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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:

What were the major goals of the project?

We first list the major and subtasks of this project. We then use the Milestones to summarize our results.

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 = 200 TBI & 25 trauma/non-TBI & 50 Stroke = 275 patients.	*1-42*	*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 and stroke 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.	*7-42*	*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.	*7-42*	*Neurosurgery*
Subtask 1.8: produce sTPI images for moderate/severe TBI patients, for stroke patients, and for trauma/non-TBI controls.	*7-42*	*Applied Physics Laboratory*
Milestone 1.1: *local IRB Approval* ***- achieved***	*3*	*Neurosurgery*
Milestone 1.2: *HRPO Approval* ***- achieved***	*6*	*Neurosurgery*
Milestone 1.3: *production of sTPI images from moderate to severe TBI patients across two classes of damage types, from stroke patients, and from trauma/non-TBI controls.* ***- achieved***	*42*	*Neurosurgery; Applied Physics Laboratory*
SPECIFIC AIM 2	***Timeline (months)***	***Participants***
Major Task 2.1: Optimize sTPI software	*7-42*	*Neurosurgery; Applied Physics Laboratory*
Subtask 2.1: compare sTPI images with clinical CT images for TBI & for stroke 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.	*7-42*	*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	*7-42*	*Neurosurgery; Applied Physics Laboratory*

images.		
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.	*12-42*	*Neurosurgery:* *Applied Physics Laboratory*
Subtask 2.4: Amend software as needed to optimize the ability of sTPI to capture diagnostically useful information regarding TBI.	*18-42*	*Applied Physics Laboratory*
Milestone 2.1**: retrospective demonstration that sTPI of TBI offers diagnostic utility comparable to CT. **– not achieved, but proxy results derived.	*42*	*Neurosurgery;* *Applied Physics Laboratory*
Milestone 2.2:** production of optimized sTPI software ready for prospective testing. **– achieved, for algorithms that don't directly image, but instead detect midline shift of brain caused by lesions.	*42*	*Applied Physics Laboratory*
Major Task 2.2: Deploy final sTPI software on a tablet-based ultrasound system.	*36-42*	*Applied Physics Laboratory*
*Subtask 2.5: enable final sTPI software on tablet-based system._Purchase, setup, and calibrate final tablet-based ultrasound system. **- achieved***	*36-42*	*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. **- achieved***	*36-42*	*Applied Physics Laboratory*
Milestone 2.3:** tablet-based ultrasound system with optimized sTPI software ready for prospective testing.* ***- achieved	*42*	*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***	*42-48*	*Neurosurgery;* *Applied Physics Laboratory*
Subtask 3.1: collect sTPI & CT images from TBI and trauma/non-TBI patients.	*42-48*	*Neurosurgery;* *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.	*42-48*	*Neurosurgery;* *Applied Physics Laboratory*
Subtask 3.3: compare, prospectively, clinical utility of sTPI for epidural or subdural bleeds, validated with clinical CT images.	*42-48*	*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.	*42-48*	*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. **– not achieved	*48*	*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. **– not achieved	*48*	*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. **– not achieved	*48*	*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 1-3*	*Neurosurgery*
Milestone 4.3: *Final report approved.*	*Year 4*	*Neurosurgery*
Major Task 2.4: FITBIR submission.	*various*	*Neurosurgery*
Subtask 4.4: facilitate FITBIR data submission	*7-36*	*Neurosurgery*
Subtask 4.5: Submit data to FITBIR.	*quarterly*	*Neurosurgery*
Milestone 4.4: *Submission of all data to FITBIR completed.* ***- achieved***	*Year 4*	*Neurosurgery*

What was accomplished under these goals – first year summary.

During the first year we earned IRB approval from the University of Washington and from DoD. We then started our data collection. Figure 1 below shows our approach for projecting the planar ultrasound data into the three-dimensional CT data. It is these comparisons that allow us to analyze the ultrasound pulsatility data in a way that compares with the CT data.

