Feasibility of Imaging Ischemic Stroke Through the Skull Using Ultrasound Tomography

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***Abstract*—Stroke is a significant cause of mortality and disability in America. Due to differences in ischemic and hemorrhagic stroke, imaging must be performed before administration of therapeutic medication; however, the nature of both CT and MRI imaging can induce delays in triage time. Recent work suggests that ultrasound tomography (UST) is capable of imaging *in vivo* tissue properties and may have potential as a diagnostic tool during stroke treatment which could be performed at the patient's location rather than at a local hospital. In this work, we investigate the feasibility of using UST imaging to detect ischemic stroke in tissue-mimicking environments in both *in silico* and *in vitro* studies. The results of this work dictate the challenges which must be overcome in order to effectively image *in vivo* stroke patients.**

***Index Terms*—Ultrasound Tomography, Ultrasound Computed Tomography, Trans-cranial Ultrasound, Bran Imaging**

I. Introduction

Per the American Heart Association, stroke is the number 5 cause of death in the United States and the leading cause of disability [1]. The majority of strokes are due to clots that block blood supply to the brain, and imaging is key to triaging and planning treatment [1], [2]. Even with optimal treatment, stroke survivors can suffer from severe long-term impairment and increased mortality [3].

Currently, imaging is a key step in triaging and planning stroke treatment. Standard clinical imaging modalities currently include CT and MRI to rule out hemorrhage, both of which require transportation of the patient to a nearby hospital. In practice, the time needed to transport the patient to a hospital and the subsequent triaging are major factors that define current door to needle time, which defines the delay in administration of thrombolytics to prevent further damage [3]. Therefore, the greatest barrier to reducing this time is the lack of a triaging method that can be deployed before the patient is transported to the ER.

To that end, some hospitals use mobile CT vans or Mobile Stroke Units [4]. However, these options are not widely available, especially in rural and under-resourced areas owing to high capital and maintenance expenses [5]. Point-of-injury brain imaging for rapid stroke assessment and triaging is a major unmet need. Ideally, a portable, low-cost device that can be carried in a typical ambulance and used at the site (e.g., patient's home), would make early interventions widely available *thereby minimizing delays in treatment and positively impacting stroke recovery.*

Ultrasound tomography (UST) has emerged as a clinical modality capable of quantitatively imaging in vivo tissue parameters which may provide improved or expedited imaging through the skull as compared to current imaging modalities [6]. Additionally, US imaging through the skull has become a topic of increased interest in recent years [7]. Therefore, in this work, we investigate the feasibility of using UST to characterize ischemic stroke utilizing simulation data, *in vitro* phantoms, and *ex vivo* tissue samples.

II. Methods

A. k-Wave Simulation Images

Initial investigation into imaging through the skull utilized *in silico* experiments with the k-Wave MATLAB toolbox to simulate the emission, propagation, and reception of sound waves through a head model [8]. The model is derived from piece-wise transforming CT pixel values (Hounsfield Units) of brain scans to sound speed and density [9]. Simulated imaging of the model is conducted using an 'ideal' low-frequency 1024 element ring transducer with a 22cm diameter (1 MHz center frequency, 75% fractional bandwidth). These simulations generated numerical RF data, both with and without noise, that were then processed and reconstructed using our existing UST algorithms. The reconstructed images were then compared to the "truth" image, as shown in Fig 1A, to benchmark ideal UST image quality and define limitations. All simulated and real data in this work were reconstructed using full waveform inversion (FWI) reconstruction. Briefly, the 2D Helmholtz equation is solved using finite difference methods, and this is compared to measured data at the ring array at discrete frequencies. For *in silico* data, the process is repeated every 10 kHz from 50 kHz to 600 kHz with three iterations per frequency. Full details of the FWI reconstruction algorithm can be found in [10].

