Communication

Standing-Wave Suppression for Transcranial Ultrasound by Random Modulation

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***Abstract*—Low-frequency transcranial ultrasound (<1 MHz) is being investigated for a number of brain therapies, including stroke, tumor ablation, and localized opening of the blood–brain barrier. However, lower frequencies have been associated with the production of undesired standing waves and cavitation in the brain. Presently, we examine an approach to suppress standing waves during continuous-wave (CW) transcranial application. The investigation uses a small randomization in the frequency content of the signal for suppressing standing waves. The approach is studied in an *ex-vivo* human skull and a plastic-walled chamber, representing idealized conditions. The approach is compared to single-frequency CW operation as well as to a swept-frequency input. Acoustic field scans demonstrate that the swept-frequency method can suppress standing waves in the plastic chamber and skull by 3.4 and 1.6 times, respectively, compared to single-frequency CW excitation. With random modulation, standing waves were reduced by 5.6 and 2 times, respectively, in the plastic chamber and skull. It is expected that the process may play a critical role in providing a safer application of the ultrasound field in the brain and may have application in other areas where standing waves may be created.**

***Index Terms*—Random frequency modulation, standing-wave suppression, transcranial ultrasound.**

I. Introduction

Transcranial ultrasound has demonstrated the potential to serve as a therapeutic tool in the treatment of a range of disorders [1]–[9]. At submegahertz frequencies, reduced aberration and absorption by the skull make such applications more practical [10]–[13]. However, low-frequency ultrasound can be associated with certain risks for adverse bioeffects. Notably, the cavitation threshold reduces with frequency [14]. There is also an increased potential of inducing standing waves [15], as a result of longer wavelengths and reduced absorption in the brain tissue. The occurrence of such standing waves at and away from the therapeutic target locations has been suggested as a source of hemorrhaging during low-frequency transcranial thrombolysis [16]–[18].

Motivated by these observations, we examine an approach for eliminating standing waves in the skull during continuous wave (CW) or near-CW application of ultrasound. We hypothesize that small randomization in the frequency content of the application signal is sufficient to significantly reduce standing waves. In this manner, the randomization will cause a break in the ultrasound symmetry between forward and reflected waves that does not allow standing waves to be established. It is further predicted that, given a sufficient spread in bandwidth, intensity fluctuations in the nearfield will be homogenized as a result of the frequency dependence on the spatial locations of nulls in the field.

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Frequency sweeps have long been understood to reduce standing waves and implemented in various ultrasound products, such as ultrasonic cleaners [19]. Mitri *et al.* [20] used a related approach to suppress standing waves in vibroacoustography, and Erpelding *et al.* [21] used a similar approach to inhibit standing waves in bubble-based radiation force measurements. Based on these studies, we compare the present randomized approach to the frequency sweep with similar frequency content.

II. Materials and Methods

A. Signal Generation

An air-backed transducer (250 kHz, 50-mm diameter, and 10-cm radius of curvature) with a −6-dB bandwidth of 50 kHz was used to generate all fields. Two different signal types were generated to compare the efficacy of the standing-wave suppression. In the first signal, the frequency was swept linearly with time. This swept signal was created by feeding a triangular wave with a frequency of 3.9 kHz from a function generator (SRS, DS345) to another function generator (Agilent, 33250 A) that modulated the 250-kHz carrier frequency with the triangular signal. The second signal was created by modulating a carrier signal with a random noise signal, so that the instantaneous frequency deviated from the center frequency in a random manner. This random-modulated signal was generated by a custom-made circuit that consist of a voltage-controlled oscillator with a center frequency of 250 kHz and a bandwidth of 50 kHz (±10% of the center frequency) fed by a random noise-modulation signal. Likewise, the center frequency and bandwidth of the swept signals were 250 and 50 kHz, respectively. Both signals were amplified by an RF power amplifier (E&I, 240 L) that excited the transducer. Control experiments with single-frequency CW excitation at 250 kHz were performed. The voltages across the transducer excited by the spread spectrum and the single-frequency signals were set to 10 V·rms and measured by an oscilloscope (Tektronix, TDS3014B). The power delivered to the transducer was less than 1 W. The frequency spectra of the measured transducer voltages with different excitations are shown in Fig. 1, and the length of waveforms acquired for averaging for the single-, swept-, and random-frequency excitations were 2, 10, and 100 ms, respectively.