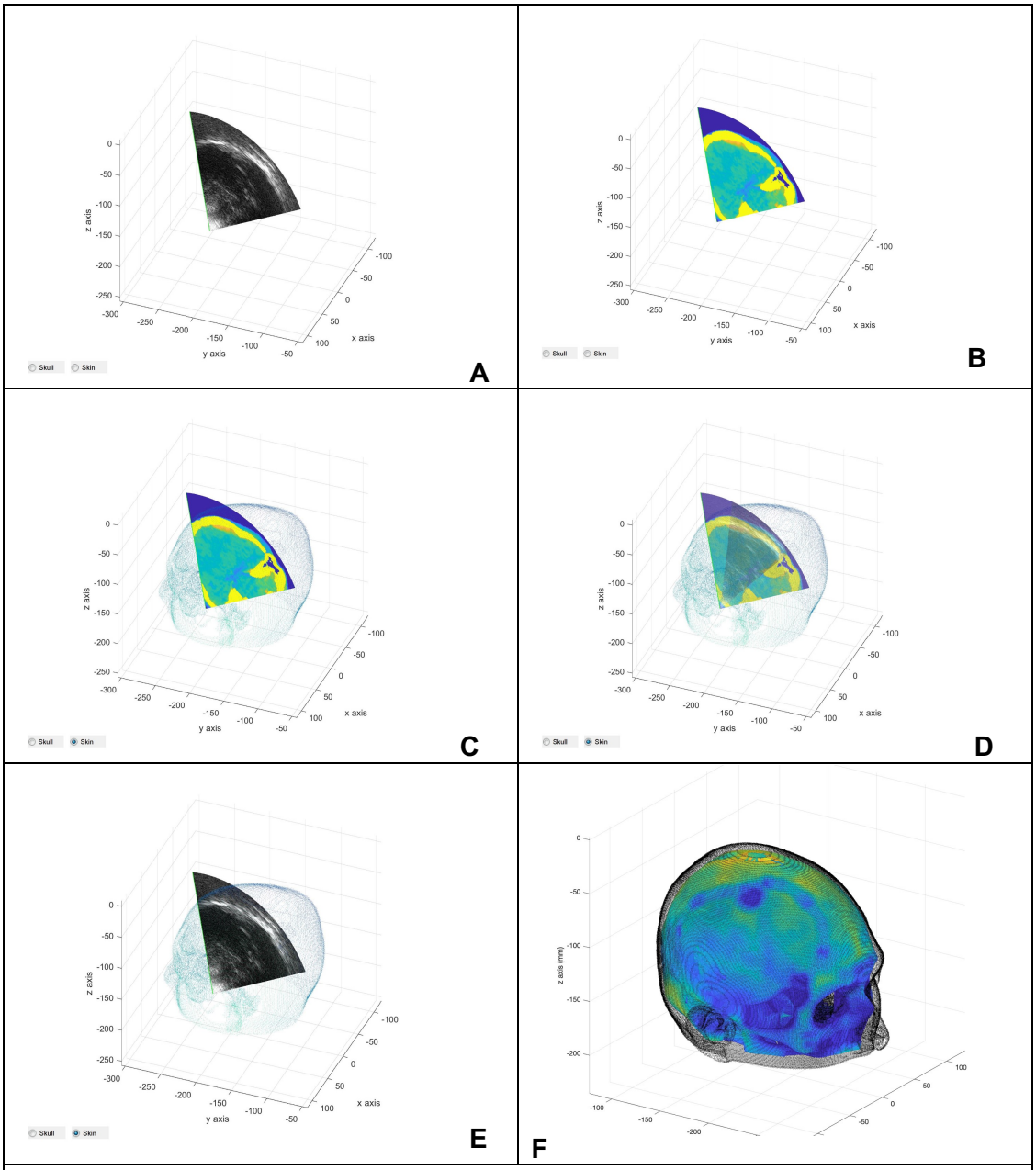


Figure1 shows registration of the CT and B-mode ultrasound images for our first test subject. **(A)** This figure shows the ultrasound image placed within the coordinate system in advance of co-registration with the **(B)** associated slice of the CT image, itself here superimposed on the ultrasound image. Figures **(C-E)** show different renderings of this co-registration, first (C) with a dominant view of the CT image, then (D) with comparable opacity and translucency, then (E) with the ultrasound image dominant. With this information we can then point to structures (hemorrhage as our main interest) in each of CT and ultrasound images. **(F)** This image shows the entirety of the CT image for this patient.

What was accomplished under these goals – second year summary.
In year two we had sufficient data to allow for development and testing of candidate algorithms. We started with individual images from a given patient for which had a fair bit of success developing ultrasound-based images using non-linear regression (Figure 2).

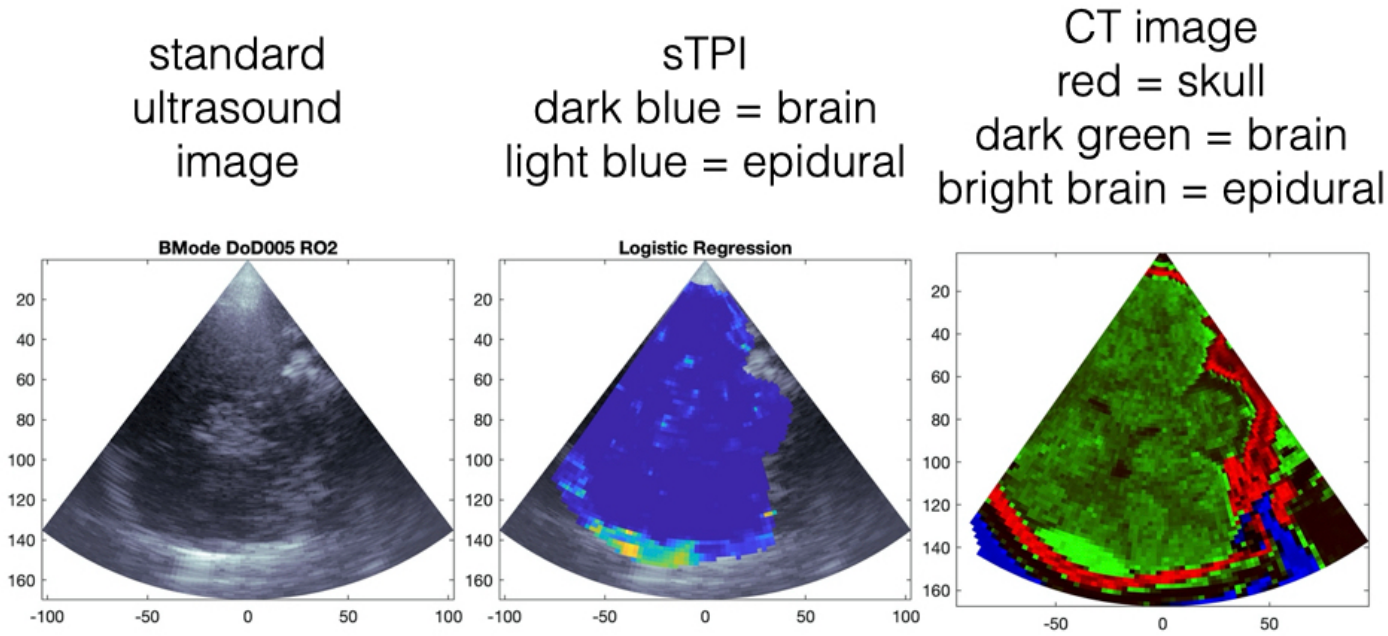


Figure 2. Epidural bleed. The left-hand image shows the B-mode ultrasound (gray scale) image derived from standard ultrasound imaging. The transducer sends sound through ipsilateral skull – here at the base of the triangular shape – and highlights a plane of tissue as well as an arc of bone (the white 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.

What was accomplished under these goals – third year summary.
Besides Covid, which slowed us down considerably (like everyone else), our continued nonlinear regression-based approach produced a mix of results, both good and bad. Sometimes we produced excellent images (Figure 3); sometimes we produced data sensitive to the *presence* of a lesion but otherwise did not capture the structure and position of the lesion (Figure 4). In all cases we achieved this level of accomplishments when we focused on a given patient. More problematic was that these approaches did not generalize well when developed on one patient (or group of patients) then applied to another, independent patient: in other words, these algorithms worked retrospectively but insufficiently so, prospectively.

