Efficient Transcranial Ultrasound Delivery via Excitation of Lamb Waves: Concept and Preliminary Results

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Abstract—Transcranial focused ultrasound is approved for non-invasive treatment of essential tremor, and is being researched as a noninvasive means of ablating brain tumors, neuro-modulation, and of increasing delivery of cancer therapeutics through the blood-brain barrier. Present technology relies on the use of an array of transducers placed in a helmet and aimed at the skull at normal incidence, leading to inefficient transmission, excess heating of the skull, and limited treatment envelope to the center of the brain. We propose an array of ultrasound wedge transducers capable of efficiently delivering focused ultrasound energy into the brain with minimal heating of the skull and expanding the treatment envelope to include the entire brain.

Index Terms—Transcranial focused ultrasound, wedge transducers, guided waves, Lamb waves, mode-conversion.

I. INTRODUCTION

Brain metastases are the most common intracranial tumors in adults, and are a common cause of morbidity and mortality in cancer patients. Surgery and radiation are the mainstays of treatment, with systemic medical treatments limited by access due to the blood-brain barrier. One possible treatment, transcranial magnetic resonance guided focused ultrasound (tcMRgFUS), is being researched as a noninvasive means of ablating brain tumors and of increasing delivery of cancer therapeutics through the blood-brain barrier [1]. Focused ultrasound has also recently been used to transiently disrupt the blood-brain barrier in humans, expanding possibilities to enhance the delivery of cancer therapies to the brain. However, the currently realized version of the device for tumor ablation operating at approximately 650 kHz has a treatment envelope limited to the center of the brain, whereas most metastases occur along the periphery of the brain, at the junction of the grey and white matter. In addition, even though the existing hemispherical transducer design seeks to distribute the energy over a broad surface area, the device aims the skull at a normal-incident angle, at which power transmission is inefficient. With this configuration, active cooling is needed to prevent skin burns, due to the absorption of much of the delivered energy by the skull.

We propose a novel wedge transducer array technology for introducing focused ultrasound waves into the brain. The array couples ultrasound into the brain through double-mode-conversion: from longitudinal wave in the wedge to a high order Lamb wave in the skull, then from the high order Lamb wave in the skull to a longitudinal wave in the brain. High transmission efficiency of the double-mode-conversion approach reduces heating in the skull, and through a proper array design, is capable of addressing points on the surface of the brain. In addition, our approach would ease the application to non-invasive neuro-modulation, which has potential benefits to treating diseases like stroke, multiple sclerosis, neuropathic pain, migraine, and depression.

II. LAMB WAVES AND WEDGE TRANSDUCERS

We propose a novel wedge transducer design capable of introducing ultrasound wave energy into the brain by selectively exciting leaky guided Lamb waves in the skull that mode-convert into longitudinal waves in the brain. The human skull bone is transversally thin, and thus effectively appears as an elastic waveguide that can support propagation of Lamb waves. Lamb waves are guided elastic waves that can propagate without significant attenuation and can leak into the surrounding medium efficiently. The feasibility of exciting and propagating Lamb waves in bone has been studied and demonstrated previously [3]. Lamb waves adjacent to an acoustic medium (such as water or soft tissue) can also leak. The leak rate is approximately a few wavelengths.

Wedge transducers are efficient transducers that have conventionally been used in Surface Acoustic Wave (SAW) devices [4] or for efficient excitation of Lamb waves [5]. They provide a suitable mechanism for selectively exciting Lamb waves. Through a proper wedge transducer one can efficiently transmit ultrasound energy into the brain. This mechanism is
schematically depicted in Figure 1. The wave generated at the surface of the wedge transducer impinges on the skull at the wedge angle. It in turn mode-converts into a suitably selected Lamb mode in the bone, which then propagates a few wavelengths (depending on the wedge length) and leaks into the brain. The premise of our approach is due to the efficiency and low attenuation of transmitting Lamb waves from a wedge transducer into the brain, through the double-mode-conversion mechanism. Upon selecting the favorable mode dictated by the frequency of interest and its marginal behavior compared to the neighboring modes at that frequency, wedge transducers can be designed to maximize the coupling efficiency of the ultrasound energy into the brain. The critical parameters in a wedge design are the wedge angle and the optimal wedge length, which are functions of the acoustic impedance mismatch between the wedge material and the substrate (the skull bone), and also the frequency. The wedge angle is given by Snell's law; the wedge angle is determined by the ratio of the speed of sound in the wedge to the speed of the guided waves, i.e., \( \sin(\theta_R) = V_L/V_W \), where \( V_L \) is the selected Lamb mode phase velocity (chose according to the dispersion curve), \( V_W \) is the speed of sound of the wedge material, and \( \theta_R \) is the wedge angle.