B. Acoustic Field Scan Experiments

The experiments were carried out inside a rubber-lined tank (tank dimensions = 111 cm × 45 cm × 40 cm, rubber thickness = 6.35 mm, and $\alpha = 8.6\ \text{m}^{-1}$ at 250 kHz) filled with degassed deionized water. A 1-mm-diameter polyvinylidene difluoride (PVDF) needle hydrophone (Precision Acoustics) was used to sense the acoustic pressure within the area of interest. This area was situated inside an *ex-vivo* human skull, in which the parietal bones of the skull were placed perpendicular to the transducer's propagation axis.

The needle hydrophone was mounted on a three-axis positioning system controlled by a PC and was aligned 45° with respect to the ultrasound propagation direction. The transducer axis of symmetry was chosen as the Cartesian z-axis, with the origin at the center of the transducer. The sagittal plane and the transducer surface are parallel to the x–y plane, and the transverse plane is parallel to the x–z plane. The distance between the skull wall closest to the transducer and the transducer surface was 12 mm. The ultrasound field in the x–z plane ($y = 0$) in the cranium was scanned. The scan range was from $(x, z) =$

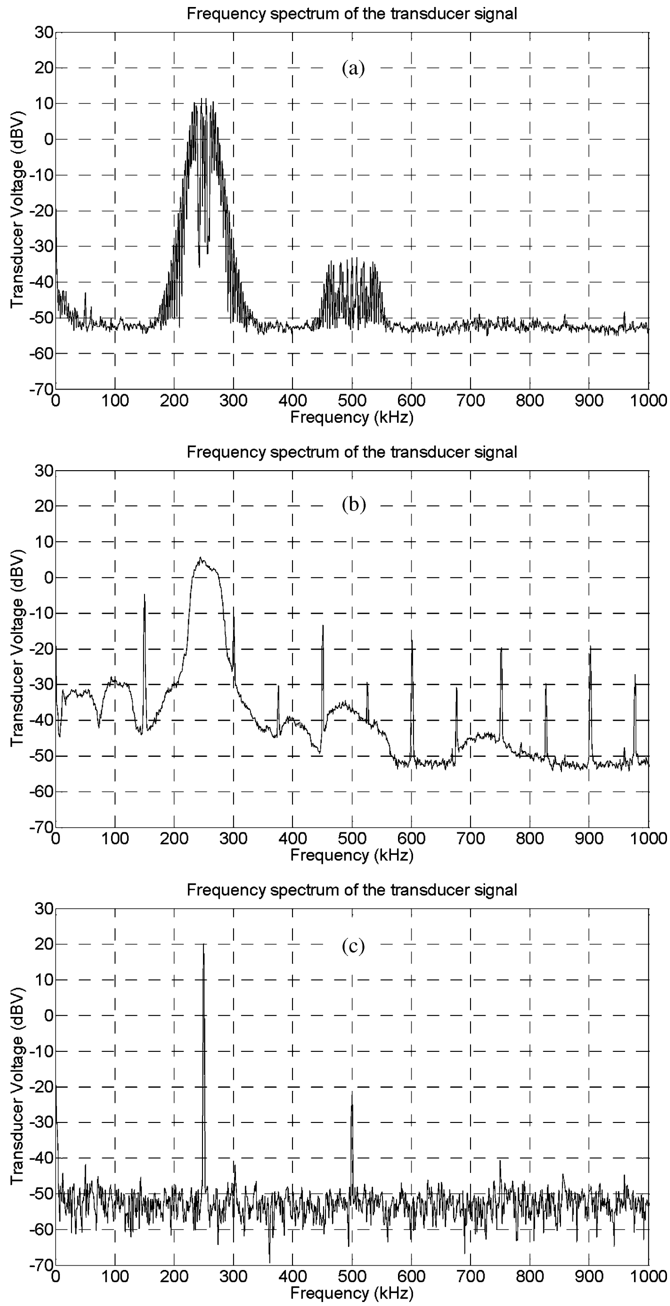

Fig. 1. Frequency spectrum of the measured voltage of the transducer excited by the signals with (a) swept frequency, (b) random-signal modulation, and (c) single frequency without modulation.