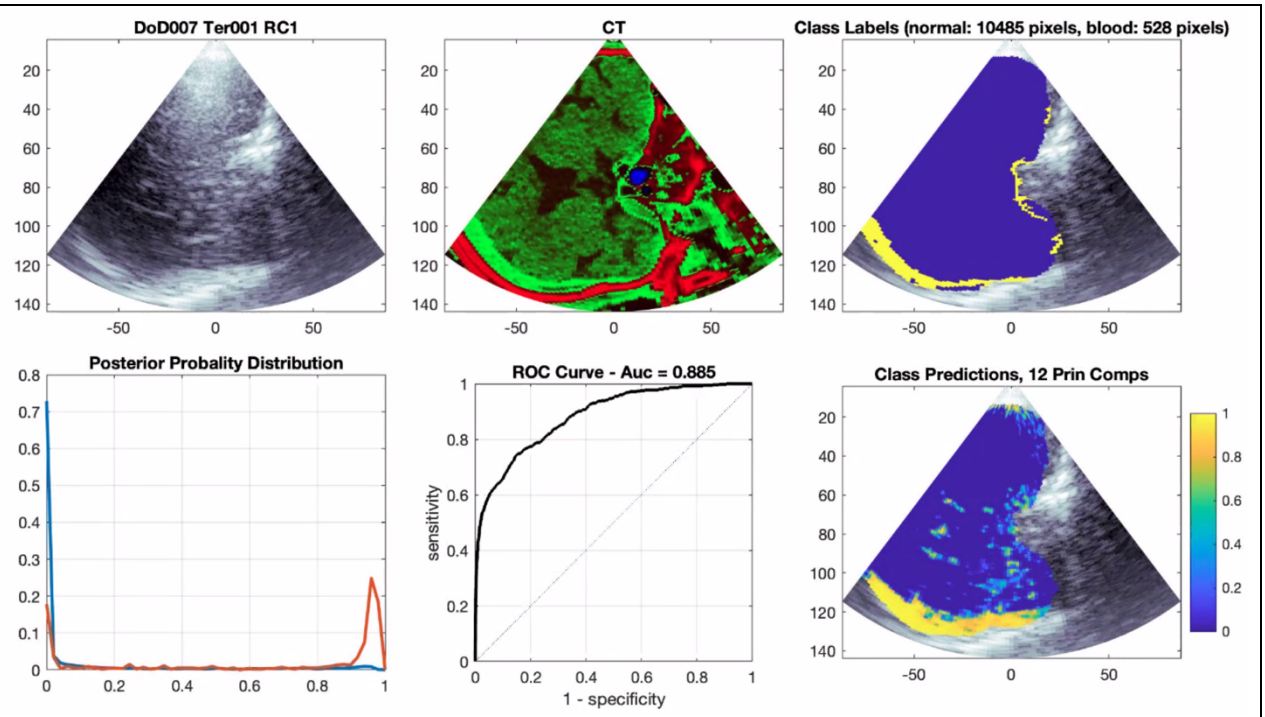


Figure 3. Epidural bleed – a successful imaging result.

Upper row. 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 middle image shows the plane within the CT image that overlaps with the B-mode image. Red highlights skull, dark green highlights brain tissue, and light green highlights the epidural bleed, all as defined by the pre-sets within the CT imaging software. The right-hand image uses the information from the middle image to identify 'bleed' from 'non-bleed' in the CT image, which we then project onto the ultrasound displacement data. That projection, in turn, allows us to characterize the brain tissue displacement in these two regions. We then use those characteristics to define a single metric for 'bleed' and another single metric 'non-bleed' for this image. With those two definitions in hand, we then apply a discriminate model to the ultrasound displacement data to determine how well that discriminate analysis can identify 'bleed' versus 'non-bleed' across all pixels in the ultrasound image plane. We show the result in the lower, right-hand image of this figure.

Lower row. The right-hand image shows the result of our retrospective analysis of brain-tissue displacement, here and throughout this report corrected for motion of the transducer relative to the patient's skull. This retrospective analysis both identifies the existence of, as well as actually images, this patient's epidural bleed (yellow arc, compare with the CT image). It also identifies a scattering of possible (but not probable) bleed sites within the parenchyma of the brain. The middle image shows the calculated sensitivity and specificity of this process of detecting blood versus non-blood containing brain tissue as a function of threshold choice (e.g., the threshold value for analyzed brain-tissue pulsatility in areas with 'blood' versus 'not blood'), with the 'area under the curve' or AUC equaling 0.89, an encouraging result. (The left-hand image is for internal analysis purposes only.)

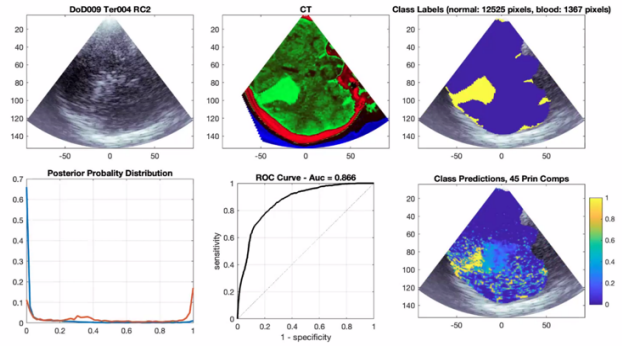


Figure 4. a primarily intraparenchymal bleed – a partially successful detection result.

Upper row. Same image *types* as in Figure 1, but for a primarily intraparenchymal bleed.

Lower row. Same image *types* as in Figure 1, but for a primarily intraparenchymal bleed. The right-hand image shows the result of our retrospective analysis of brain-tissue displacement for this case, analysis that both identifies the existence of and suggests the extent of an intraparenchymal bleed (a reasonable detection) while unfortunately only hinting at a subset of small subarachnoid and subdural bleeds.

This mixed success led us to adding machine learning to our armamentarium, which produced a range of *prospective* success, (Figure 5 & 6), an improvement over or relative failure with prospective application of our nonlinear regression algorithms.