Wedge transducers can be arranged over a ring. This arrangement provides a tight focusing at the focal point that is controlled by the radius of the ring. The ring can be adjusted to have different radii. Figure 2 shows conceptual arrangements of a wedge transducer over a ring, which results in focusing of the leaky Lamb waves inside the brain. The geometry of a human skull is composed of surfaces with different radii of curvature. The arrangement of the wedge transducers can be over any contour of any shape, in which case the focusing would be at the center of the area enclosed by the contour. The arrangement can similarly be realized over any three dimensional surface with a particular radius of curvature. For example, Figure 2a shows a ring-wedge transducer over a flat section of the skull and Figure 2b shows a ring-wedge transducer over a curved portion of the skull with a finite curvature.

A. Mode conversion efficiency

Mode conversion efficiency of a wedge transducer has been the subject of extensive research for diverse applications of both surface and Lamb waves since the early days of ultrasonic guided wave technologies. Since skull bone exhibits significant impedance mismatch to tissue, the transmission at around the megahertz regime is inefficient (less than 30%) [6], [7]. On the other hand, mode-conversion provides over 80% coupling efficiency one-way [8], [9]. Therefore, a double-mode-conversion process improves the transmission by over 35%, corresponding to 4-5 dB improvement.

B. Attenuation

Attenuation in skull is mainly due to two factors: (1) absorption of ultrasound energy, and (2) multiple scattering inside the skull due to its sub-wavelength heterogeneous structure. In the literature, there exist a large body of works on both theoretical and experimental quantification of attenuation, however, mainly targeted at the normal-incidence wave propagation [3]. These results and models do not directly translate into guided propagation phenomena in the bone and the associated attenuation. Recently, there have been research results on quantification of bone anisotropy and more in depth analysis of attenuation [10], [11], portraying more realistic models of attenuation due to wave phenomena such as guided waves and surface waves [12]. According to these models and results, Lamb waves exhibit in general about 50% less attenuation than the normal-incident transmission approach at around 1 MHz frequency.

C. Total Loss of Wedge vs. Normal-Incident Techniques

In summary, for a wedge transducer, the total loss of transmitting ultrasound energy though skull is the sum of the loss due to attenuation and the loss due to mode-conversion. The loss of Lamb modes is about 1 dB/mm at 1 MHz [12] for a 5-6 mm thick bone. The propagation path of the desired mode in the skull is about 5-6 mm. This gives around 5-6 dB of loss in the bone. 80% mode-conversion efficiency one way, as argued above, leads to about 4 dB loss due to the double mode-conversion mechanism. Therefore, there exists around 10 dB total transmission loss. On the other hand, for the conventional normal-incident transducer, an average loss of 2 dB/mm at 1 MHz has been reported [13]. This for a 5-6 mm bone results in around 12 dB loss due to attenuation. The direct normal-incident transmission is less than 30%, which gives around 10-11 dB transmission loss. So, in total there is around 22 dB transmission loss for the normal-incident approach. Therefore, the wedge technique outperforms the normal-incident technique by over 10 dB.

D. Robustness to Thickness, Heterogeneous Bone Structure, and Overlying Tissue

Wedge transducer elements, due to their finite length, provide a certain spatial-frequency bandwidth and angular tolerance. Spatial-frequency bandwidth provides a measure as to how much of other Lamb modes will be excited by the same wedge transducer [14]. For the target wedge transducer in this proposal, the bandwidth is about 15%, which provides a selective excitation of the Lamb mode of interest. The wedge elements can also be phase-shifted. The proposed mechanism,
once designed at a specific (average) thickness, is robust to the range of the thicknesses of the skull bone. Furthermore, it is anticipated that the wedge transducer will work robustly with presence of the skin, because of its low impedance mismatch to the wedge material. However, wedge transducers can be modified with the knowledge of the average skin thickness, by looking at the skin and skull as one waveguide.

FIG. 3: Focusing achieved by the wedge transducer for 1 MPa surface pressure. The pink spot indicates the focusing of the leaky Lamb waves (dissected three-dimensional view).

III. SIMULATION RESULTS

We have conducted several preliminary simulations to verify the concept. A preliminary simulation study showing the performance of a conceptual wedge design is demonstrated in Figure 3. This prototype was designed using the third asymmetric Lamb mode of the skull at 1 MHz, which has the phase velocity of 2105 m/s. In a wedge with a sound speed of 1500 m/s, the wedge angle would be 45° and the optimal wedge length would be 4λ, where λ = 2.105 mm (the Lamb wavelength).

