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Modeling ultrasound propagation through material of increasing geometrical complexity

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ABSTRACT

Ultrasound is increasingly being recognized as a neuromodulatory and therapeutic tool, inducing a broad range of bio-effects in the tissue of experimental animals and humans. To achieve these effects in a predictable manner in the human brain, the thick cancellous skull presents a problem, causing attenuation. In order to overcome this challenge, as a first step, the acoustic properties of a set of simple bone-modeling resin samples that displayed an increasing geometrical complexity (increasing step sizes) were analyzed. Using two Non-Destructive Testing (NDT) transducers, we found that Wiener deconvolution predicted the Ultrasound Acoustic Response (UAR) and attenuation caused by the samples. However, whereas the UAR of samples with step sizes larger than the wavelength could be accurately estimated, the prediction was not accurate when the sample had a smaller step size. Furthermore, a Finite Element Analysis (FEA) performed in ANSYS determined that the scattering and refraction of sound waves was significantly higher in complex samples with smaller step sizes compared to simple samples with a larger step size. Together, this reveals an interaction of frequency and geometrical complexity in predicting the UAR and attenuation. These findings could in future be applied to poro-visco-elastic materials that better model the human skull.

1. Introduction

Ultrasound is increasingly being explored as a therapeutic modality for diseases of the brain [1]. Established applications in peripheral tissue include lithotripsy and physiotherapy, whereas emerging applications for the brain include tissue ablation by inducing hyperthermia, for example to treat essential tremor [2], and microbubble-facilitated opening of the blood–brain barrier (BBB) to deliver drugs past the BBB as exemplified by anti-cancer antibodies in the treatment of gliomas [3]. We and others have shown in transgenic mouse models that microbubble-mediated opening of the BBB with ultrasound is also an efficient method to reduce two key pathologies of Alzheimer's disease [4–8], and that treating wild-type mice with ultrasound is safe long-term [9]. In a subset of these studies, cognitive impairment was restored and ultrasound on its own, without delivery of a therapeutic agent, was able to achieve therapeutic outcomes. Safety studies have also been performed in larger animals including beagles [10], sheep [11] and macaques [12]. Together, these results have prompted clinical trials in humans.

However, applying the principles established in mice to larger animals is not simply a matter of scaling up; ultrasound is also affected by the human skull, that different from mice, consists of two outer layers and a central spongy cancellous bone (diploë) with liquid-filled pores, which cause ultrasound to be reflected by the layer boundaries and pores and absorbed by the skull, resulting in a significant temperature increase in the bone [13,14]. As a consequence, insufficient energy is transmitted into the brain. Magnetic resonance imaging (MRI) and computed tomography (CT) has been instrumental in determining both the profile and internal structure of the skull [15].

In order to overcome the skull and determine its acoustic properties, a stepwise approach of modeling is required. In the current study, we modeled the human skull bone by simple resin samples with a bone-like density and a defined geometry in order to predict wave propagation and determine their acoustic properties using a signal processing approach. This allows simulating the process in a system of building blocks that produce a clear illustration of sample behavior towards ultrasonic waves, termed Ultrasound Acoustic Response (UAR). Based on previous work by Langton and colleagues, the initial assumption was made that the waveform shows a linear behavior as it passes along different paths through the samples [16]. However, we found that such a linear behavior is not applicable when the complexity of the sample's geometry increases. Moreover, a Finite Element Analysis (FEA) was performed to investigate ultrasound refraction and scattering that affects the direction of wave propagating, an analysis not possible by

