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Image-guided Application and Monitoring of Transcranial Focused Ultrasound in Realistic Human Head Phantom

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***Abstract*—Dual-mode ultrasound arrays (DMUAs) have been used for monitoring and delivery of transcranial focused ultrasound (tFUS) in small-animal models *in vivo*. Synthetic-aperture (SA) imaging can be used for stereotaxic guidance, while high frame rate imaging modes, such as single-transmit focus (STF) imaging, can provide feedback for thermal and mechanical closed-loop control of lesion formation and neuromodulation. The objective of this study is to demonstrate the feasibility of DMUA guidance and control of tFUS application in a realistic human head phantom. A DMUA was used to image through the temporal bone of the phantom in SA and STF modes. Results from the SA imaging mode demonstrates the ability to image fine targets such as vessels with aneurysms. Additionally, subaperture processing of SA data shows it is possible to reduce reverberation. Results from the STF imaging mode show the feasibility of speckle tracking using transranial echo data, both with and without subaperture processing. These results demonstrate the value of judicial design of subaperture beamforming for identifying tissue structure and improving speckle statistics for high fidelity thermography and elastography. Results from tFUS-monitoring experiments will be given.**

***Index Terms*—Subaperture beamforming, Realistic Phantom, Transcranial FUS**

I. Introduction

Transcranial focused ultrasound (tFUS) is currently being investigated as a potential treatment modality for a range of neurological disorders such as epilepsy and stroke [1], [2]. One exciting development in tFUS research is the demonstration of blood brain barrier (BBB) opening in animals by Kullervo Hynyn and his co-workers [3], [4].

The key advantage of tFUS is the potential for very precise spatiotemporal control of the therapeutic patterns. In principle, tFUS bioeffects can be confined to volumes on the order of $300 \times 500 \times 2000$ μm^3 (corresponding to the focal spot size). It is possible to maintain this resolution in transcranial applications when using a transducer array with phase and amplitude control of individual array elements to correct for the aberration incurred by the skull. Even without this correction, it is still possible to deliver targeted therapy. In [5], we have shown that tFUS beams, while distorted, still produced localized heating very near the target point. However, the degree of distortion was dependent on the geometry of the skull.

Distortions caused by the skulls have been a general problem in tFUS applications. The groups of Hynynen [8] and Fink [9] have employed numerical modeling of the propagation through the skull to account for its distortion. The 3D propagation model was obtained from x-ray CT or MRI scans of the subject prior to the application of tFUS and performed off line as a form of treatment planning. Because the therapy and imaging modes share a common coordinate system, one advantage of using a DMUA for therapeutic applications is that the distortion of the imaging beam will inherently correspond to the distortion of the therapy beam. Thus, if a transcranial target can be identified and targeted using the imaging modality, it is possible to say with a high degree of confidence that therapy modality will be successfully applied to the same target. In this paper, we present how the DMUA can be used for three-dimensional, imaging-based targeting for guiding tFUS therapy in a human skull phantom.

We have recently demonstrated a sterotaxic approach to targeting specific structures with rodent brains *in vivo* using dual-mode ultrasound arrays (DMUAs) [6]. Three-dimensional synthetic aperture (SA) imaging was used to render the skull surface and identify the suture lines (bregma, lambda and medial) as anatomical markers for precise placement of the tFUS beam. In addition, we have developed real-time imaging techniques for monitoring and control of tFUS application *in vivo* [6] as well as image-based refocusing *in vitro* [7]. In this paper, we present the first results of applying our guidance and monitoring techniques on a realistic human head phantom. We present first imaging demonstrating access through the temporal bone at frequencies in the 2.5 - 4.8 MHz using SA imaging. In addition, we present results from sub-aperture processing of SA data that demonstrate the potential advantages in reducing or eliminating reverberation artifacts to enable quantitative imaging and speckle tracking for monitoring and assessment of tFUS application.

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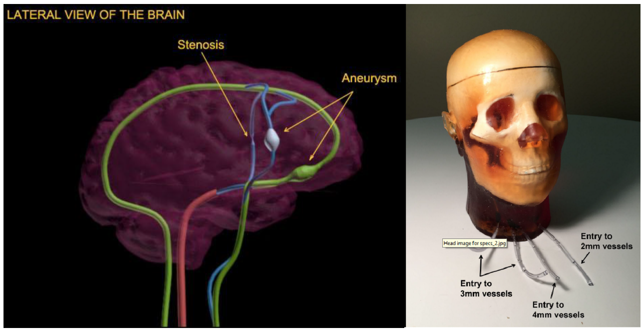

Fig. 1. Standard Adult Head Flow Phantom (True Phantom Solutions Inc.)

