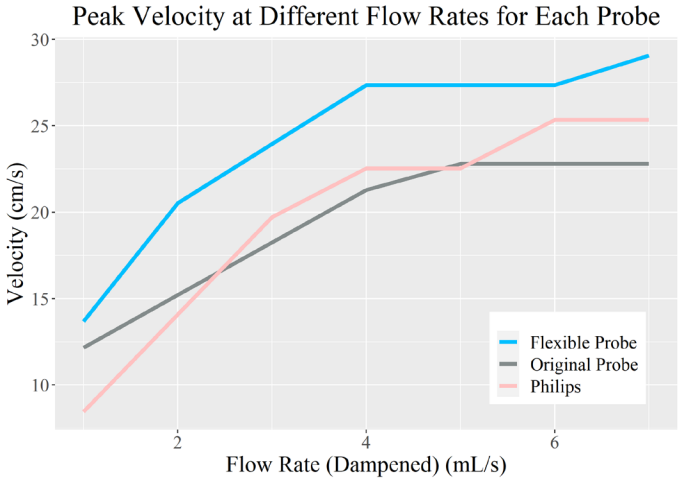

FIGURE 4: PEAK SYSTOLIC VELOCITY CAPTURED USING SPECTRAL DOPPLER IMAGING ON THREE DIFFERENT PROBES. THIS PLOT WAS GENERATED BY THE CARDIAC DOPPLER PUMP PUSHING 2ML OF VOLUME THROUGH THE SYSTEM AT 7 DIFFERENT FLOW RATES. A PULSE DAMPENER WAS WIRED INTO THE SYSTEM FOR THIS EXPERIMENT TO AVOID ALIASING. THERE WERE NO STATISTICALLY SIGNIFICANT DIFFERENCES BETWEEN THE VALUES CAPTURED BY EACH PROBE ($P > 0.05$).

The custom probe designed for this study was successfully used as a hands-free device in all data acquisition, both *in vitro* and *in vivo*. It remained flat and attached to the tissue phantom and a human arm. Placement on the arm required reinforcement with Self-Adherent Gentle Wrap (CVS Health, Rhode Island, USA) to reduce noise from fidgeting. In addition, software developed for the Verasonics system minimized data storage requirements and would enable continuous ultrasound monitoring for two years, assuming no hardware failures. This calculation was found by determining that each saved sample is 8 bytes captured at approximately 30Hz, and the maximum memory for an array in MATLAB is 13.8 gigabytes.

No statistically significant difference existed between PSV values detected by any of the ultrasound probes reported in Section 2.2.1. (Fig. 4). These velocities were captured at twenty-one different combinations of volume (three options) and flow rate (seven options) as dispensed by the cardiac Doppler flow pump, and all *p*-values were greater than 0.05.

The custom probe was also capable of running pulsed wave spectral Doppler imaging over the course of an hour (Fig. 5**A**,**B**). Although the pump was programmed to a constant volume (2mL) and flow rate (3mL/sec), both the velocity and the amplitude of the velocity detected by the probe decreased over time (Fig. 5**A**). It was suspected that the heat released by the pump (Fig. 6**A**) and the probe (Fig. 6**B**) may have affected both the pump's ability to dispense Doppler fluid through the system and the transducer's accuracy, respectively. As seen in Fig. 6**C**, the temperature of the probe increased to a value (105°F) near the burn threshold for human skin (111°F [5]) after only 30 minutes. Therefore, one limitation made evident by this experiment is the device's inability to dissipate heat. In the future, re-wrapping the electronic casing with copper or additionally wrapping the eCAP with aluminum will be explored as options for heat sinks, and the device will be programmed to operate at a lower power and duty cycle. Adding metal particulates to the flexible rubber housing may also aid in heat dissipation [6].

The device was able to track changes in flow rate and volume dispensed (Fig. 5**C**,**D**). A previous study on long-term ultrasound monitoring argued that recognition of severe or sudden changes in patient vital signs is more important as a device feature than replication of ground truth values [2]. Therefore, the ground truth comparison is less important in this example than the degree of change itself, although ground truth is shown as a gray dashed line (Fig. 5**C**,**D**). The data from this

