Short paper

Towards a non-invasive cardiac arrest monitor: An *in vivo* pilot study

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Abstract

Introduction: Hemodynamic-guided cardiopulmonary resuscitation (HGCPR) achieves better outcomes than standard resuscitation. Currently, HGCPR requires an invasive procedure, infeasible during resuscitation. Non-invasive measures of blood flow could provide useful hemodynamic guidance to rescuers.

Objective: We describe initial efforts to develop a device that detects, analyzes, and measures the velocity of carotid artery blood flow (CABF) towards the brain at pre-arrest baseline ('baseline') and during cardiopulmonary resuscitation, here tested in a swine model of cardiac arrest (CA). A key element of that device consists of non-imaging diagnostic ultrasound, due to its simplicity and small form factor, hence potential for deployment during HGCPR in a bandage placed on the neck.

Methods: Sixteen mixed-breed domestic swine were sedated, anesthetized and paralyzed, followed by endotracheal intubation and mechanical ventilation. Cardiac arrest was induced with a 3-s 100 mA transthoracic shock or bolus of fentanyl, after which all animals received mechanical CPR. A non-imaging ultrasound probe was manually applied to the neck over the carotid artery to capture CABF during baseline, as verified with diagnostic ultrasound imaging, and during mechanical resuscitation.

Results: We successfully collected CABF measurements at baseline in 14/16 swine and during attempted resuscitation with mechanical chest compression in 5/16 swine. Signal characteristics include peak blood flow both towards (90.4 +/−20.4 cm/s) and away from the brain (−44.2 +/−31.8 cm/s) during resuscitation, each larger than flow towards (41.7+/−14.8 cm/s) and away from brain (−3.0 +/−7.8 cm/s) during baseline.

Conclusion: Measurement of CABF before and during CPR in swine with a non-imaging ultrasound probe is feasible before CA and informative when achieved during CPR. For example, observations of reverse flow within the carotid artery during CPR merits further study for its prevalence and effect on resuscitation outcomes. Also, tissue motion represents a significant obstacle for CABF measurement during CPR. Additional work will determine the feasibility and utility of non-imaging ultrasound measurements of CABF during resuscitation.

Keywords: Ultrasound, Resuscitation guidance, Pig model, Doppler ultrasound

Introduction

Cardiac arrest (CA) strikes more than 530,000 people each year in the United States.[1] Despite considerable effort, patient survival after out-of-hospital cardiac arrest (OHCA) remains low.[2] American Heart Association guidelines define specific CPR methods during resuscitation, with a deterioration in their quality during manual CPR.[3–8] For this reason, and observations using animal models[9–11] and in humans,[12] current evidence-based guidelines[13] recommend hemo-dynamic monitoring of CPR to improve outcomes, an invasive hence impractical prospect for routine use.

The rate of survival after CA varies widely between communities,[14] suggesting that there remains room for improvement of CPR implementation. Here we consider non-invasive ultrasound to provide hemodynamic guidance. Diagnostic ultrasound imaging systems have been used to directly assess cardiac activity after CPR administration.[15] We previously reported their use to measure carotid flow in human subjects during CPR.[16] Doppler interrogation using diagnostic ultrasound imaging systems requires, however, considerable training and easy availability for successful deployment, inconsistent with current critical care practice. Moreover, their complexity and large form factor makes problematic their integration into mechanical resuscitation devices.

Long term, we seek to develop an easy-to-deploy and hands-free non-imaging ultrasound device, whose small transducers, deployable in a bandage[17] and capable of easily guided placement over the carotid artery, could provide real time feedback during resuscitation through display of CABF towards the brain. Here we report results of pilot studies with an animal model of CA, that demonstrate the feasibility, potential advantages, and limitations of collecting non-imaging ultrasound data without a bandage for this first study, during mechanically assisted resuscitation.

