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Toward a Miniature Ultrasound Device for Imaging TBI Under PFC Scenarios

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14. ABSTRACT

Tissue pulsatility imaging (TPI) of brain structure -- hence sTPI -- of individual moderate to severe TBI brains can (a) identify the presence of and quantify the spatial extent of epidural and subdural hematomas as well as (b) differentiate those brain injuries from others that arise due to closed-head trauma and from the brains of trauma/non-TBI patients, in a manner comparable to computed tomography (CT) imaging. The focus of our study is to develop and test on civilian patients a field-deployable (tablet-based) ultrasound imaging device for brain structure after moderate to severe TBI. We observed TBI features within sTPI images that correlate with the damage associated with TBI highlighted by corresponding CT or magnetic resonance (MR) images. After 3 years, we expect to deliver a prospectively tested (in the setting of a preclinical study) final sTPI ultrasound-data processing algorithm, deployed on a tablet-based and otherwise standard diagnostic ultrasound system. Aim 1: We are collecting sTPI of brains of moderate to severe TBI patients and of controls. Aim 2: We have made very significant progress in developing sTPI software and deploy on a tablet-based ultrasound system. We use trauma/non-TBI patients as controls.

15. SUBJECT TERMS

Tissue pulsatility imaging, Traumatic Brain Injury, epidural and subdural hematomas, Brain imaging, CT scans, Tablet based diagnostic ultrasound for brain injury.

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TABLE OF CONTENTS

1. Introduction.

We seek to provide portable technology able to image abnormal brain structure after acute TBI as encountered at and near battlefields that lack on-site CT and MR imaging modalities. Our core technology consists of images of the pulsation of brain tissue: tissue pulsatility imaging (TPI) derived via novel analysis of standard diagnostic ultrasound. Since here we target imaging of abnormal brain structure we call this 'structural TPI' or sTPI. We will work with civilian patients with moderate and severe TBI. Successful completion of our proposed work will demonstrate that sTPI images of TBI yield diagnostically useful information comparable to that derived from CT images. Moreover, we will do so using a diagnostic ultrasound system with a form factor of a tablet. Of critical importance, this approach represents novel reinterpretation of standard B-mode diagnostic ultrasound imaging. Specifically, we work with the ultrasound data collected by standard diagnostic ultrasound imaging systems and process that data in a way different than that used to create gray-scale (B-mode) ultrasound images. Therefore, as we emphasize below, our anticipated tablet-based diagnostic ultrasound system can perform basic gray-scale imaging of the body – critical for Focused Assessment with Sonography in Trauma (FAST) analysis of potential intra-abdominal bleeding – as well as structural tissue pulsatility imaging of brain. Moreover, because our approach requires only modification of the software on extant diagnostic ultrasound systems, we anticipate that sTPI algorithms can embody rapidly into whatever portable diagnostic ultrasound imaging system the military targets for its use.

We therefore seek with this proposal to refine (Aim #2) structural tissue pulsatility imaging (sTPI) of moderate to severe TBI using retrospective analysis of images collected from civilian moderate to severe TBI patients (Aim #1) then (2) test prospectively, in a pre-clinical study, our sTPI algorithms deployed in a tablet-based form factor on moderate to severe TBI (Aim #3).

Objective: Tissue pulsatility imaging (TPI) of brain structure – hence sTPI – of individual moderate to severe TBI brains can [a] identify the presence of as well as quantify the spatial extent of epidural and subdural hematomas as well as [b] differentiate those brain injuries from others that arise due to closed-head trauma and from the brains of trauma/non-TBI patients, in a manner comparable to CT imaging.

2. Keywords.

Tissue pulsatility imaging, Traumatic Brain Injury, epidural and subdural hematomas, Brain imaging, CT scans, Tablet based diagnostic ultrasound for brain injury.

3. Accomplishments.

We first list the major and subtasks of this project. We then use the subtask number so the reader can correlate our description of our accomplishments to the subtask.

SPECIFIC AIM 1	***Timeline (months)***	***Participants***
Major Task 1.1: Collect sTPI of brains of TBI and control patients for retrospective analysis of sTPI algorithm. ***N = 100 TBI & 25 trauma/non-TBI = 125 patients.***	*1-27*	*Neurosurgery;* *Applied Physics Laboratory*
Subtask 1.1: Obtain UW IRB Approval for human studies.	*1-3*	*Neurosurgery*
Subtask 1.2: HRPO Review and Approval for human studies, including an IDE from the FDA by month 12 if necessary.	*4-12*	*Neurosurgery*
Subtask 1.3: enable desktop-based research ultrasound system and clinical ultrasound system. Purchase, setup, and calibrate desktop and clinical ultrasound systems.	*2-4*	*Applied Physics Laboratory*
Subtask 1.4: demonstrate, in vitro, capabilities of ultrasound systems from Subtask 3. Embody within the desktop and clinical systems sTPI software, with devices tested on tissue phantoms.	*3-5*	*Applied Physics Laboratory*
Subtask 1.5: train residents for image collection and interpretation duties.	*5-6*	*Neurosurgery;* *Applied Physics Laboratory*
Subtask 1.6: gather ultrasound and CT data from moderate/severe TBI patients. Collect ultrasound data from civilian patients with moderate to severe brain injury after closed-head trauma of two classes [1] epidural and subdural hemorrhage; [2] other e.g., subarachnoid or intraparenchymal hemorrhage or diffuse brain injury.	*7-27*	*Neurosurgery*
Subtask 71.: gather ultrasound and CT data from trauma/non-TBI controls. Collect ultrasound and CT data from civilian patients who have experienced trauma but not TBI.	*7-27*	*Neurosurgery*
Subtask 1.8: produce sTPI images for moderate/severe TBI patients and for trauma/non-TBI controls.	*7-27*	*Applied Physics Laboratory*
Milestone 1.1: *local IRB Approval*	*3*	*Neurosurgery*
Milestone 1.2: *HRPO Approval*	*6*	*Neurosurgery*
Milestone 1.3: *production of sTPI images from moderate to severe TBI patients across two classes of damage types, and from trauma/non-TBI controls.*	*27*	*Neurosurgery;* *Applied Physics Laboratory*
SPECIFIC AIM 2	***Timeline (months)***	***Participants***