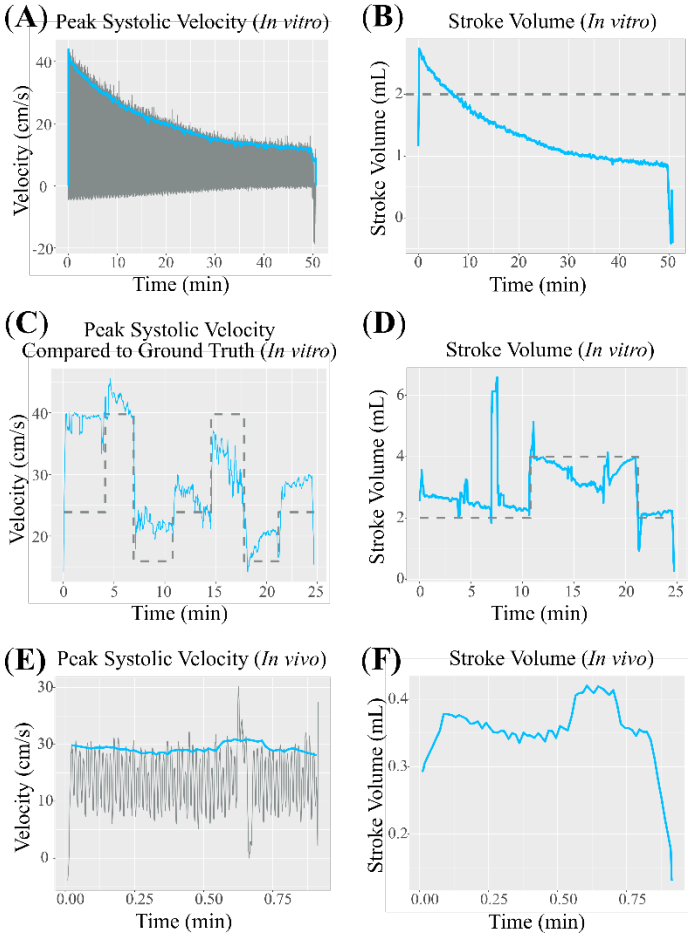

FIGURE 5: PEAK SYSTOLIC VELOCITY (PSV) AND STROKE VOLUME (SV) TRACKED (**A**, **B**) OVER ONE HOUR *IN VITRO*, (**C**, **D**) OVER 30 MINUTES *IN VITRO* WITH FLUCTUATING VOLUME AND FLOW RATE INPUTS, AND (**E**, **F**) OVER ONE MINUTE *IN VIVO*. (**A**, **E**) GRAY REPRESENTS VELOCITY AS CAPTURED BY THE CUSTOM PROBE. (**C**, **D**) GRAY REPRESENTS THE GROUND TRUTH VELOCITY OR VOLUME, RESPECTIVELY, AS PROGRAMMED BY THE CARDIAC DOPPLER PUMP. IN ALL PLOTS, BLUE REPRESENTS THE CALCULATED PSV OR SV.

experiment is noisy, potentially as a result of electromagnetic interference (EMI) generated by the pump and/or the Verasonics system. It is possible that replacing the copper casing surrounding the electronics (shown in Fig. 2**A**) with eCAP reduced the device's ability to shield the transducer from these EMI signals. Further validating this hypothesis, an oscilloscope (PicoScope 4000 Series) detected EMI signals correspondent with the cardiac Doppler pump's on/off state. The next model of this custom transducer will experiment with different electrically conductive materials to ground and shield the device, for example, reusing the copper shielding after creating the perpendicular bend at the transducer tip rather than using eCAP.

In vivo data demonstrated the device's ability to detect velocities seen in human vessels, specifically tracking PSV and SV in the brachial artery (Fig. 5**E**,**F**). Although ground truth values do not exist for this example, the curves are shaped as expected, with a faster and relatively constant heart rate. It is important to note the volunteer fidgeted approximately forty seconds into the recording, leading to noise in the recorded signal. Future iterations of the device will feature improved algorithms for filtering noise.

Long-term monitoring and point-of-care medicine using ultrasound are currently limited by the necessity for constant expert manual guidance during imaging [7], yet even recent attempts at hands-free ultrasound cannot be commercialized due to slow and costly production, poor imaging techniques, and short battery lives. Wang *et. al.* constructed a stretchable ultrasound patch for imaging the carotid artery and jugular vein [1]. However, their claim that the patch secures air-tight against the skin is unlikely outside a vacuum. Additionally, they lack matching and backing layers as a part of their transducer. The matching layer allows for nearly seamless acoustic transition between the transducer and skin, while the backing layer forces sound waves forward into the body. Without these, one would require a large amount of power to ensure enough sound waves enter the skin. Kenny *et. al.* recently constructed an ultrasound patch for continuous spectral Doppler monitoring of the carotid artery as well; however, the reported patch adhesive wears out after one day, and their battery lasts only three hours. The reported device is also unable to switch between 2-D and spectral Doppler imaging, limiting its use for patient monitoring [2].