B. Ex Vivo Thrombus Characterization

For all experiments, UST imaging was performed on a Verasonics Vantage 256 system (Verasonics Inc., Kirkland, WA) with a 1024-element ring array (TransducerWorks, LLC, Centre Hall, PA; 3 MHz center frequency, 1-4 MHz Bandwidth) [11]. The transducer was driven at 700 kHz to ensure appropriate low frequency content in the waveform to begin full waveform inversion image reconstruction [10]. In the first

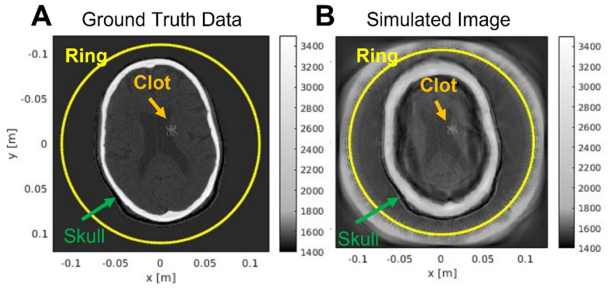

Fig. 1. A) Image of the ground truth sound speed values of the simulated media with a simulated blood clot inserted digitally near the ventricle. B) K-wave simulated data propagated through the medium in (A) were reconstructed using FWI reconstruction.

experiment, mechanically retrieved blood clots from standard treatment of two ischemic stroke patients were obtained using an IRB-approved protocol. After retrieval, clots were flash-frozen and stored until the imaging day, at which point they were thawed and inserted into a condom filled with isotonic saline in order to preserve physiological relevance. Once the clots reached room temperature of approximately 20°C, they were imaged with UST to characterize tissue properties in vitro (Fig. 2A). For all physically-acquired UST images in this study, reconstruction was performed using FWI techniques (350-800 kHz, 50 kHz step size) to generate sound speed and attenuation images, while traditional reflection images were also generated to aid with localization of the features.

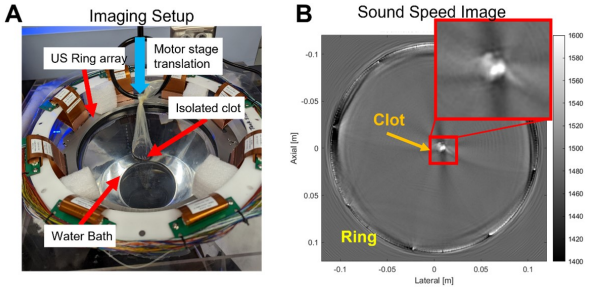

Fig. 2. A) Image of the experimental 3D imaging setup for ex vivo blood clots. B) Reconstructed sound speed image slice from an ex vivo blood clot.

C. In Vitro Phantom Imaging and Characterization

After validating that ex vivo clots could be visualized, a human replica skull (Skulls Unlimited Inc., Oklahoma City, OK) was used to demonstrate our current ability to image through bone-mimicking material. The skull phantom was filled with an 8% gelatin mixture (Sigma-Aldrich, Inc., St. Louis, MO) along with two inclusions which were filled with a mixture of 8% gelatin and 20% isopropyl alcohol to create high sound speed imaging targets (i.e., ~1600 m/s; Fig. 3 A, B) [12]. UST images were taken of a representative cross-section of the phantom, and FWI reconstruction was performed with standard parameters as listed previously.

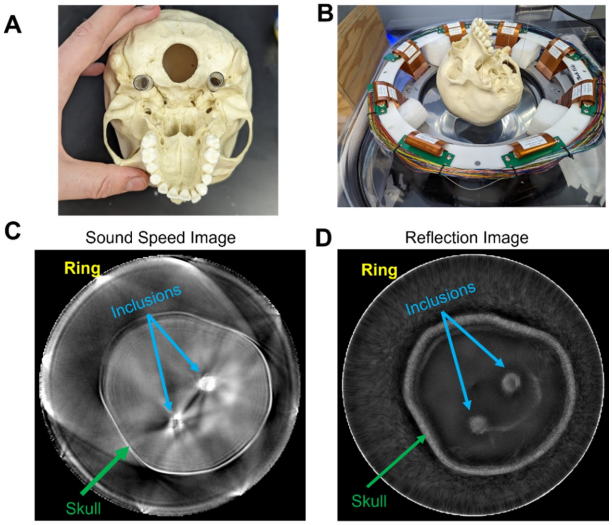

Fig. 3. A) Depiction of where high sound speed inclusions were created in the skull phantom. B) Photograph of the skull phantom while preparing for UST imaging. C) Sound Speed image of a representative slice showing the skull boundary and two high sound speed inclusions, along with cycle skipping artifacts. D) Matched reflection image to (C), validating the locations of the skull boundary and the inclusions.