II. Methods

Experiments are performed using a static adult head flow imaging phantom from True Phantom Solutions (Windsor, Ontario). The head is composed of tissue- and bone-mimicking materials, as seen in Fig. 1. Inside the cranial cavity, there is a network of tubing to simulate vasculature with two simulated aneurysms, one stenosis, and a few vessel bifurcations. The white aneurysm in Fig. 1 behind the temporal bone is used as the target, as it is a good specular reflector, demonstrates the feasibility of targeting shallow internal structures, and is located in a region of the brain which is a good candidate for other tFUS applications, such as treating temporal lobe epilepsy or glioblastomas.

Two dual-mode ultrasound arrays (DMUAs) prototypes are used to insonicate the head phantom. The first DMUA was a 3.5 MHz spherical transducer array with a radius of curvature of 50 mm. The array has 64 elements, split into an upper and lower row of 32 elements each. This DMUA is supported by the HIFU Synthesizer^{TM} (International Cardio Corporation (ICC)), hereafter referred to as the Synthesizer. The Synthesizer is supported by a 64-channel linear amplifier. This transducer is coupled to the phantom using a water bolus and connected to 3 orthogonal stepper motors which serve as a 3D-positioning system to accurately move the transducer to specific target locations on the phantom 2. The second DMUA is a 2.25 MHz center frequency, spherically-focused, 64 element array with a radius of curvature of 100 mm. The second DMUA is placed in a waterbath with the phantom to view the skull, aneurysm, and the simulated brain tissue deeper in the skull.

A. Imaging Modalities and Methods

Single Transmit Focus (STF) imaging is the spherically focused array equivalent of plane wave imaging used in linear arrays. This imaging modality has several advantages. Firstly, it has a high frame rate; this is useful for real-time monitoring and quantitative feedback about the effects of sub-therapeutic ultrasound delivery during therapy. Additionally, the focal point of this imaging modality inherently corresponds to the focus of the therapy beam, thereby providing information about the distortions of the therapy beam incurred by the skull. Finally, the focal point provides increased energy deposition

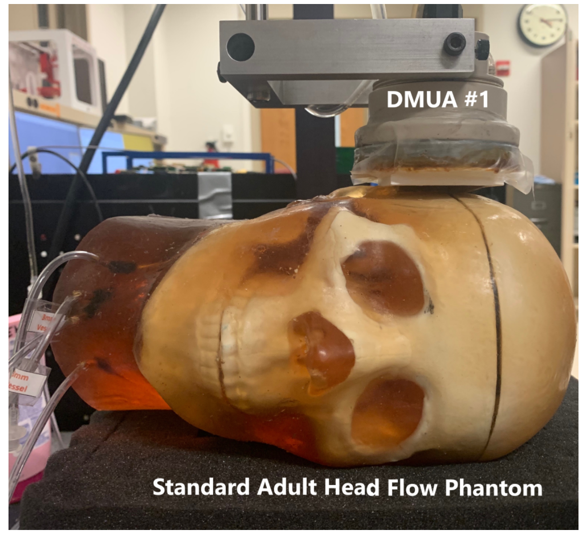

Fig. 2. Experimental Setup with DMUA Bolus and 3D positioning System

and resolution of the target before therapy. Synthetic Aperture (SA) transmits an imaging pulse for each transducer individually in the array, and subsequently collects echo data for each element. The individual transmissions allows for the subaperture beamforming developed in this work. Subaperture analysis gives information about the angular dependence of specular reflections from targets, such as the skull and aneurysm. SA imaging is also very useful in the detection and stereotaxic location of transcranial targets.

III. Results and Discussion

Figure 3 shows a -60 dB screen captures from the Synthesizer^{TM}. The images shows several specular reflections from the bolus membrane near the top, the outer and inner tables of the skull as well as the aneurysm (arrow). The echo from the aneurysm is evidence of tFUS transmission through the temporal bone (equivalent) and its appearance was confirmed in 3D scans (where it comes in and out of view). Furthermore, in the lower image, the speckle around the aneurysm appears mixed with reverberation components due to the multiple reflections in the low attenuation layer of encapsulating the skull. Figure 4 shows the sub-aperture imaging results demonstrating the feasibility of accessing brain tissues through the temporal bone. The images were formed by beamforming on all receive channels while transmitting on 8-element subapertures with 4-element overlap. The top 8 panels are images from 7 such supapertures from the top row of elements and the 8th image is a compounded from all transmissions. The lower 8 panels were obtained by using the same procedures with the lower row of array elements. The images are displayed with a dynamic range of 60 dB.