This work will lead to a hands-free approach to point-of-care medicine. The next major step towards implementing this device in the clinic focuses on reducing the operational temperature of the probe during pulsed wave doppler imaging. Lowering the power or duty cycle is an immediate approach to reduce overheating[8, 9]. Additionally, experimenting with new materials for the flexible housing as well as the electronic encasing will help improve heat dissipation and EMI shielding. Furthermore, re-programming the device to simultaneously acquire 2-D and spectral Doppler ultrasound scan would allow the calculation of SV to include the changing CSA that fluctuates as blood flows through a vessel. This additional time-series variable will improve the accuracy of calculating local vascular output and CO. The device could also be improved by incorporating a machine learning algorithm to automatically

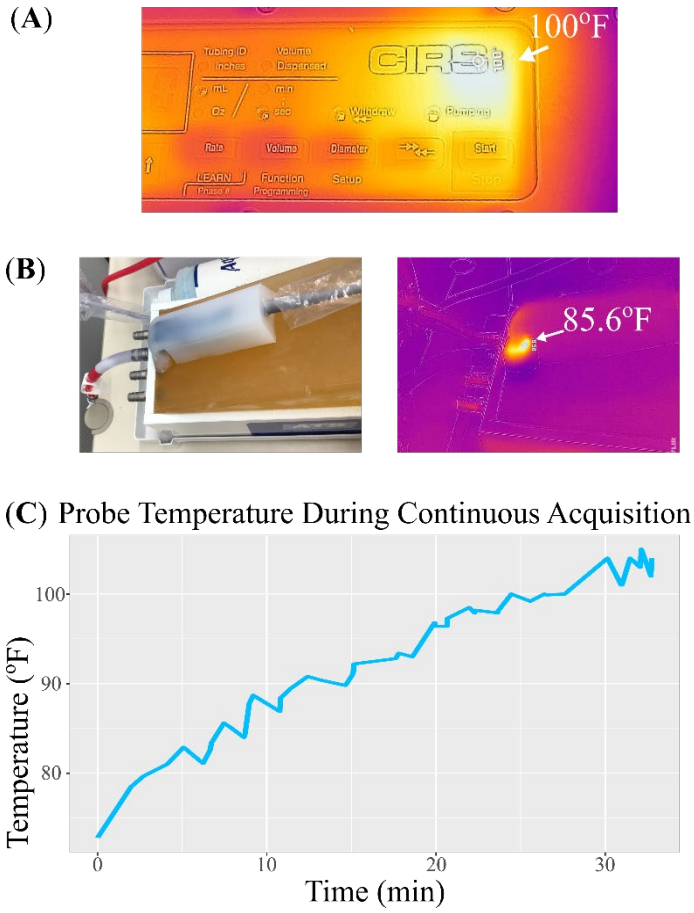

FIGURE 6: THERMOSENSOR IMAGING OF THE SYSTEM USING A FLIR CAMERA DEMONSTRATES OVERHEATING AFTER A PERIOD OF TIME. (**A**) THE PUMP HEATED UP TO 100°F AFTER 30 MINUTES. (**B**) THE CUSTOM PROBE RESTING ON THE TISSUE PHANTOM (LEFT) IS SHOWN AS A HEATMAP (RIGHT). THE TIP OF THE PROBE REACHED 85.6°F IN 9 MINUTES. (**C**) THE TEMPERATURE OF THE CUSTOM PROBE WAS TRACKED OVER A 30 MINUTE ACQUISITION OF SPECTRAL DOPPLER ULTRASOUND IMAGING.

steer the ultrasound waves to monitor blood flow in key vessels. This algorithm could be programmed to alert clinicians to sudden changes in patient health status as well as predict patient vitals during interspersed ultrasound acquisition (*e.g.*, when operating at a lower duty cycle), which could reduce power consumption and heat emission. Ultimately, the goal of this technology is a transformation of the hands-free device into a wireless patch for use in the intensive care unit for imaging any body part and monitoring, for example, cardiac or pulmonary health. This patch would be an inexpensive, ubiquitous, and user-friendly solution to long-term monitoring that would enable immediate response to changes in patient status.

4. CONCLUSION

This study presented a custom ultrasound probe that is flexible, semi-conformal, hands-free, and able to capture data

over long periods of time (i.e., one hour). *In vitro* and *in vivo* results demonstrated the calculation of SV, which is directly proportional to local vascular "output," from spectral Doppler ultrasound imaging. Implementation of this device in the intensive care unit could ease continuous patient monitoring and decrease response time to critical changes in patient health.

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