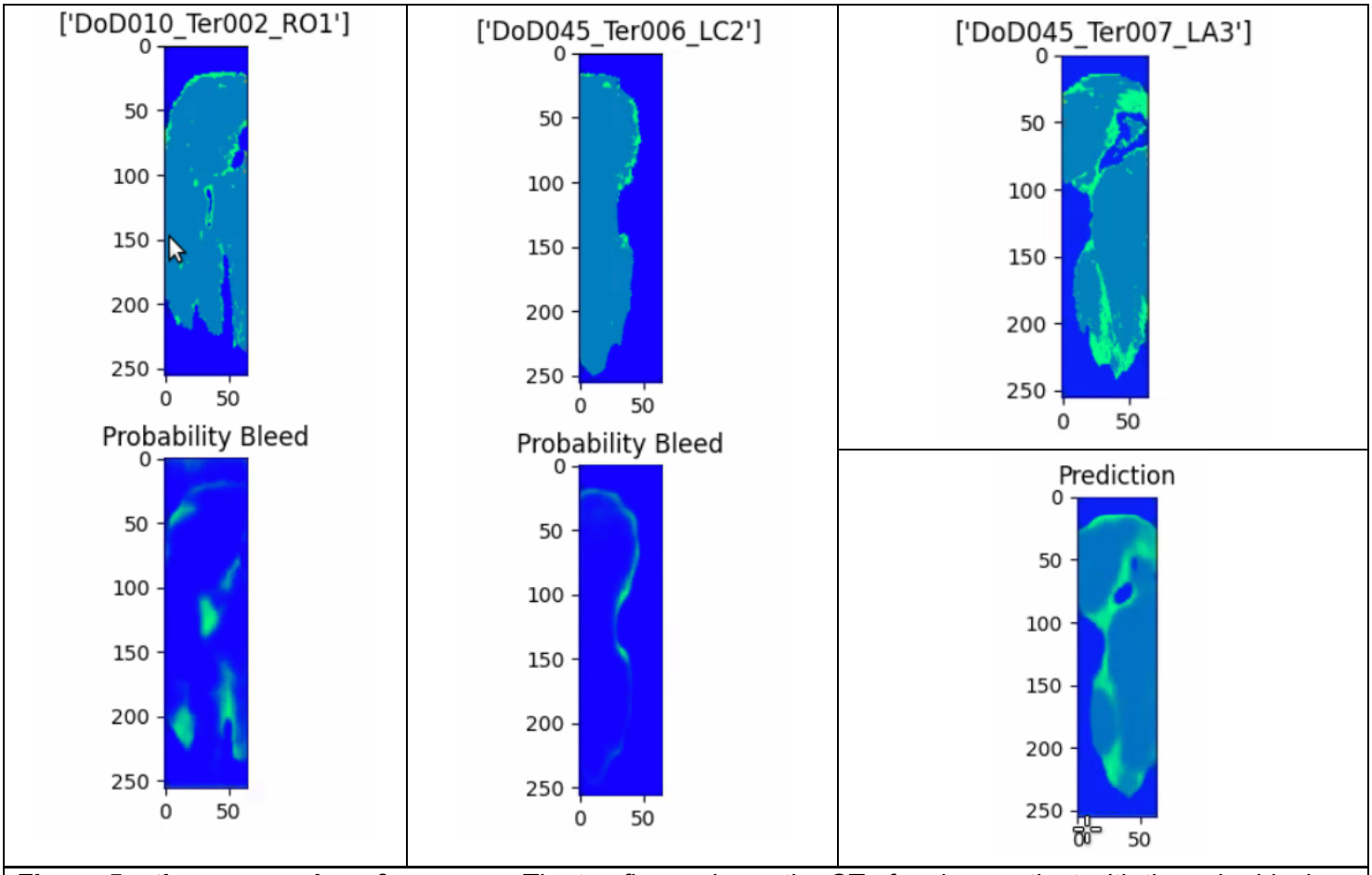


Figure 5 – three examples of success. The top figure shows the CT of a given patient with the color black denoting the extracranial space, the dark green denoting brain tissue and light green denoting blood. The bottom figure shows the prediction of bleed (light color) based upon machine-learning (ML) algorithms *not* used to build the ML model.