Methods and materials

Probe for pulsed Doppler

Ultrasound data were collected with a Hokanson (Issaquah, WA) CP-1B single-element pulsed-Doppler with a hand-held, 0.25" diameter, 5 MHz 'pencil probe' transducer. Ultrasound quadrature data were digitized using an AlazarTech (Pointe-Claire, Canada) ATS-460 analog-to-digital converter and custom-built MATLAB (Natick, MA) acquisition software. Sixty-four quadrature samples were recorded per pulse over a time interval that spanned a 1-cm long region centered on the depth of the middle of the carotid artery and deeper than the jugular vein. Diagnostic ultrasound imaging (Fujifilm Sonosite, Inc, Bothell WA) was used during baseline to locate the carotid artery (Fig. 1) and guide the placement of the Doppler transducer ultrasound field. Data collection yielded 26.7 ensembles of 128 pulses per second at a pulse repetition frequency of 8.1 kHz.

Animal model

All experiments were performed at the University of Pittsburgh Medical Center with approval by the University of Pittsburgh Institutional Animal Care and Use Committee, performed in compliance with the Guide for Care and Use of Laboratory Animals. Ultrasound data for the present study were collected as ancillary endpoints of three separate experimental series as determined by investigator availability.

Female 25–50 kg swine were sedated with ketamine (10 mg/kg) and xylanzine (4 mg/kg), paralyzed (4 mg vecuronium), intubated with a 5-0 cuff endotracheal tube, and then anesthetized with fentanyl (50 mcg/kg). The electrical CA group underwent a 3-s, 100 V transthoracic shock, followed by disconnection of the ventilator and 8 min of untreated arrest. The overdose CA group received a fentanyl bolus (30 mcg/kg) plus 10 mg vecuronium, followed by disconnection of the ventilator and occlusion of the endotracheal tube for 9 min. For both, mechanical chest compression was then initiated using a commercial LUCAS2 (Physio-Control, Inc., Lund, Sweden) compressor or a custom-built, programmable compressor.

Ultrasound data collection from 16 swine was attempted during pre-arrest baseline (termed 'baseline' below) and during chest compressions following the primary experimental protocol. During baseline, the Hokanson transducer was manually placed over the neck until it received blood flow signals from the common carotid artery (CCA) as verified with simultaneous Sonosite Doppler imaging. Once located, the operator fixed the depth of Hokanson data acquisition on the observed carotid artery. During resuscitation, the operator removed the Sonosite probe and held the Hokanson transducer in place, at an approximately 45° angle with respect to the orientation of the CCA throughout resuscitation.

Signal analysis

Only data from within the 1 cm focus of the Doppler device and centered on the CCA was used, after inspection for signs of multiple blood vessels. Doppler spectrograms were generated using MATLAB (MathWorks, Natick, MA), including use of a high-pass filter in the 200–400 Hz range during baseline, and adaptively during resuscitation, to screen out slow and bright, hence tissue-related backscatter signals. To enhance their temporal resolution, multiple cardiac cycles were aligned and averaged yielding composite waveforms. All composite waveforms are visualized over the same time (0.5 s) and velocity (+/−86 cm/s) scales, with manually measured peak flow. Artifacts such as a low-frequency constant signal were removed via filtering before additional data processing that yielded the averaged data.