The wedge elements are arranged over a ring with a radius of 20 mm facing a flat 6-mm thick piece of bone. Figure 3 shows the focusing of the wedge transducer inside the brain. By adjusting the radius of the wedge ring, different areas of the brain can be targeted. Figure 4 shows a preliminary numerical calculation that benchmarks a wedge design against a conventional single element normal-beam transducer, both transmitting ultrasound energy through a flat piece of bone.

Fig. 4: Relative (normalized) temperature elevation inside the brain compared to the temperature elevation inside the skull. (a) Conventional normal-beam transducer. (b) Wedge transducer.

IV. EXPERIMENTAL RESULTS

To provide supporting preliminary data, we have utilized a 1 MHz single element commercial immersion transducer (Olympus A303S, 0.5 in diameter) to emulate a wedge transducer configuration. The coupling material between the transducer element and the samples is water, mimicking the effect of the wedge material. Considering water as the wedge material and 2104 m/s the desired Lamb wave phase velocity in the bone leads to a 45° wedge angle.

A. Lamb Mode-Conversion Efficiency

As a proof-of-concept for mode-conversion efficiency, we conducted tests on a 3-mm thick aluminum plate. Aluminum has low attenuation, in turn providing a suitable way to demonstrate the double mode-conversion efficiency. The tests were conducted in water, with a speed of sound around 1500 m/s. A suitable mode at 1 MHz is A0, for which the wedge angle is about 32°. The plate was placed at the axial distance corresponding to S1 (i.e., the onset of far-field) of the transducer, given as S1 = a²/λ, where a is the aperture radius and λ is the wavelength. For the transducer radius of 0.25 in, S1 = 2.9 cm. The plate first was placed perpendicular to the ultrasound beam to measure the normal-incident transmission and then tilted at 32° to test the wedge transmission approach. We performed spatial pressure scans using a hydrophone (ONDA HGL-0200). The RF data at the peak pressure location of both scans are shown side-by-side with the free field scan (i.e., field scan with no sample on the path of the US beam) in Figure 6, demonstrating a maximum peak-to-peak transmitted pressure of 44 kPa using the wedge compared to 18 kPa by the normal incident approach. Analysis of the RF data indicates around 78% double-mode-conversion efficiency compared to around 32% normal-incident transmission efficiency.

Fig. 5: Pressure field scan setup with the 3-mm thick Aluminum plate placed between the transducer and hydrophone, at two different angles to emulate the normal-incident and wedge techniques. (a). Normal-incident transmission. (b). Wedge transmission.
B. Proof-of-Concept Result Using Skull Fragment

A skull fragment, which had been immersed in water for several days, was used along with the single element transducer to benchmark the wedge transmission technique against the normal-incidence transmission technique. Figure 7 demonstrates the experimental setup. In the first configuration, the skull fragment was placed perpendicular to the ultrasound beam at S1 distance from the surface of the transducer. In the second configuration, the skull fragment was tilted by 38°, to emulate the wedge transmission. The field measurements are shown in Figure 8. The wedge technique data shows around 14 dB total loss as opposed to the normal-incident technique, which shows around 21 dB total transmission loss. This is still around 4 dB more loss than expected, which is likely due to the lack of proper alignment of the wedge angle. The true value of the wedge angle must be 45°. However, due to tight spacing between the instruments and fragment, the maximum reachable angle was 38°. This however demonstrates robustness of our approach to angular variability of the wedge.

Fig. 6: RF data recorded at the location of peak transmitted pressure in both normal-incident and wedge transmission cases and their relative amplitudes compared to the free field measurement.

Fig. 7: Pressure field scan setup with the skull fragment placed between the transducer and hydrophone, at two different angles to emulate the normal-incident and wedge techniques. (a) Normal-incident transmission. (b) Wedge transmission.

Fig. 8: RF data recorded at the location of peak transmitted pressure in both normal-incident and wedge transmission cases.

V. CONCLUSIONS

We propose an array technology concept for improving on transcranial focused ultrasound delivery into the brain. The array couples ultrasound into the brain through double-mode-conversion: from longitudinal wave in the wedge to a high order Lamb wave in the skull, then from the high order Lamb wave in the skull to a longitudinal wave in the brain. Compared to existing techniques, the benefits of our approach is in improved efficiency, reduction in heating of the skull, the ability to address regions in the brain that are close to the skull, and freedom in operating at a wider range of frequencies. We presented preliminary data proving the feasibility and concept. This technology can potentially be impactful on therapeutic and neuromodulation applications.

REFERENCES