Major Task 2.1: Optimize sTPI software	7-27	Neurosurgery; Applied Physics Laboratory
Subtask 2.1: compare sTPI images with clinical CT images for TBI patients. Compare, retrospectively and on a patient-by-patient basis, the size, shape, extent and other features of brain damage in sTPI of TBI patients with those in their CT images.	7-27	Neurosurgery; Applied Physics Laboratory
Subtask 2.2: compare sTPI images with clinical CT images for trauma/non-TBI control patients. Compare, retrospectively and on a patient-by-patient basis, the size, shape, extent and other features of brain damage in sTPI of trauma/non-TBI control patients with those in their CT images.	7-27	Neurosurgery; Applied Physics Laboratory
Subtask 2.3: perform retrospective comparison of diagnostic utility of sTPI versus CT of moderate to severe closed TBI. Here we will use the structural information from Subtasks 1 & 2 to differentiate between [1] epidural or subdural bleeds versus [2] other brain damage and versus [3] trauma/non-TBI brain, with CT images as the gold standard.	12-27	Neurosurgery: Applied Physics Laboratory
Subtask 2.4: Amend software as needed to optimize the ability of sTPI to capture diagnostically useful information regarding TBI.	18-27	Applied Physics Laboratory
Milestone 2.1: retrospective demonstration that sTPI of TBI offers diagnostic utility comparable to CT.	27	Neurosurgery; Applied Physics Laboratory
Milestone 2.2: production of optimized sTPI software ready for prospective testing.	27	Applied Physics Laboratory
Major Task 2.2: Deploy final sTPI software on a tablet-based ultrasound system.	24-27	Applied Physics Laboratory
Subtask 2.5: enable final sTPI software on tablet-based system. Purchase, setup, and calibrate final tablet-based ultrasound system.	24-27	Applied Physics Laboratory
Subtask 2.6: demonstrate in vitro the final tablet-based ultrasound system's capabilities. Embody within the final, tablet-based system optimized sTPI software, with device tested on tissue phantoms.	24-27	Applied Physics Laboratory
Milestone 2.3: tablet-based ultrasound system with optimized sTPI software ready for prospective testing.	27	Applied Physics Laboratory
SPECIFIC AIM 3	**Timeline (months)**	**Participants**
Major Task 3.1: **Prospective studies of sTPI algorithm deployed on an ultrasound tablet.** **N = 50 TBI & 15 trauma/non-TBI = 65**	27-36	Neurosurgery; Applied Physics Laboratory
Subtask 3.1: collect sTPI & CT images from TBI and	27-33	Neurosurgery;

trauma/non-TBI patients.		Applied Physics Laboratory
Subtask 3.2: compare, prospectively, ability of sTPI to detect epidural or subdural bleeds relative to other TBI sequela, validated with clinical CT.	30-36	Neurosurgery; Applied Physics Laboratory
Subtask 3.3: compare, prospectively, clinical utility of sTPI for epidural or subdural bleeds, validated with clinical CT images.	30-36	Neurosurgery; Applied Physics Laboratory
Subtask 3.4: For patients with brain injury other than epidural or subdural hematomas, produce prospective analysis of clinical utility of sTPI as compared to clinical CT images.	30-36	Neurosurgery; Applied Physics Laboratory
Milestone 3.1: Prospective demonstration that analysis of sTPI of TBI patients can differentiate those patients with epidural or subdural bleeds from those with other brain injuries associated with TBI, in a manner comparable to that of CT.	36	Neurosurgery; Applied Physics Laboratory
Milestone 3.2: Prospective demonstration that analysis of sTPI of TBI patients can quantify the structural extent of epidural or subdural bleeds due to TBI, in a manner comparable to that of CT.	36	Neurosurgery; Applied Physics Laboratory
Milestone 3.3: Prospective demonstration that sTPI of TBI patents with brain injury other than epidural or subdural hematomas has diagnostic utility comparable to that of CT.	36	Neurosurgery; Applied Physics Laboratory
ADMINISTRATIVE	**Timeline (months)**	**Participants**
Major Task 4.1: Delivery of reports	various	Neurosurgery
Subtask 4.1: produce quarterly reports.	quarterly	Neurosurgery
Subtask 4.2: produce annual reports.	annually, yrs 1-2	Neurosurgery
Subtask 4.3: produce final report.	Year 3	Neurosurgery
Milestone 4.1: Production of quarterly reports.	quarterly	Neurosurgery
Milestone 4.2: Annual reports approved.	annually, yrs 1-2	Neurosurgery
Milestone 4.3: Final report approved.	Year 3	Neurosurgery
Major Task 2.4: FITBIR submission.	various	Neurosurgery
Subtask 4.4: facilitate FITBIR data submission	7-27	Neurosurgery
Subtask 4.5: Submit data to FITBIR.	quarterly	Neurosurgery
Milestone 4.4: Submission of all data to FITBIR completed.	Year 3	Neurosurgery

<u>Major goals and associated accomplishments for the time period covered by this report.</u>

Subtask 1.6: gather ultrasound and CT data from moderate/severe TBI patients …

- We have estimated 'identified' and 'approached' in order to get this report out the door. We will revise these numbers before the end of April 2020.
- We identify an average of ~one patient per day during the five days per week we can perform our study. We lose approximately a third of the patients we identify before we can approach them for reasons that include, primarily, the movement of the patients to the OR, or they die, consistent with the moderate to severe head injuries that we are studying. We successfully consent ~80% of the patients we approach. We have studied ~80% of the patients we have consented, with the drop off due to emergent patient procedures that arose after consent but before we arrived at Harborview to perform the study, or patient/family irritability after we arrive.
- In total, we have collected data from approximately 25% of the patients we identify, without any adverse events or unanticipated problems.
- This last quarter included significant holiday time, hence the reduced number of identified patients relative to average.

human data	Identified	Approached	Consented	Studied	Data Sets Collected
Total	~200	~71	59	49	49
This quarter (16Nov'19 - 15Feb'20)	~30	~15	11	11	11

Subtask 1.7: gather ultrasound and CT data from trauma/non-TBI controls …

- We have started to collect data from the controls (one thus far); of note, they are hard to collect data from because they, thus far, tend to leave the hospital by the time we identify and consent them.