The appearance of the aneurysm varied depending on the orientation of the transmit suapertures, but it was visible in all images. For example in the tSub-1 images (upper left), the aneurysm appears as a blob (arrow). The tSub-1 subaperture is on the posterior side while tSub-7 is on the anterior side

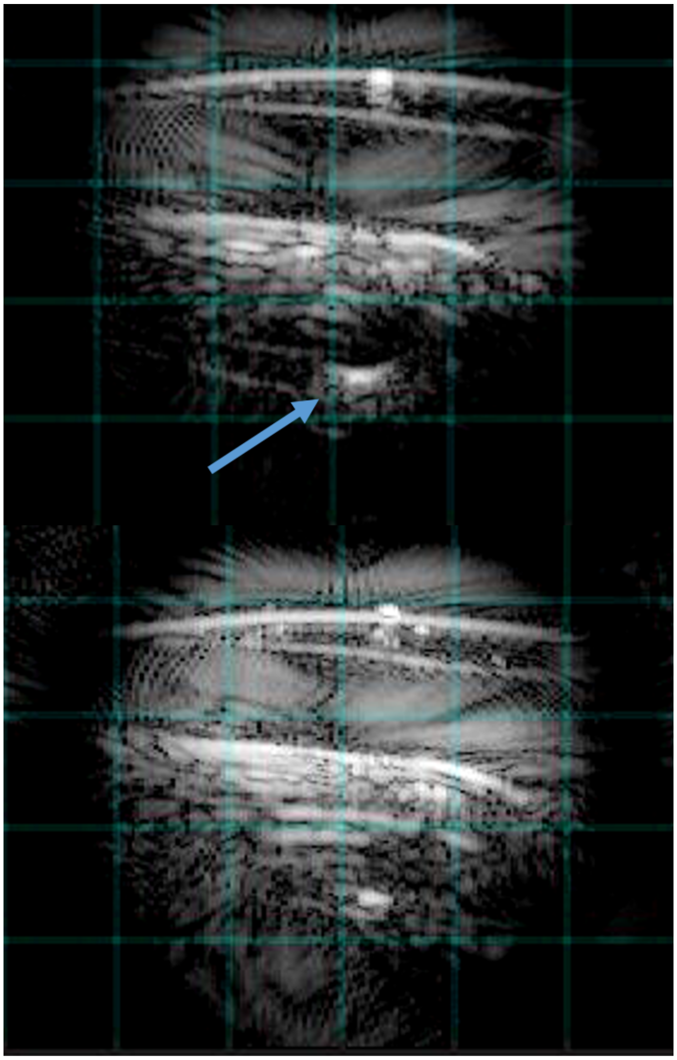

Fig. 3. Grayscale images (60 dB) screen captures from the Synthesizer^{TM} showing the aneurysm (arrow) with maximum echogenicity (top) and relatively lower echogenicity.

of the head. It is interesting to see that the aneurysm appears to have an extended echo in the tSub-7 images. It should be noted that the aneurysm appears with good contrast in 4 out of 7 subaperture images as well as the compounded images. However, the compounded images do not show the same level of contrast as some of the subaperture images, which suggests the need for more intelligent forms of compounding.

Reverberation is likely to feature significantly in DMUA imaging through human scale skulls due to the use of a water bolus with the existing system. However, the subaperture processing results shown herein suggest that we can identify reverberation patterns and develop effective solutions to mitigate degragation of the echo data. Speckle statistics near the geometric center in 4 out of 7 subapertures were consistent with statistics from a standard QA phantom (CIRS Model 40) and were suitable for speckle tracking. By tracking changes in speckle using STF imaging, it is possible to observe spatially-dependent temperature changes induced by tFUS therapy. The lower row subapertures were more aligned with the skull surface and produced strong specular reflections and reverberations (arrows, tSub-2 and tSub-3, Lower 32 Elements).