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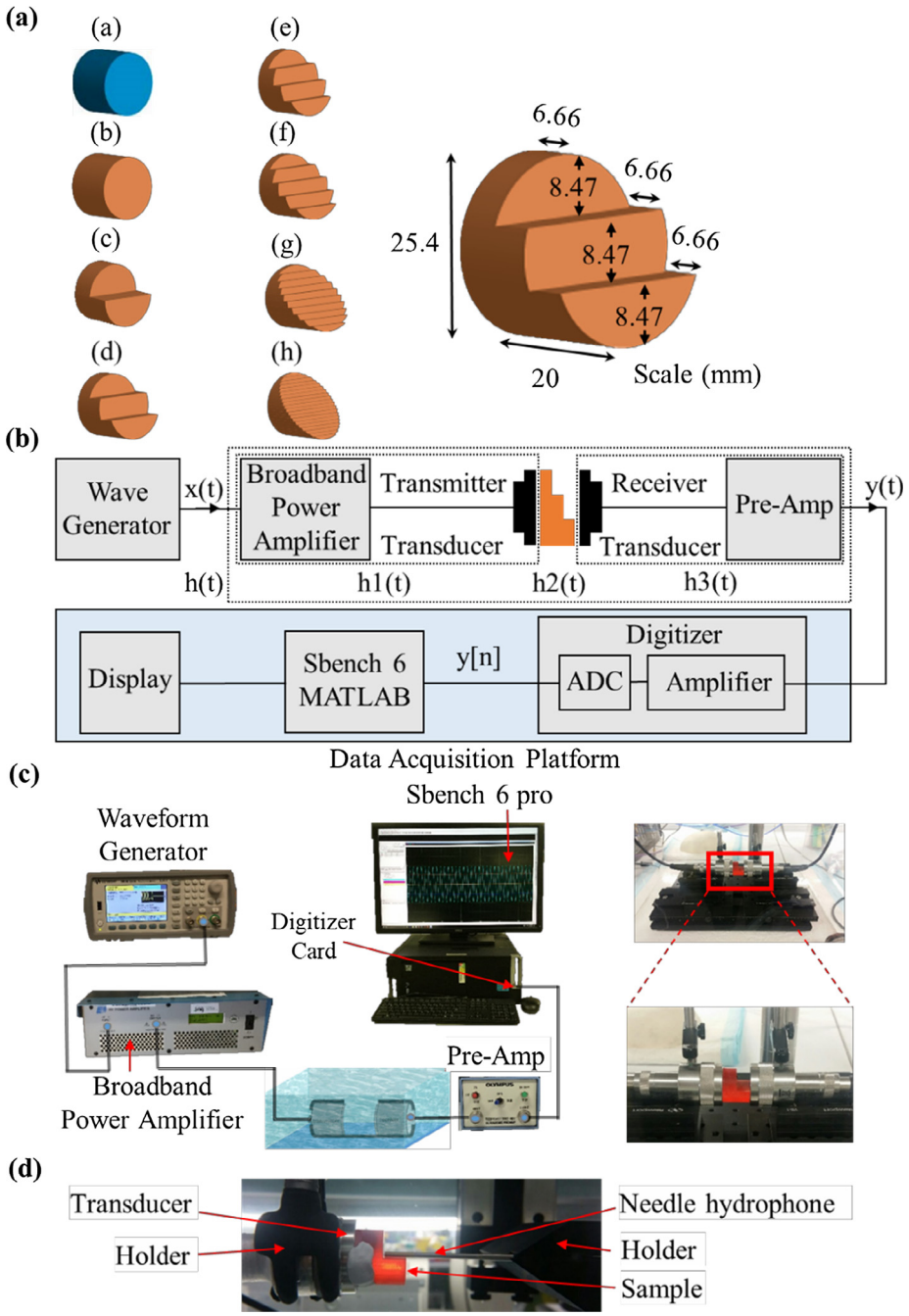

Fig. 1. Series of printed resin samples and experimental setup to measure the UAR. (a) Series of 3D-printed resin samples including reference sample (a) of water and step samples (b–h). A 3-step sample is shown as a close-up with the actual dimensions. (b) Schematic setup of the test platform. (c) Experimental setup. (d) Setup of the Onda tank.

UAR. Together, this serves as a foundation for follow-up studies using layered and poro-visco-elastic models (that more faithfully represent the human skull) and human skulls.

2. Methods

2.1. 3D printing of step samples

A series of full and partial cylindrical samples was generated with a 50 µm resolution 3D printer (Kudo3D, Titan1 Kudo3D, Pleasanton, California, United States, www.kudo3d.com) using resin (ultrasound velocity was measured as 2200 m/s, 3DM-ABS, 3D-Materials, Feldkirch, France). Seven samples (b) to (h) with increasing complexity were generated using water (sample (a)) as reference (Fig. 1a). The simplest sample (b) comprised a cylinder of 20 mm length and 25.4 mm diameter covering the surface of the active transducer elements fully. The other samples were designed with equal step heights. As illustrated for the 3-step sample (close-up), the path length of the acoustic wave in the second and third step is 2 and 3 times that of the first step, respectively. A similar principle applies to the other samples (ranging from the 2 to 20 steps), with the steps varying in length and size (Table 1).

2.2. Ultrasonic testbed and data acquisition platform

The acoustic setup consisted of a pair of single-element transducers (Olympus Immersion Transducer, 1-inch (25.4 mm) diameter, with 0.5,