Subtask 1.8: produce sTPI images ...

- We have generated such images using a wide range of techniques for all our data sets, see discussion in Subtask 2.3 and the Appendix.

Subtask 2.1: compare sTPI images with clinical CT images for TBI patients …

- We have analyzed many of our ultrasound images and offer one here (Figure 1, overleaf), with a deeper discussion in Subtask 2.3 and much more extensive discussion with several examples in the Appendix.
- As mentioned in recent quarterly reports, we have identified a new, VR-based technology that should help us collect ultrasound images that have even more refined alignment with the patient's CT image. This requires us to provide a ~$40K contract with VSOM, Inc, a local startup here in Seattle, which we have started.

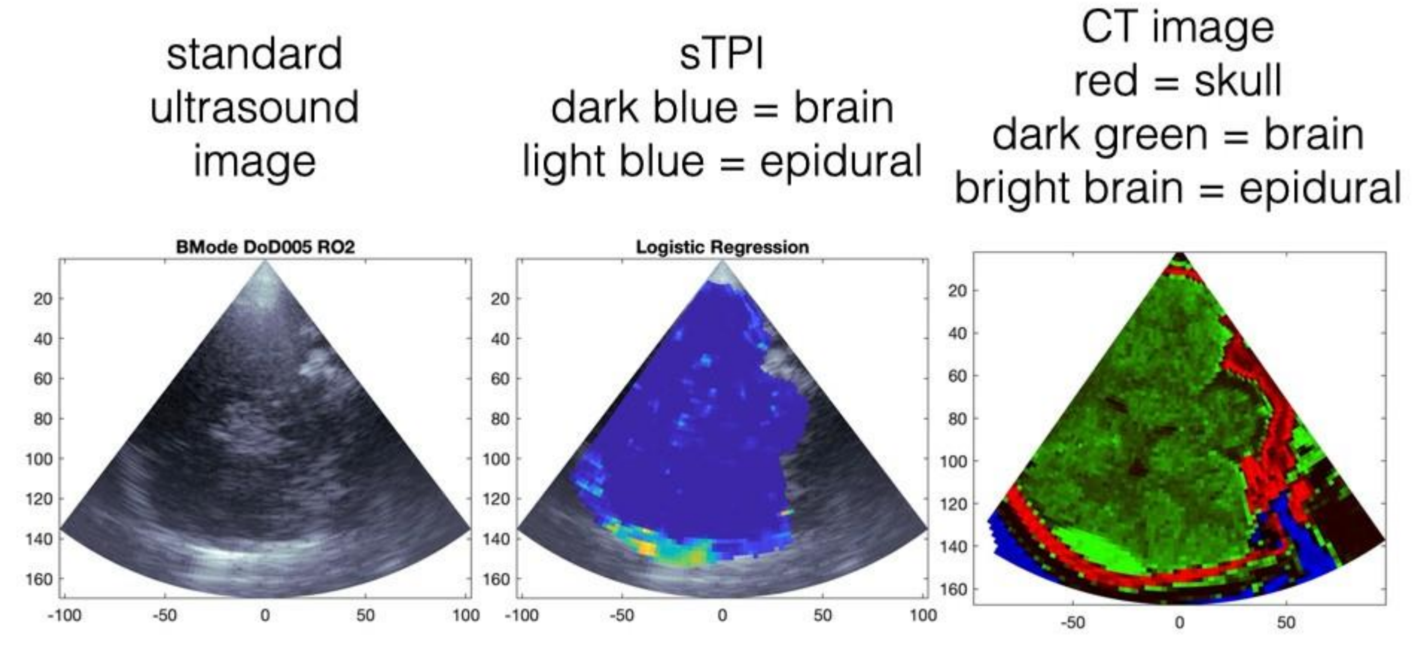

Figure 1. Epidural bleed. The left-hand image shows the B-mode ultrasound (gray scale) image derived from standard ultrasound imaging. The transducer sends sound through ipsilateral skull – here at the base of the triangular shape – and highlights a plane of tissue as well as an arc of bone (the white portion near the bottom of the image. The right-hand image shows the plane within the CT image that overlaps with the B-mode image. Red highlights skull,m dark green as brain tissue, and light green as the epidural bleed, all as defined by the pre-sets within the CT imaging software. The middle image shows the result of our analysis of the raw signals that through one kind of processing creates a B-mode image, here processed in a different way that yields local measures of brain-tissue pulsation (that is, local displacement) and velocity, here and throughout this report corrected for motion of the transducer relative to the patient's skull. This retrospective analysis highlights the epidural bleed.

Subtask 2.3: perform retrospective comparison of diagnostic utility of sTPI versus CT of moderate to severe closed TBI.

- For a given patient, we have the ability to define within the volume of CT data a plane that plausibly aligns with their ultrasound image plane. With this in hand we have projected the CT image information onto the ultrasound image plane that defines epidural or subdural bleeds, intra-parenchymal bleeds, ventricles (another fluid-filled space) and other anatomical structures. We have started the process of determining whether or not the pulsatility of brain tissue within these different structures differ from one another in a usefully sensitive and specific way. We offer an Appendix to this report that gives significantly more details as to the methods and the results. Differentiation between skull and its contents using ultrasound only and in a prospective fashion remains an important technical task to refine: for the purposes of this report we use the CT image to define the skull, although B-mode images do a decent job of defining the skull.

Subtask 2.4: Amend software as needed to optimize the ability of sTPI to capture diagnostically useful information regarding TBI.

- This represents an on-going effort as we (a) collect more data and (b) learn more from that collected data and on-going analysis efforts.

Subtask 2.5: enable final sTPI software on tablet-based system. Purchase, setup, and calibrate final tablet-based ultrasound system.

- We have purchased, setup and calibrated the final tablet-based ultrasound system. We will put the final algorithm on it when ready.

Subtask 4.4: facilitate FITBIR data submission.