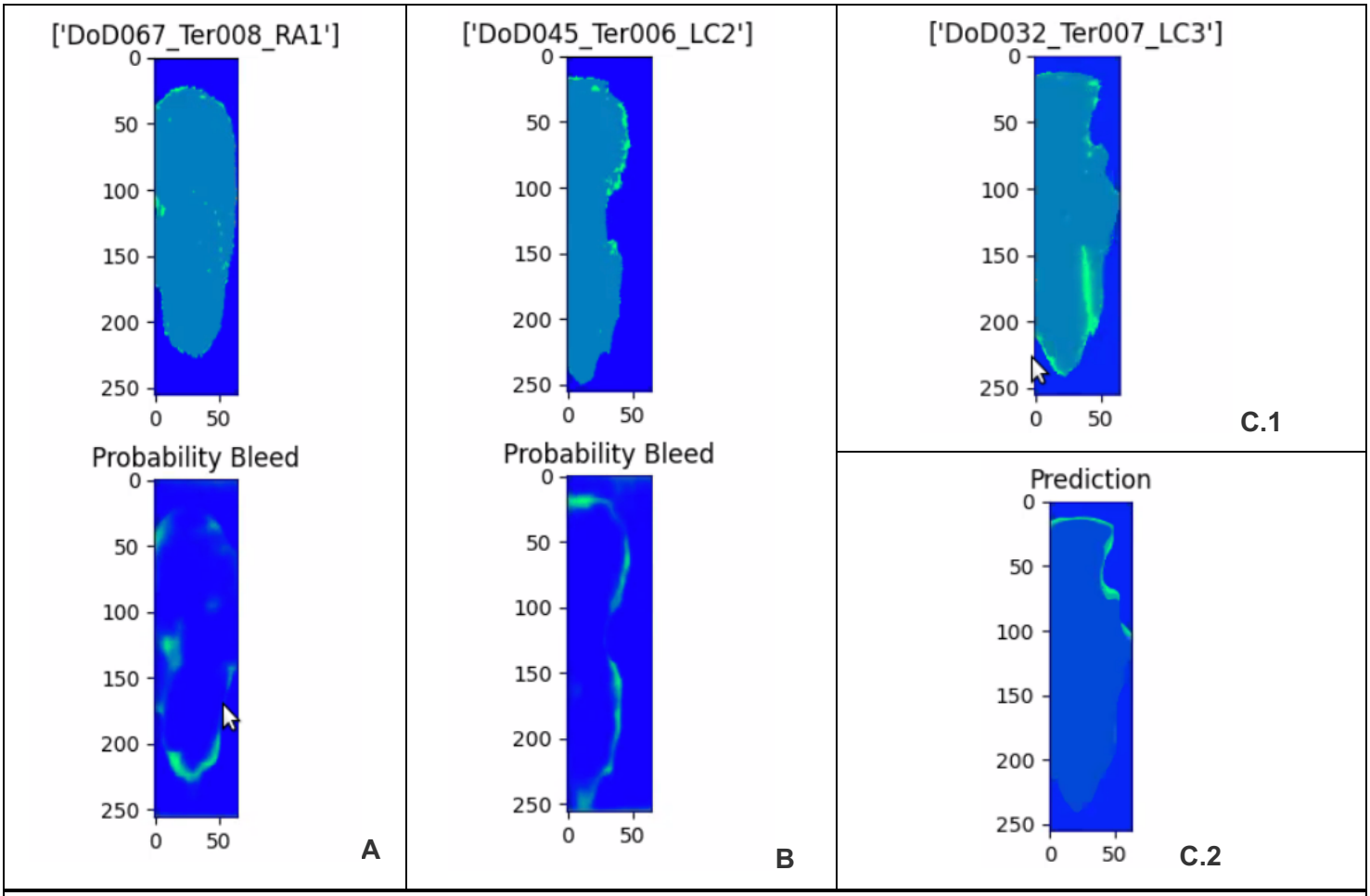


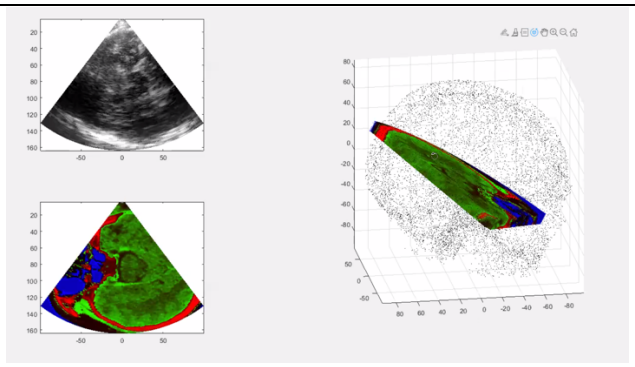
Figure 6 – three examples of mixed success. The figure pairs are the same as in Figure 1. In figure A, the model picks up some of the extra-axial bleed at the top and left-hand side of the CT image while missing a large extra-axial bleed t the bottom of the CT image. In Figure B each of the CT and predicted images highlight substantial extra-axial bleeds but the prediction misses the extra-axial bleed near the bottom of the CT image. In Figure C the prediction over-predicts the extra-axial bleed at the top of the CT image and completely misses the other bleeds.

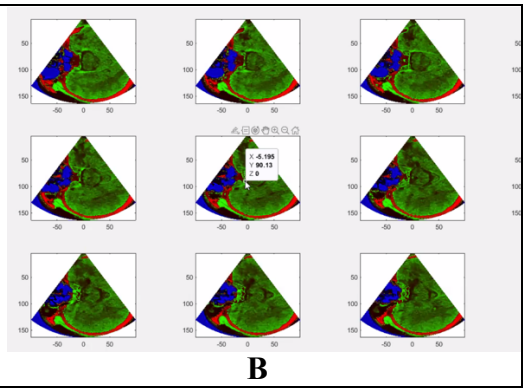
What was accomplished under these goals – final (fourth) year.

Covid continued to slow us down, reducing the amount of new data we could collect. Nonetheless, we collected the planned amount of retrospective CT and ultrasound data from TBI patients and trauma/non-TBI patients (Table 1).

Table #1 human data collected	Identified	Approached	Consented	Studied	Net Useful Data Sets Collected
Total	~477	272	156	130	130

We were also able to continue to analyze the data, albeit in a reduced way, continuing with our mix of nonlinear regression and machine learning. Also, we generalized our analysis that projected the ultrasound plane into the CT volume to mitigate against uncertainty in that projection (Figure 7).





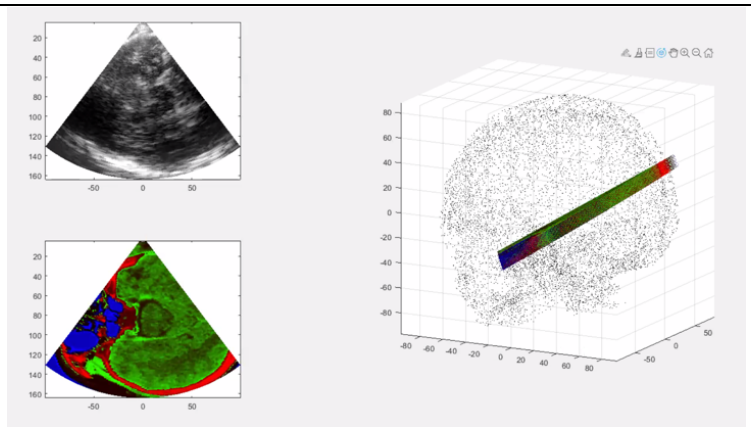


Figure 7. 'Thick' CT slices for comparing with our ultrasound images. (A) A composite image of diagnostic ultrasound (gray), the thin slice of CT image most likely corresponding with the ultrasound image (green and red, below), and the corresponding 'thick' CT image super-imposed on a rending of the patient's skull. **(B)** The eleven separate thin CT imagers whose summation builds into the thick CT image. **(C)** As in **A** but viewed from a different orientation.

In addition, we finished our ultrasound-based tablet, making it able to deploy any of our algorithms, here the midline shift calculation, discussed below (**Figure 8**).

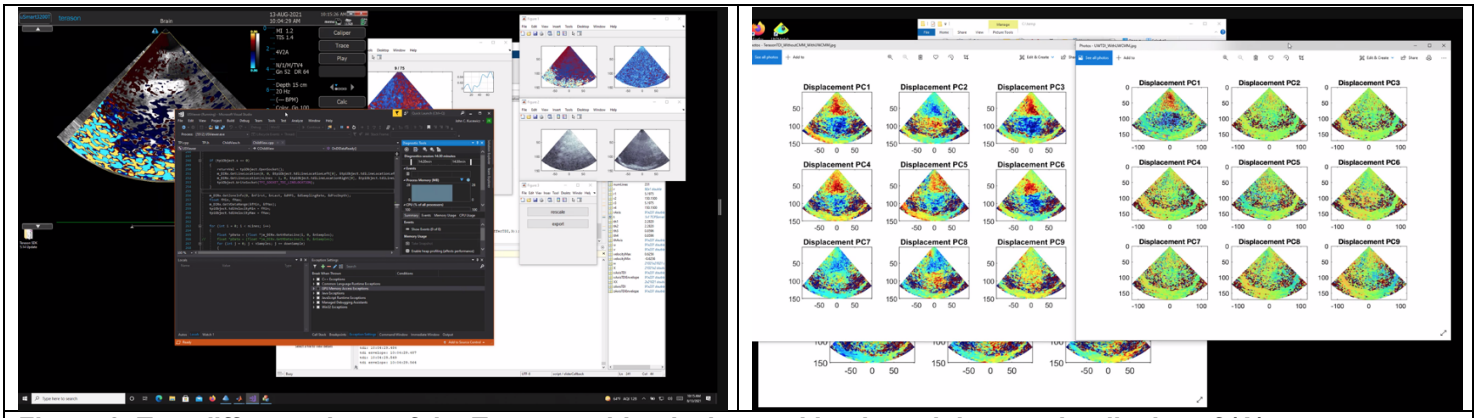


Figure 8. Two different views of the Terason tablet device working in real time on the display of (A) raw ultrasound data and **(B)** plots of brain-tissue pulsatility emphasizing different brain hemispheres (left) and skull detection (right).