Results

Peak CABF measurements (Table 1) were successfully collected from 14/16 swine at baseline and from 5/16 swine during CPR, where robust movement of the swine during mechanical resuscitation impeded successful collection of ultrasound data from the majority of swine. Instantaneous (Fig. 2A) and averaged (Fig. 3, top row) Doppler waveforms collected during baseline demonstrated a consistent temporal pattern across all animals: maximum forward flow during peak flow at systole (typically around 0.1 s after the start of a cardiac cycle), followed by a diminishing oscillatory flow during diastole, in the range of 0.25–0.4 s, with minimal reverse flow. During resuscitation, instantaneous (e.g. Fig. 2B) cardiac waveforms collected exhibited greater temporal variability than during baseline, including examples of substantial instantaneous blood flow away from brain, and tissue motion. Consistent features in composite waveforms (Fig. 3, bottom row) include observations of high velocity blood flow towards the brain during chest compression (5/5 swine), tissue motion artifacts (3/5 swine), and reverse blood flow away from the brain (4/5 swine).
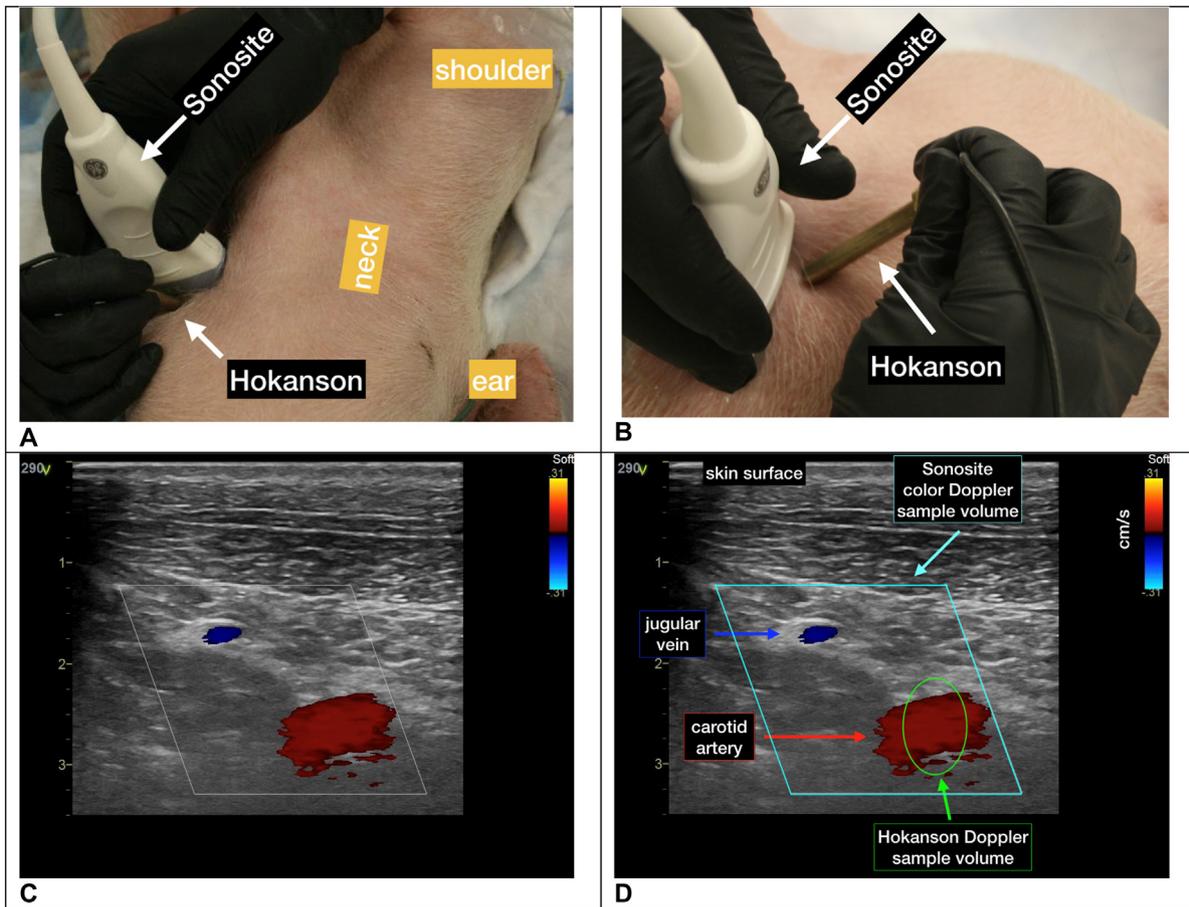
Fig. 1 – Doppler ultrasound probes and color Doppler image of vascular anatomy.
(A) This figure shows a plan view of the experiment, a supine swine with deployment of the Sonosite's diagnostic imaging probe and the Hokanson's non-imaging Doppler probe. (B) Closeup of probe deployment, from a different perspective. (C) Unannotated color Doppler image of tissue within the neck of swine taken using the Sonosite ultrasound diagnostic imaging system. (D) Corresponding annotated color Doppler image, denoting the skin surface, the carotid artery and jugular vein within the sample volume for the Sonosite device, and the sample volume of the non-imaging Hokansan Doppler device, the latter encompassing only the carotid artery.

Table 1 – Peak Forward Velocity (PFV) and Peak Reverse Velocity (PRV) at baseline and during mechanical chest compression (CPR) after cardiac arrest (CA).