IV. Conclusions

The synthetic aperture imaging results demonstrate the feasibility of imaging through the temporal bone at frequencies in the range of 2.5 - 4.8 MHz and obtain echo data from brain-mimicking tissues with good speckle statistics. Internal targets such as the anurysm and the vessels were clearly visible and identifiable on DMUA imaging. In fact, DMUA imaging produced more identifiable vessel images than a diagnostic phased array probe used for echocadiography (2.5 MHz center frequency). These results also demonstrate the value of judicial design of subaperture beamforming for identifying tissue structure and/or improving speckle statistics for high fidelity thermography and elastography.

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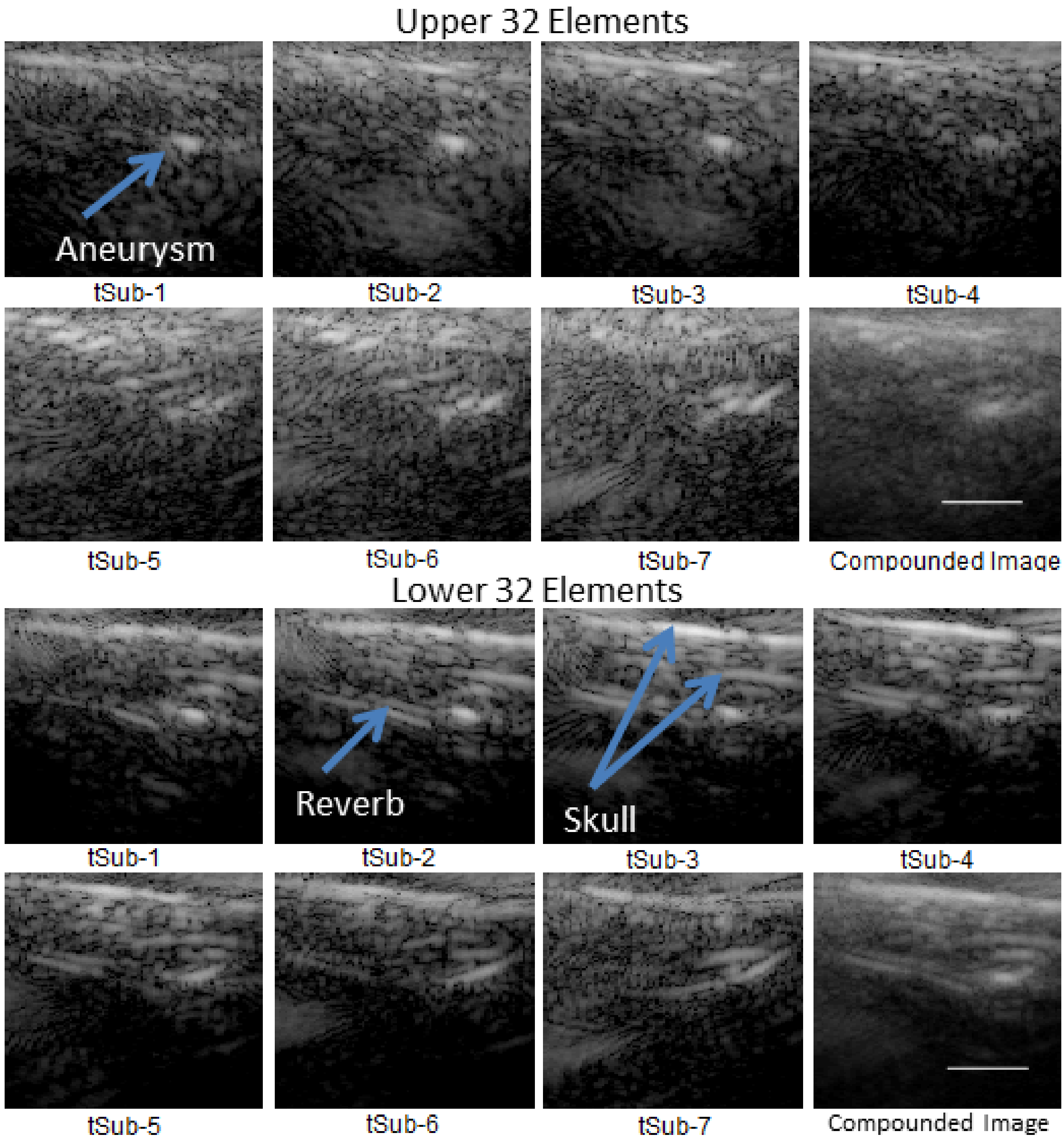

Fig. 4. Grayscale images (60 dB) obtained using supaperture processing of DMUA synthetic aperture imaging data.