- We established a FITBIR account and started uploading data.

Opportunities for training and professional development for the time period covered by this report.

We have had the excellent help of neurological surgery residents – Ariana Barkeley, MD and John Williams, MD – who together have made quite critical contributions to the interpretaqtion of the data, how best to collect the data including how to read the charts to gain a sufficient interpretation of the patient's condition relative to what we seek for our study. Also, we have engaged several undergraduates into this project, who help in a mentorship scenario with a variety of the secondary efforts – not the detailed analysis that I've put in the hands of our lead scientists.

Results disseminated to communities of interest.

Nothing to report.

Plans for the next reporting period.

- We plan to collect data from as many TBI patients, and trauma/non-TBI patients as we can.
- We will to re-open a dialogue about post-study consent.
- We will continue our analysis of the data to refine a robust sTPI algorithm
- Differentiation between skull and its contents remains an important technical task to refine.
- Post-COVID-19, we will establish sites beyond Seattle, perhaps Charlottesville VA and/or Boston MA.
- We plan to extend our results to date to see if we can identify generalizable characteristics of different internal bleeds (epidural, subdural, intra-parenchymal) versus normal tissue.

4. **Impact**

What was the impact on the development of the principal discipline(s) of the project?

We can report that our colleagues from neurological surgery, from neurology, from critical care, and from emergency medicine are excited about the possibility of our device. We can anticipate that a hand-held device capable of rapidly determining the presence and grade of intracranial bleed will have a profoundly positive impact on the practice of civilian emergency medicine. We also see the possibility of using this device to quickly determine the presence of ischemic stroke.

What was the impact on other disciplines?

We anticipate that we will develop novel algorithms beyond the state of the art tissue pulsatility algorithms in ways specifically applicable to brain. There exist a one group that use tissue pulsatility algorithms to study brain function, for example. We believe our advances will help them.

What was the impact on technology transfer?

We anticipate that, as above, we will develop novel algorithms beyond the state of the art tissue pulsatility algorithms in ways specifically applicable to brain. Commercial opportunities may include direct development of our tablet-based ultrasound system embodying sTPI. Terason, the privately held company from which we have purchased our clinical system and anticipate purchasing our tablet-based system has an interest in this possibility. More broadly, with its anticipated form factor and possibility of measuring brain *function* not just brain *structure*, we have some hope that our device will evolve into what one could call functional tissue pulsatility imaging (or fTPI).

What was the impact on society beyond science and technology?

We anticipate that a hand-held device capable of rapidly identifying and differentiating between different intracranial maladies will help reduce the cost of health care.

5. Changes/Problems

Changes in approach and reasons for change

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

We have had unseasonably mild winters hence a reduction in TBI, good for the general population, of course but not for our study. We wish to consider opening up new study sites, and, consenting after collection of data so we can capture patients more serious intra-cranial bleeds before the systems whisks them off to the OR. Also, COVID-19 arrived just after the end of this reporting period, which has stopped collection of new data though has not stopped analysis of existing data.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

Significant changes in use or care of human subjects

None anticipated.

Significant changes in use or care of vertebrate animals.

NA

Significant changes in use of biohazards and/or select agents

NA

6. Products

Publications (journals; book chapters), conference papers, and presentations.

Nothing to report yet

Websites or other internet sites.

Nothing to report.

Technologies or techniques

Nothing to report, yet, but, under consideration is the algorithm we use to correct for the motion of the transducer relative to the patient's head, and our algorithm that, thus far in a retrospective way, identifies different kinds of intra-cranial bleeds.

Inventions, patent applications, and/or licenses.

Nothing to report, yet.

Other Products.

Nothing to report, yet.

7. Participants and Other Collaborating Organizations

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Name: Pierre D Mourad, PhD
Project Role: PI
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.1/month
Contribution to Project: Principle investigator

Name: John Kucewicz, PhD
Project Role: Research Scientist
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.70/month
Contribution to Project: writing code for the devices; collecting and analyzing data

Name: Michael S Bobola, PhD
Project Role: Research Scientist
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.5/month
Contribution to Project: organizing data, assisting with procedures, oversight of devices, collecting data, analyzing data, attending to FITBIR.

Name: Nina Lapiana
Project Role: Research Scientist
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.0/month
Contribution to Project: organizing data, assisting with procedures, oversight of devices, collecting data, analyzing data, attending to FITBIR.

Name: Chikodi Ezeokeke
Project Role: Research Scientist
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.5/month
Contribution to Project: organizing data, assisting with procedures, oversight of devices, collecting data, analyzing data, attending to FITBIR

Name: Caren Marzban, PhD
Project Role: Research Scientist
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 0.33/month
Contribution to Project: Analyzing data

8. Special Reporting Requirements

We have submitted a Quad Chart.

9. Appendices

Detailed analysis of representative images of intracranial bleeds immediately follow this page.

Appendix

Tissue Pulsatility Imaging and other variants of Doppler ultrasound are generally only able to measure the scalar projection of velocity in the direction of the ultrasound beam, away from the transducer face, in a radial direction when thinking in terms of polar coordinates with the transducer at the point of origin.

In 2019 we started developing and implementing methods of estimating 2D vector velocity fields from scalar velocity fields, that is, to pick up the more subtle tangential movement of tissue as well as the directly computable radial component of tissue movement. This was initially motivated by the need to correct for relative motions between the ultrasound transducer and the patient during data collection. We have worked to extend these methods to better measure tissue pulsatility in regions dominated by tangential motion, i.e. locally perpendicular to the direction of the ultrasound beam.

Least Squares Vector Processing

In order to resolve 2D motion, ultrasound data needs to be collected from different directions and the projected scalar data can then be used to estimate the 2D vector field. The radial velocity for an individual pixel is:

$$v_{!} = v_{"} u_{\#} + v_{\#} u_{\#}$$

where v is velocity and u_x and u_y are the x and y components of a unit vector pointed away from the origin of the ultrasound transducer. Least squares regression is used to solve for v_x and v_y within a region-of-interest assuming the velocity is uniform over the region. We developed this method originally to estimate and compensate for common-mode motion due to relative motion between the patient and the hand-help ultrasound transducer. A challenge of this method thus far is that can overestimate tangential motion, especially in relatively small regions-of-interest such as near the skull, the position of the bleeds of greatest interest. Nonetheless initial application of this approach has retrospectively produced images tissue pulsatility images that highlight regions and sometimes extent of intracranial bleeds.