Moreover, and importantly, we did not generate ultrasound-based images of intracranial bleeds with sufficient quality to compare one-to-one with CT images. Instead, as primary achievements, we demonstrated two other findings. First, we showed that our machine-learning based algorithms that used brain-tissue pulsatility, plus GCS (a readily available clinical marker) produced a sensitive means of detecting the presence of intracranial bleeds that would benefit from neurosurgical intervention (Mourad PD, report, Table #2). To improve this algorithm, we need data from patients with larger bleeds, patients excluded from our analysis because they received treatment before we could enter them in our study. We intend to pursue further funding that would ask for access to patients as they enter the emergency department.

Table 2.
For patients across all GCS scores, sensitivity/specificity between US+GCS and CT+GCS was 0.80 and 0.71, respectively.
F**or patients with mild to moderate GCS score** (GCS >=9), which represents the cohort of patients for which GCS would not automatically preclude intervention, sensitivity/specificity between US+GCS and CT+GCS was 0.80 and 0.38, respectively.
For patients with mild GCS score (GCS 13-15) sensitivity/specificity was 0.79/0.40.
For patients with moderate GCS score (GCS 9-12), sensitivity/specificity was 0.85/0.17.

Furthermore, we demonstrated that other analysis (not based on machine learning) produced a statistically significant and clinically significant metric for midline shift caused by intracranial bleeds (Kucewicz et al, **Figure 9a**; Marzban et al, **Figure 9b)**. For each method, we posit the existence of a 'center of brain pulsation' – supported by MR elastography analysis as centered in the middle of the brain for healthy test subjects. These two different approaches assay for differences between the actual center of pulsation of a brain with where it should be. In each case we compare against the midline shift measured from the patient's CT image. As above, to improve this algorithm, we need data from patients with larger bleeds, hence larger midline shifts, patients excluded from our analysis because they received treatment before we could enter them in our study. We intend to pursue further funding that would ask for access to patients as they enter the emergency department

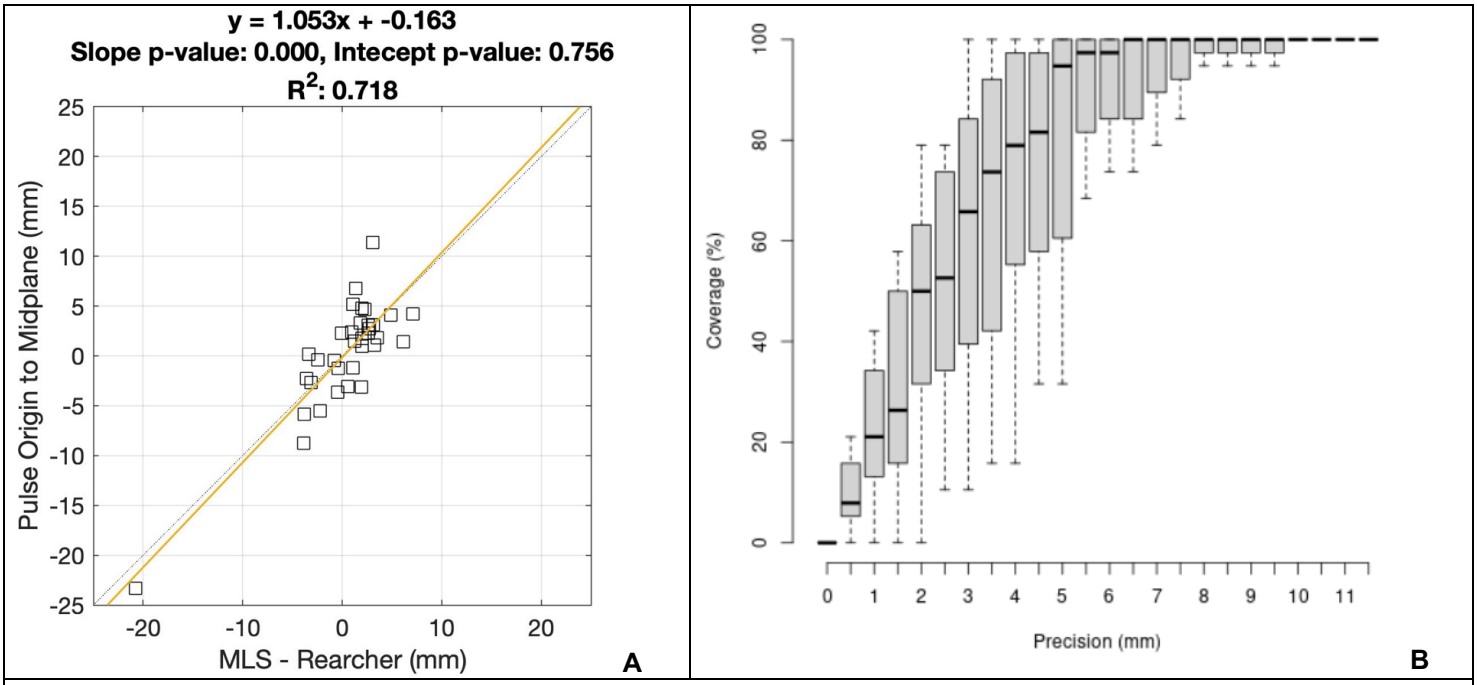


Figure 9. Novel analysis of brain-tissue pulsatility can quantitatively predict the extent of midline shift caused by intracranial bleeding. **(A).** Comparison of the 'pulse origin' inferred for a given patient based upon analysis of ultrasound images of their brain-tissue pulsation produces a strong correlation with midline shift (MLS), here derived from CT images by our research scientists (which strongly conform with the radiologist's defined MLS). Note the two regression lines: one includes the outlying point at 20 mm while the other doesn't. **(B)** Boxplots of MLS estimate ("coverage") as a function of precision in millimeters. For example, if the required precision is ±5mm, then the center of pulsation is correctly estimated in 95% of the scans on average; and that percentage can vary from around 30% to 100%. That precision increases as the criterion for identifying larger bleeds increases in size.

As secondary achievements, we demonstrated various ways to detect skull in ultrasound images, as a way of supporting algorithms that differentiate between skull and an adjacent bleed (epidural land subdural). For example, K-mean analysis of brain-tissue pulsatility usefully differentiated between bone and brain (Leotta et al, **Figure 10**).