Experiment Number	CA	CPR	baseline PFV (cm/s)	baseline PRV (cm/s)	CPR PFV (cm/s)	CPR PRV (cm/s)
1	Electrical	custom	46	−17	63	−63
2	Electrical	custom	59	0	105	−84
3	Overdose	LUCAS2	42	0	74	−32
4	Overdose	LUCAS2	17	0	–	–
5	Overdose	LUCAS2	21	0	–	–
6	Electrical	LUCAS2	–	–	–	–
7	Electrical	LUCAS2	32	0	–	–
8	Electrical	LUCAS2	63	0	–	–
9	Electrical	LUCAS2	34	0	–	–
10	Electrical	LUCAS2	–	–	–	–
11	Electrical	custom	42	0	105	0
12	Electrical	custom	53	0	–	–
13	Electrical	custom	38	0	–	–
14	Electrical	LUCAS2	67	−25	–	–
15	Electrical	LUCAS2	38	0	105	−42
16	Electrical	LUCAS2	32	0	–	–
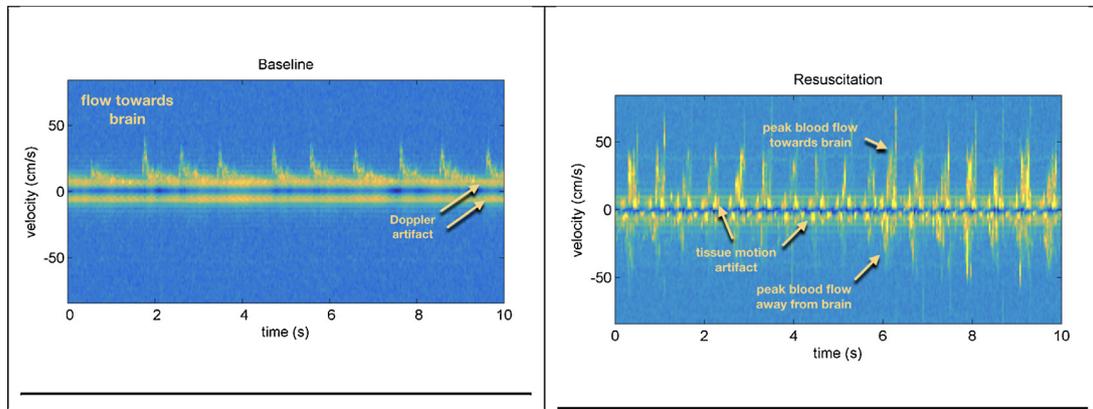
Fig. 2 – Instantaneous blood flow within the carotid artery of swine. Ultrasound Doppler-measured blood flow over ten seconds (A) before CA [baseline], and (B) during mechanical resuscitation. Mechanical resuscitation produced signals consistent with blood flow both towards and away from brain.
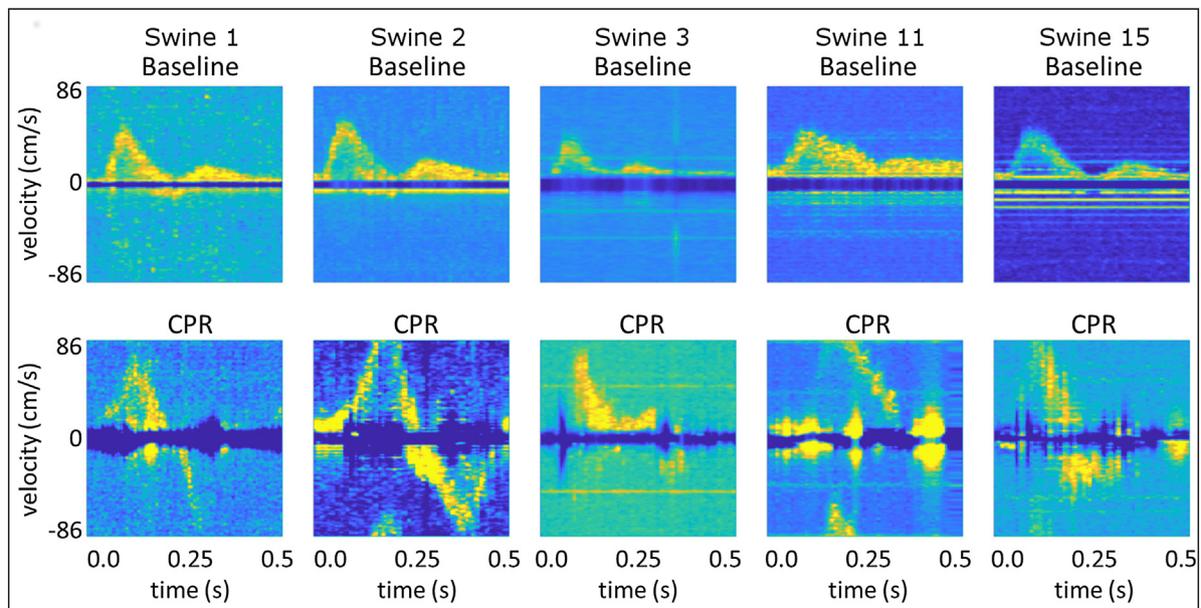
Fig. 3 – Average Doppler waveforms collected at baseline (top row) and during resuscitation (bottom row). Five of sixteen swine provided ultrasound data for each baseline (top) and resuscitation (bottom). All show large systolic peaks, at approximately 0.1 s. Tissue-motion (bright, low-velocity signals) occur during CPR in swine #s 1 (at ~0.15 s),11 (throughout) and 15 (at 0.5 s). Reverse flow (negative velocity values) appear in Swine #s 1 (at 0.25 s), 2 (within 0.25–0.4 s), 3 (at 0.3 s) and 15 (at 0.2–0.3 s). Aliasing artifacts appear in Swine #s 2, 11 and 15 (negative signal within 0.1–0.2 s).