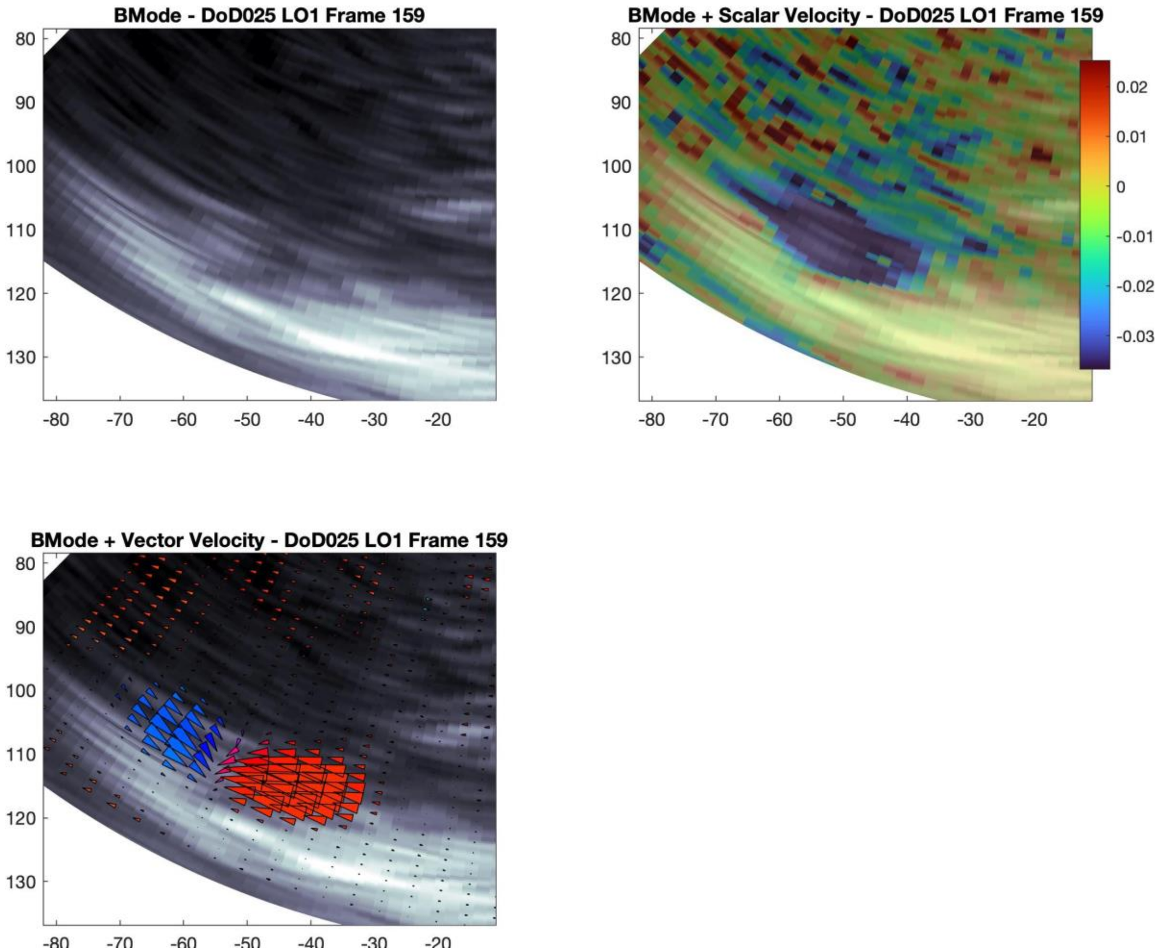

Figure 1 – an example of a gun-shot wound, with greatest tangential velocity near the skull, at the point of entry of the bullet into the brain through the skull. *(Upper left image)* This image shows a close up of a standard 'B-mode' ultrasound image, created by an ultrasound transducer placed far above this imaged sub-region and its bright arc at along the bottom due to the skull. *(upper right image)* Amplitude of vector velocity field, with its peak negative value at systole, hence away from the transducer, towards the bullet's entrance point on the skull. *(lower image)* Least squares estimate of vector field during systole in proximity to gun shot skull defect. Velocities near the skull defect are sufficiently large and largely tangential that they yield good estimates for radial and tangential motion, with the latter dominating in this case.

Optical Flow

Optical flow is an established technique for motion tracking especially in image sequences. It is a very robust technique when used on ultrasound BMode images with good signal-to-noise ratios (Yamshita et al., PMID: 32158076). We have been testing the use of optical flow with the raw radiofrequency ultrasound signals which should give better estimates of motion compared to BMode images (Figure 2, overleaf).