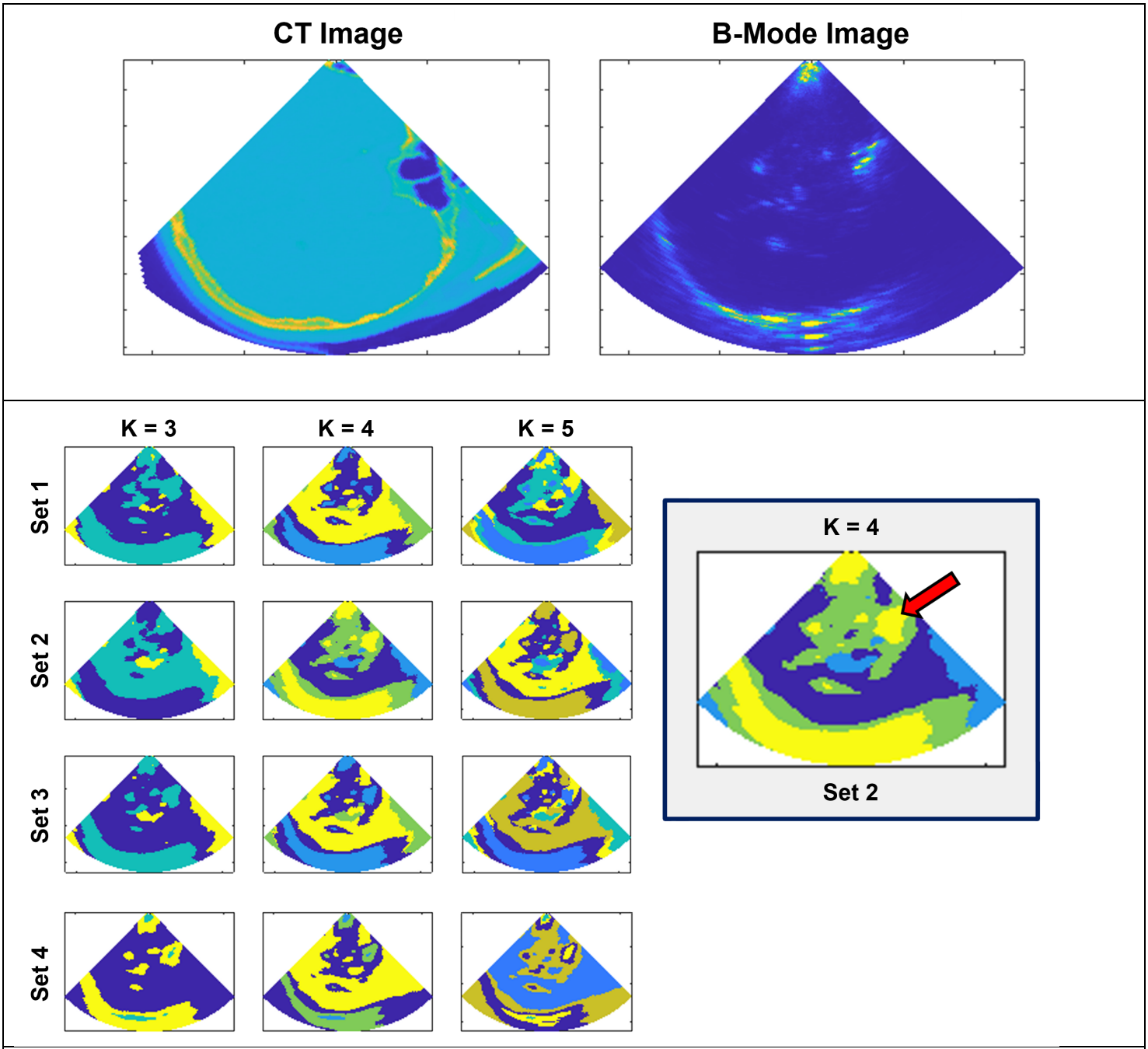


Figure 10. **(A)** CT image (left) and corresponding ultrasound B-mode image (right). **(B)** Multiple K-means results for the ultrasound pulsatility image corresponding with the images in A. A search is performed in each set of data for a discrete connected component in the region where a shadowing bone is likely (inset). If an object is identified in at least 5 of the 12 data sets then the brain mask is modified to include a shadow. In this case 7 of the 12 sets have a cluster that meets the criteria for a shadowing bone (red arrow).

We achieved similar bone-imaging results with machine-learning algorithms (**Figure 11a**), also as a step towards detecting intracranial bleeds next to bone. We also produced plausible images of ventricles (**Figure 11b**) without, unfortunately, adequately imaging intracranial bleeds (Phan, MS Thesis; also Thomas, MS Thesis).

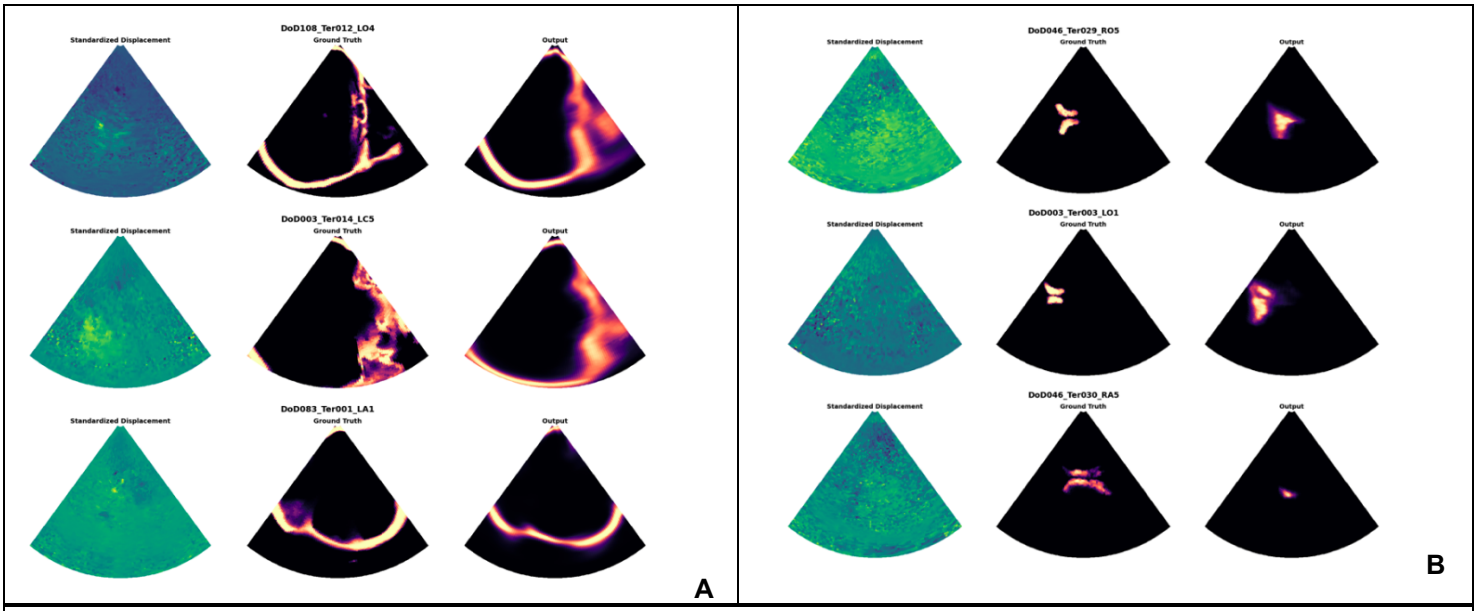


Figure 11. (A) Example skull imaging using machine learning algorithms, specifically the U-Net model: (A-left) ultrasound-derived displacement image; (A-middle) CT data showing skull in white; (A-right) model prediction of skull. **(B)** Example ventricle imaging using machine learning algorithms, also thel U-Net model: (B-left) ultrasound-derived displacement image; (B-middle) CT data showing ventricles in white; (B-right) model prediction of ventricles.