Quantitatively, average signal characteristics during resuscitation include peak blood flow both towards (90.4 +/− 20.4 cm/s) and away from brain (−44.2 +/−31.8 cm/s), each larger than flow towards (41.7 +/−14.8 cm/s) and away from brain (−3.0 +/−7.8 cm/s) during baseline.

Discussion

We have demonstrated non-invasive measurements of carotid artery blood flow (CABF) using non-imaging, non-invasive ultrasound, with data collected successfully at baseline from 14/16 swine and during

resuscitation from 5/16 swine. We observed average CABF reversal during resuscitation, suggesting it is possible that CABF directed towards the brain can exceed the capacity of the brain to receive blood, consistent with our measurements using diagnostic ultrasound during human resuscitation.[16]

If differences in CABF structure affect resuscitation outcomes, changes to chest compression strategy could optimize net forward flow of blood towards the brain, a possible explanation for increased short-term survival of animals undergoing goal-directed resuscitation.[12–14] Continuous non-invasive hemodynamic measures by ultrasound may therefore offer the potential to improve resuscitation outcomes by giving rescuers a therapeutic target during their efforts.

Limitations

Without ultrasound imaging during resuscitation, we could not accurately determine the orientation of the ultrasound probe. We therefore reported velocities assuming an insonation angle of 45°, noting that deviations from the true angle would change the velocity scale but not the overall appearance of the Doppler spectrograms. Systems that include imaging with simultaneous Doppler measurements would address this issue, at the cost of taking the device design away from a resuscitation monitor that uses small, non-imaging ultrasound probes deployable in a bandage.

We visualized all Doppler data within the sample volume for each experiment, always finding only one blood vessel, as observed during baseline. Future studies would benefit from the use of intra-carotid and intra-jugular pressure monitoring catheters in conjunction with ultrasound measurements.

Relative motion between the transducer and skin induced by the mechanical chest compressor made difficult the maintenance of blood flow measurements during resuscitation. Also, tissue motion signals required significant post-processing to remove their contribution to blood-flow statistics. These challenges limited our ability to collect high quality CABF data during resuscitation. Therefore, any clinically feasible cardiac arrest device that relies on ultrasound-based CABF for hemodynamic guidance must address the effects of tissue movement while facilitating easy deployment with minimal training.

Conclusion

A simple to use, non-invasive cardiac arrest monitor could provide useful feedback during CPR. Small, non-imaging ultrasound transducers, were they robustly deployable, could offer one such possibility. We have presented preliminary data showing it feasible, though difficult, and, potentially important to do so, with identification of significant limitations at this time. Successful refinement of this approach, with its promise of providing measurement of blood flow to the brain that can guide refinement of CPR in real time, may one-day improve outcomes after cardiac arrest.

Conflicts of interest statement

No conflict of interest to report.

Acknowledgments

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