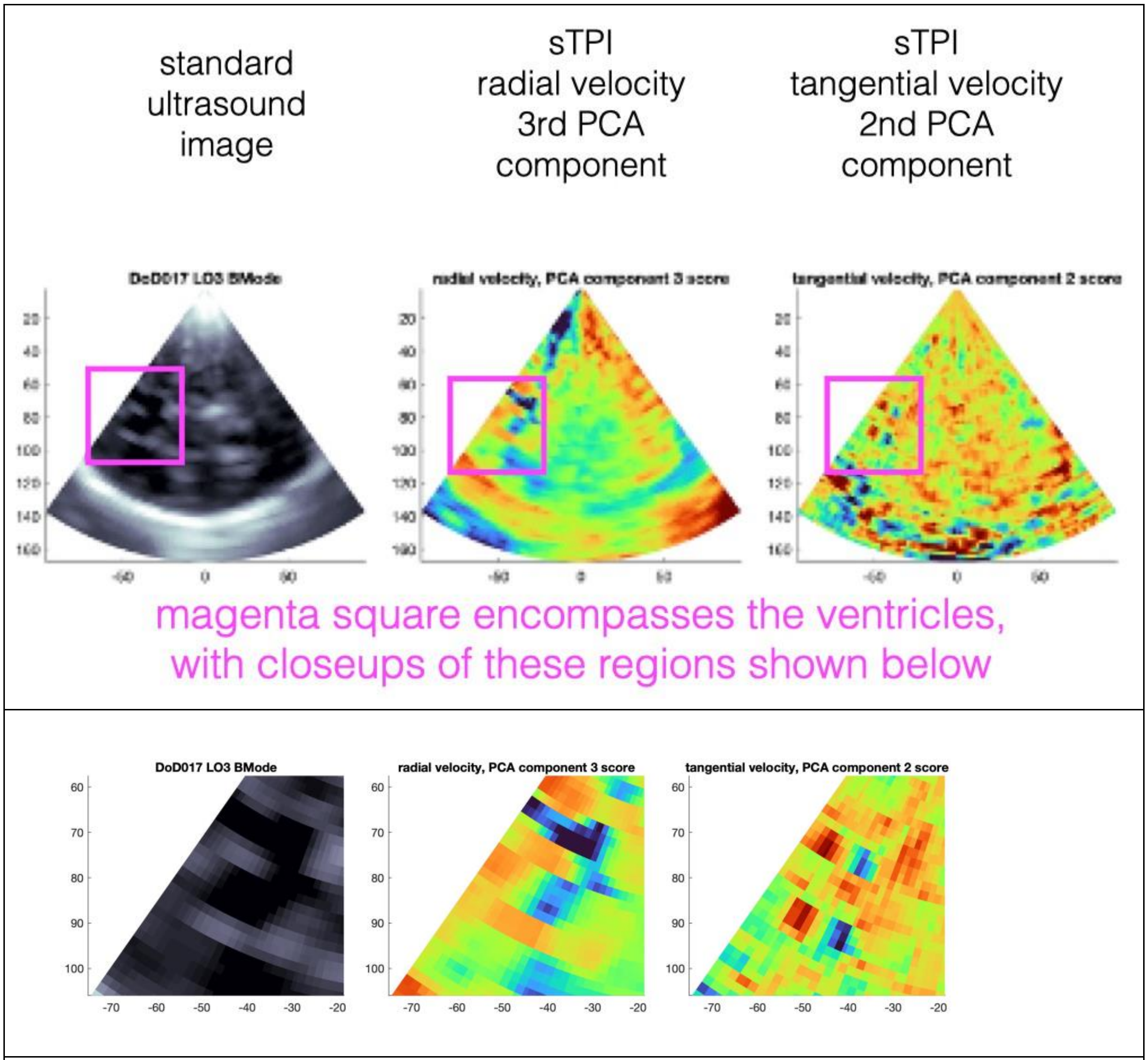

Figure 2 – Principal component scores for radial and tangential pulsatility waveforms associated with a pair of ventricles estimated using Optical Flow imaging – large-scale view on the first line of images, closeup on the second line of images. We chose these components because they retrospectively highlighted motion associated with the ventricles while the lower set of images shows a closeup of the ventricles. Red and Blue in each velocity component indicate compression and expansion of the tissue adjacent to the lateral ventricles over the cardiac cycle, respectively.

Vector Flow (Least Squares Vector Processing with Regularization)

Vector Flow is a vector Doppler method developed primarily for estimating 2D and 3D blood flow velocity in the chambers of the heart. There are a few variations on this approach; we have been working with Assi's "intraventricular vector flow mapping" method (Assi et al, PMID: 28800300). This is a closed form method with regularization terms for divergence, smoothness, and flow at the chamber wall (or skull in our case). Part of the challenge with this method is determining how much weight to assign to each regularization term. We are in the process of constructing a phantom to validate this method.

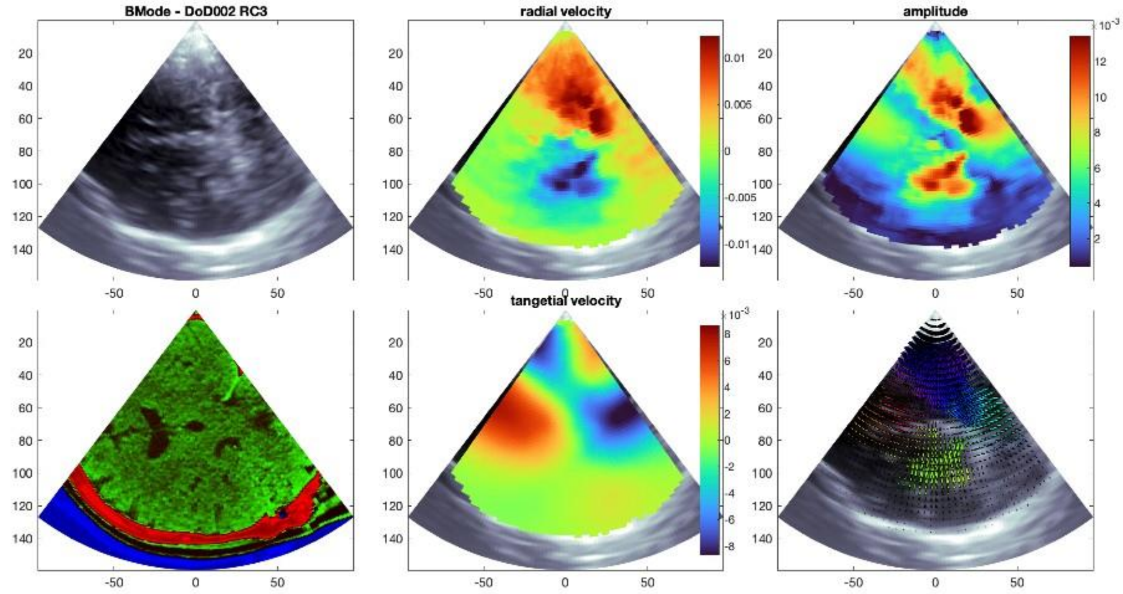

Figure 3. Mean systolic velocity for subject DoD002 – RC3 {"right coronal, third image"}, here highlighting ventricles, without an intra-cranial bleed. Upper images, left to right: B-mode image, with the arc of bone appearing as a white arc along the bottom of the image and contralateral to the point of contact of the ultrasound probe placed here at the apparent point of origin of the ultrasound image; radial velocity image; total amplitude of radial and tangential velocities. Lower images from left to right: CT image – red = bone, dark green equals brain tissue, light green equals blood; tangential velocity image; vector velocity image. Here the ventricles appear to have large radial and tangential velocities, the bright that dominate the radial and tangential velocity images. Note also the reduced velocity amplitude adjacent to the skull. We see this as background displacement of an undisturbed brain against which we compare brain images that contain intracranial bleeds.