D. In Vitro Phantom containing ex vivo thrombus

Finally, a third *ex vivo* blood clot was sourced and then embedded in an 8% gelatin mixture within the skull phantom (Fig. 4A) and imaged to determine the feasibility of resolving a clot through the skull with both sound speed and reflection imaging. UST images were taken of a representative cross-section of the phantom, and FWI reconstruction was performed with standard parameters as listed previously.

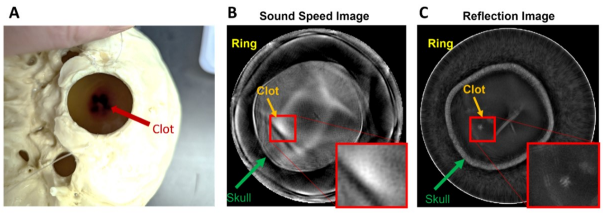

Fig. 4. A) Retrieved blood clot inserted into the same skull phantom from Fig. 3. B) Sound speed image of a representative slice showing the skull boundary as well as the clot. C) Matched reflection image to (B), validating the location of the clot as well as the skull boundary.

III. Results

K-Wave simulations support our hypothesis that UST is capable of imaging pathologies through the skull, providing a roadmap for experimental work (Fig. 1B). The two retrieved stroke blood clots showed heterogeneous sound speed values ranging from 1520-1630 m/s when imaged in water at room temperature (Fig. 2B). Using our current hardware setup, we successfully imaged the high sound speed inclusions through the replica skull, albeit with cycle skipping due to the relatively high-frequency content of the waveform (Fig. 3 C,D). We also successfully visualized a retrieved human blood clot within

a replica skull, thereby defining the baseline challenges (i.e., cycle skipping, skull mapping) that will guide future technique development. (Fig. 4 B,C).

Discussion

In this work, we present validation that UST imaging can detect a blood clot in a realistic simulation environment, while also detecting both generalized regions of high sound speed such as *ex vivo* blood clots in real experimental data. These results show that UST imaging is feasible through a skull-mimicking phantom, although further work is needed to optimize the imaging and reconstruction due to the presence of significant artifacts.

Retrieved *ex vivo* blood clots displayed contrast in all imaging reconstructions performed (i.e., reflection and sound speed), and sound speed values recorded were consistent with literature values at similar temperatures and clot ages [13]. High sound speed inclusions within the skull phantom were also visible in all three reconstructions; however, the presence of artifacts in both reflection (due to refraction) and sound speed (due to cycle skipping) images demonstrate the need for improvement. These artifacts continue to provide challenges in the final experiment with a retrieved *ex vivo* clot inside the skull phantom.

The artifacts present in this work can be overcome by addressing two sets of issues that can be loosely grouped into hardware and software concerns. Hardware concerns to address include low signal to noise ratio (SNR) at our desired imaging frequencies and lack of signal at sub-300 kHz levels, leading to cycle skipping artifacts [10]. As the skull attenuates ultrasound waves more significantly than soft tissue, additional techniques such as virtual sources must be investigated in order to improve SNR after through transmission. Additionally, starting FWI reconstruction at lower frequencies can help to overcome cycle skipping artifacts in imaging samples with high sound speed discontinuities as we expect to see with the skull. Software concerns include investigation of adaptive waveform inversion [14] and the introduction of a two-component model [15] in order to help generate additional low frequency content and provide an accurate starting model, respectively.

Conclusions

This work shows that UST imaging is feasible through a skull-mimicking phantom for a variety of targets. Simulations of realistic blood clots, as well as *in vitro* examples could all be visualized in sound speed images despite the presence of cycle skipping artifacts.

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