What opportunities for training and professional development has the project provided?

Nina LaPiana, a biology major at the University of Washington, became an expert in analyzing CT- and ultrasound-based images of brain. She now works for another researcher, learning how to use MRI to analyze brain.

Lucas Chen, a biology major at the University of Washington, has moved on to medical school, where he continues to focus on ultrasound, anticipated it as part of his medical practice.

Cory Kelly, a masters-level research technician, helped analyze our data as well, and now works for NIH as a program officer and has entered graduate school in bioengineering.

William O. Thomas developed machine-learning algorithms that allowed him to receive his master's degree and will go on to industry.

Nutt Pham, also developed machine-learning algorithms that allowed him to receive his master's degree and will go on to industry.

How were the results disseminated to communities of interest?
I have given grand rounds talks at the University of Washington. We have submitted one paper, have three others under construction, all as listed below.

Next steps and relevant strategies required to move the candidate product to the next phase of development and/or commercialization, including property.
We intend to work with our industrial partner to retrospectively refine then prospectively test our novel midline shift algorithm as deployed on their device, with a novel headset. We have disclosed to the University of Washington our invention of a midline shift detection algorithm and supporting device.

Future direction and next steps for this project.
Follow-on-funding for this project.
Not yet, though we intend to go to NIH for SBIR funding and remain interested in further DoD funding.

Next step(s) for this project?
Seek further funding to move the midline shift algorithm forward.

Lead candidate product?
(b)Diagnostic & (c)Device

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project (e.g., so what)?
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 therefore anticipate that a hand-held device capable of rapidly determining the presence of neurosurgically treatable intracranial bleeds (via our ML+GCS algoritm and our midline shift detection algorithm) 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 versus hemorrhagic stroke: if an ischemic stroke, the on-site medical providers can push drug-based therapies without fear of damaging the hemorrhagic stroke patient.

What was the impact on other disciplines?
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 have developed novel algorithms beyond the state-of-the-art tissue pulsatility algorithms: midline shift quantification most notably, along with a novel headset design. Terason, the privately held company from which we have purchased our tablet-based system will shortly begin to negotiate with UW to license this technology, to embody our midline shift algorithm on their tablet-based ultrasound system embodying our midline shift algorithm.

What was the impact on society beyond science and technology?
We anticipate that a hand-held device capable of rapidly identifying neurosurgically treatable intracranial lesions, which will help improve patient outcomes by facilitating patient triage in the field rather than in the hospital as currently required. With improved patient outcomes we expect to also reduce the cost of health care.

How does your candidate product aid the Warfighter, Veteran, Beneficiary, and/or General Population?
We anticipate that re-analysis of our algorithms with inclusion of more patients with large lesions will allow us to finalize our algorithm and make it available to deploy in civilian and military contexts. As stated above, we anticipate the availability of our algorithm, deployed on the Terason mini, to improve patient outcomes as well as reduce th cost of health care.

5. CHANGES/PROBLEMS:
Final report, so nothing to report.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

  Leotta DF, Kucewicz JA, LaPiana NJ, Mourad PD. Automated Brain Segmentation for Guidance of Transcranial Tissue Pulsatility Image Analysis. *Submitted to Computer Methods and Programs in Biomedicine***.**

  Kucewicz JA, LaPiana NJ, Moore A, Marzban C, Mourad PD. Ultrasound-based measure of the center of brain pulsation of trauma patients. *Under construction for Ultrasound in Medicine and Biology.*

  Marzban C, Kucewicz JC, Leottta DF, LaPiana NJ, Mourad PD. A Method for Estimating the Location of the Brain's Center of Pulsation Using Ultrasound. Under construction for Ultrasound in Medicine and Biology.

  Thomas WO. Human Cranium, Brain Ventricle and Blood Detection Using Machine Learning on Ultrasound Data. (2022) Master's thesis, Computer Science, University of Washington, Bothell campus.

  Phan N. Deep Learning Methods to Identify Human Cranium, Brain Ventricles, and Intracranial Hemorrhage Using Tissue Pulsatility Ultrasound Imaging. (2022) Master's thesis, Computer Science, University of Washington, Bothell campus.

- **Technologies or techniques**

  Novel application of diagnostic ultrasound to detect midline shift due to intracranial lesions, reported above.

- **Inventions, patent applications, and/or licenses**

  Reported above; provisional patent under construction, licensing under consideration

- **Other Products**

NA.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Only members of the University of Washington participated in this project.

Individuals who have worked on the project.

Name. **Project Role.** **Nearest Person Month.** **Contribution to project.**	Pierre D. Mourad, PhD PI 33%/month leadership
Name. **Project Role.** **Nearest Person Month.** **Contribution to project.**	John Kucewicz, PhD Scientist/engineer 80%/month data-collection & analysis
Name. **Project Role.** **Nearest Person Month.** **Contribution to project.**	Nina LaPiana Scientist 100%/month Data collection and organization; attending to FITBIR
Name. **Project Role.** **Nearest Person Month.** **Contribution to project.**	Caren Marzban, PhD Mathematician 20%/month Data analysis
Name. **Project Role.** **Nearest Person Month.** **Contribution to project.**	Cory Kelly Scientist 50%/month Identifies candidate patients; interprets images
Name. **Project Role.** **Nearest Person Month.** **Contribution to project.**	Various undergraduates Neurobiology 30%/month Data organization/processing
Name. **Project Role.** **Nearest Person Month.** **Contribution to project.**	Jason Caucutt Research Coordinator 10%/month Informs/consents patients
Name. **Project Role.** **Nearest Person Month.** **Contribution to project.**	Dan Leotta, PhD Scientist/engineer 30%/month data analysis

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS: provided separately.

9. APPENDICES:

I have uploaded separate documents that detail our results, draft or submitted copies of our papers.