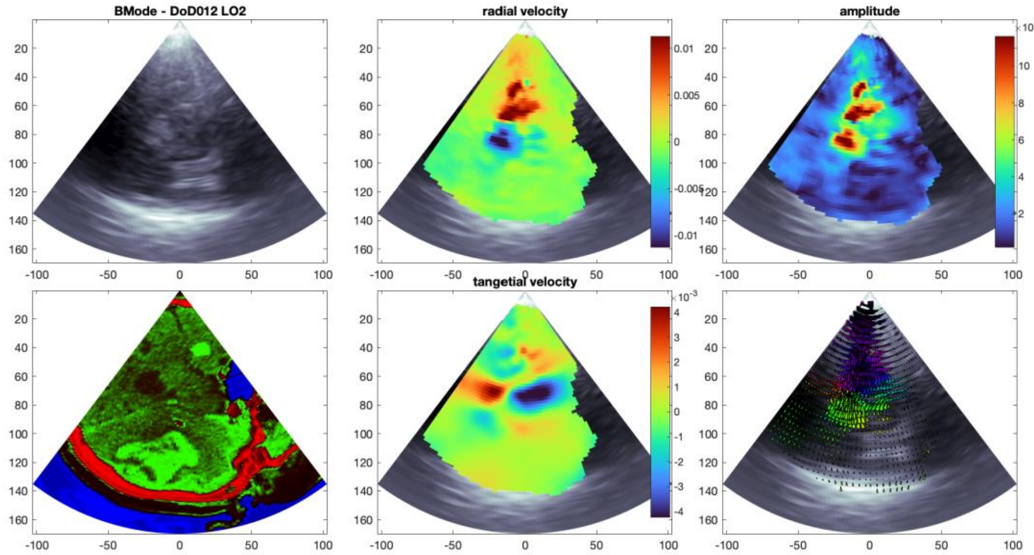

Figure 4. Mean systolic velocity for subject DoD012 – LO2, a right temporal intraparenchymal hematoma and acute subdural hematoma. Upper images, from left to right: B-mode image, with the arc of bone appearing as a white arc along the bottom of the image and contralateral to the point of contact of the ultrasound probe placed here at the apparent point of origin of the ultrasound image; radial velocity image; total amplitude of radial and tangential velocities. Lower images from left to right: CT image – red = bone, dark green equals brain tissue, light green equals blood; tangential velocity image; vector velocity image. Here the adjacent intraparenchymal and subdural bleed-containing region has much lower values of velocity amplitude associated with it, over a larger extent of space, than in Figure 3. The single lateral ventricle (dark circular structure) still appear to have large radial and tangential velocities, with smaller bright spots than in Figure 3, displaced upwards towards the upper portion of the radial and tangential velocity images. These peak displacement regions associated with the ventricles are also smaller than in Figure 3 .

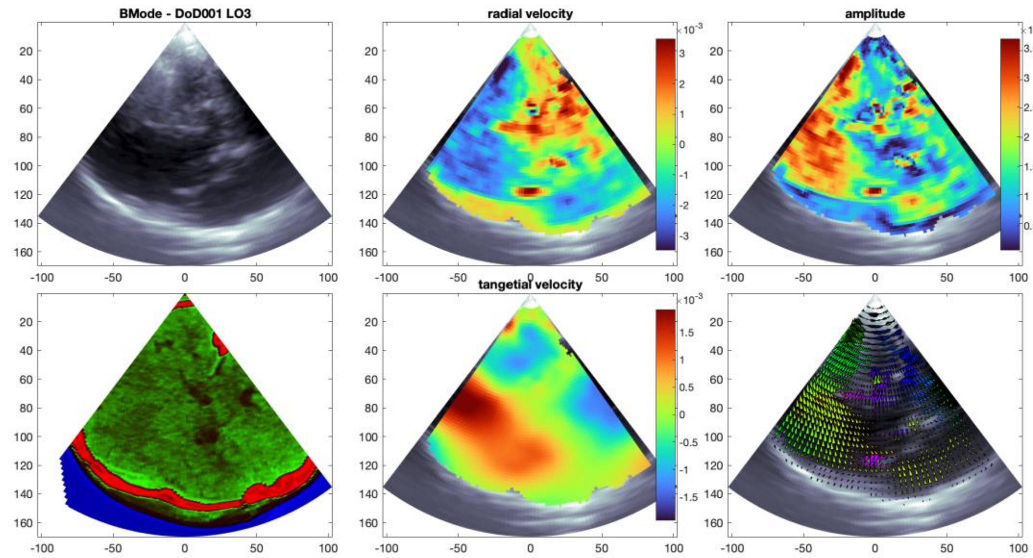

Figure 5. Mean systolic velocity for subject DoD001 – LO3, with an epidural hematoma along the skull. Upper images, from right to left: B-mode image, radial velocity image, total amplitude of radial and tangential velocities. Lower images from left to right: CT image – red = bone, dark green equals brain tissue, light green equals blood; tangential velocity image; vector velocity image. Note the epidural hematoma in the CT image (thin light green region along the bright-red skull) and its correspondence with relatively high radial velocity near the skull, moderately low tangential velocity, and the low amplitude of velocity in the 'amplitude' image. The ventricles (two separate and dark ovid regions in the CT image) appear to superimpose on the velocity-component images large variations in radial and tangential velocities, which complicates the images of the bleeds.

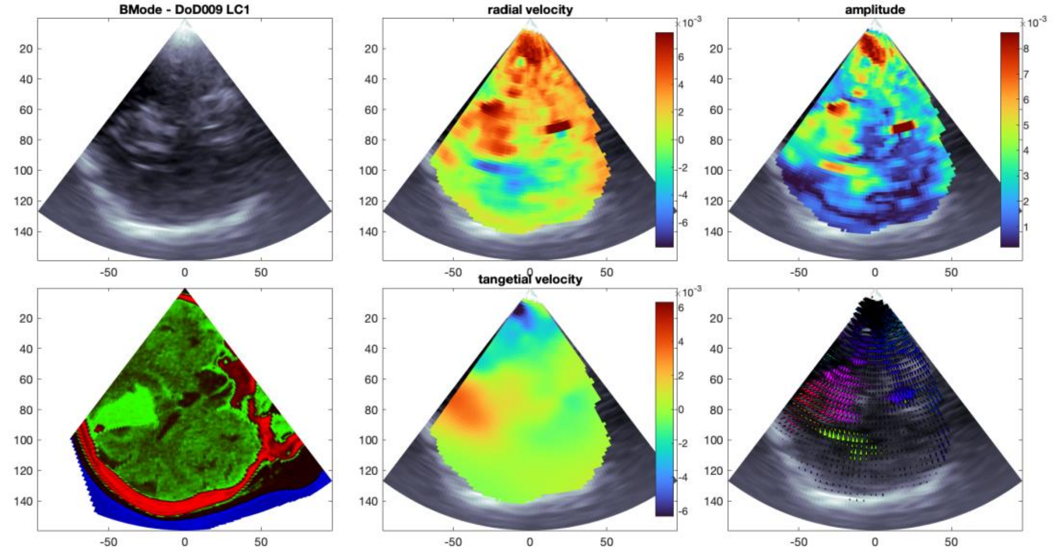

Figure 6. Mean systolic velocity for subject DoD009 – LC1 with a left parafalcine sudural hematoma and small left intraparenchymal hematoma. Upper images, left to right: B-mode image, with the arc of bone appearing as a white arc along the bottom of the image and contralateral to the point of contact of the ultrasound probe placed here at the apparent point of origin of the ultrasound image; radial velocity image; total amplitude of radial and tangential velocities. The intraparenchymal hematoma appears as a region of high radial and especially tangential velocity with, however, a complicated velocity pattern perhaps associated with the small adjacent ventricle (a single dark ellipse tangential to the lower right hand corner of the intraparenchymal hematoma. The subdural hematoma does not show up in a distinct fashion, perhaps because it sits within a low-velocity region due to brain swelling and/or perhaps it is too small to detect.

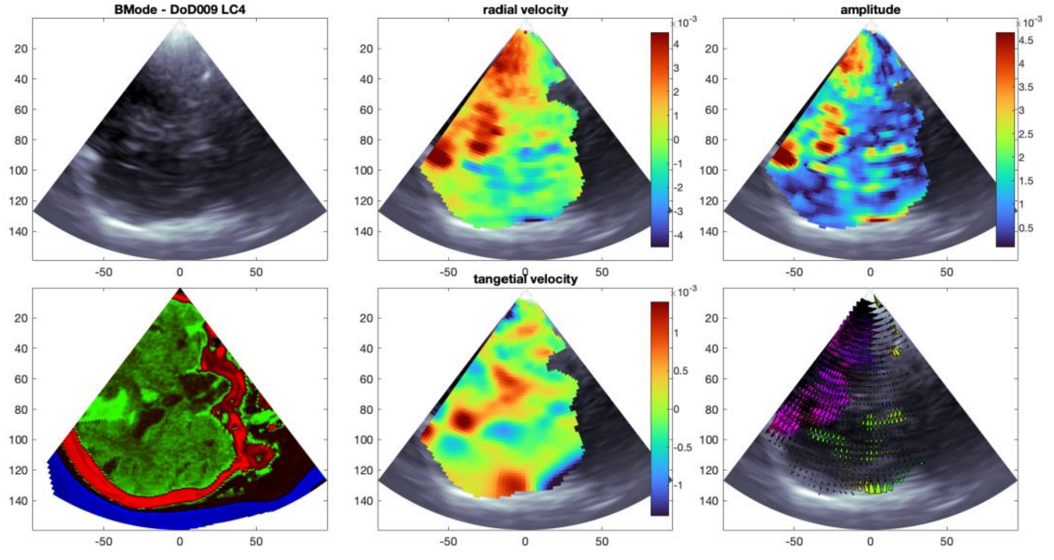

Figure 6. Mean systolic velocity for subject DoD009 – LC4, with a left parafalcine sudural hematoma and small left intraparenchymal hematoma. *As in Figure 5, with analysis based on a different left-coronal (LC) image.* Upper images, from right to left: B-mode image, radial velocity image, total amplitude of radial and tangential velocities. Lower images from left to right: CT image – red = bone, dark green equals brain tissue, light green equals blood; tangential velocity image; vector velocity image. The intraparenchymal hematoma appears as a region of elongated (left-right) high radial and tangential velocity with, however, a complicated velocity pattern perhaps associated with the adjacent ventricles. The subdural hematoma does not show up in a distinct fashion, perhaps because it sits within a low-velocity region due to brain swelling and/or perhaps it is too small to detect.

Next Steps

Vector processing of skull motion has been critical for compensating for common-mode motion introduced by hand-held scanning of patients. We have found, retrospectively, some utility in its application to identifying brain regions that contain bleeds.

Our next steps are as follows:

1. Increase the sensitivity and specificity of our vector-based imaging procedure.
2. Refine vector flow method with tissue phantom. We have built a mold that we will use to construct a tissue-mimicking phantom. This is currently on hold due to limited lab access due to the novel coronavirus.
3. Explore feasibility to combining data sets collected from the left and right temporal windows. Regularization with vector flow is based in part on zero motion boundary constraint at the skull. With data collected from a single window, we are thus far challenged to consistently use ipsilateral skull as a boundary condition. Combining data sets from both windows will improve our vector velocity estimates.
4. We will refine our means of identifying skull in ultrasound images; as of how our analysis has used the CT image information to retrospectively identify skull.