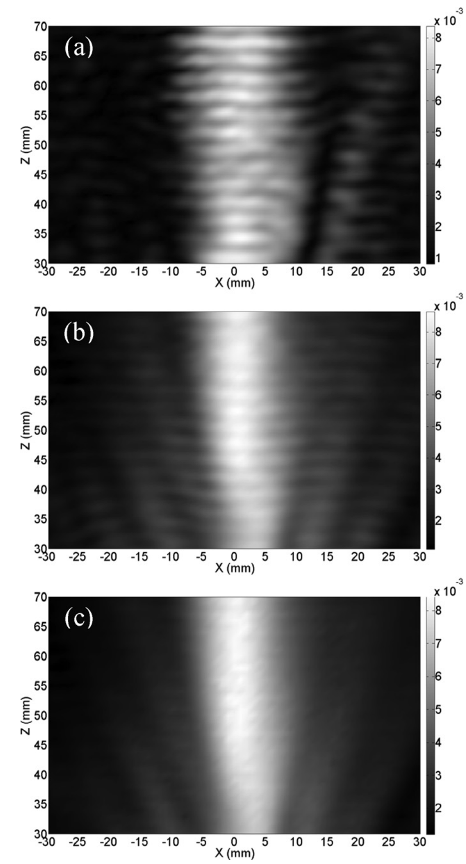

Fig. 2. Measured hydrophone rms voltage in the x–z plane in an *ex-vivo* human cranium, when the transducer was excited by the signal with (a) single frequency, (b) swept frequency, and (c) random-signal modulation in linear scale.

(−30 mm, 30 mm) to (30 mm, 70 mm). With the single- and swept-frequency excitations, the length of waveform data acquired at each hydrophone position were 2 and 10 ms, respectively, and the spatial resolution was 0.5 mm for both excitations. The spatial resolution and the length of the waveform data acquired for the random modulation were 1 mm and 100 ms, respectively.

Similar experiments were performed with two parallel acrylic plates replacing the *ex-vivo* human skull in order to evaluate the performance of the standing-wave suppression methods in an idealized condition. The plates (150 mm × 90 mm × 5 mm) were parallel to the transducer, and the plate separation was 129 mm. The scan area ranged from $(x, z) = (-30$ mm, 20 mm) to (30 mm, 70 mm) with spatial resolution of 0.5 mm.

III. Results

A. Acoustic Field Scans

The averaged relative acoustic pressure field plots in the x–z plane ($y = 0$) inside an *ex-vivo* human cranium, with single frequency, swept frequency, and random-signal modulation excitations are shown in Fig. 2. The field patterns illustrate that the swept-frequency method provided an improvement on the reduction of the standing-wave effect compared to the single-frequency excitation. However, the standing-wave effect with the swept excitation was still clearly visible. The distance between two adjacent peaks along the ultrasound propagation direction is 3 mm, which is half of the wavelength of the excitation center frequency. The plots also reveal that the random-modulation scheme substantially suppresses the standing-wave effect in the ultrasound main beam ($|x| < 5$ mm). An inconspicuous standing-wave effect was observed outside the main beam, but the intensity was significantly lower than that inside the main ultrasound beam. Both the average and the peak intensities at $x = -15$ mm (outside the main beam) were more than three times less than that at $x = 0$ mm (inside the main ultrasound beam) from $z = 40$ m to 60 mm.

B. Effectiveness of Standing-Wave Suppression

The effectiveness of the standing-wave suppression method is quantified by a comparison of the amplitude peak $p_{\max}$ to minimum $p_{\min}$

TABLE I
STANDING-WAVE EFFECT WITH DIFFERENT EXCITATIONS QUANTIFIED IN TERMS OF THE RATIO R AND THE SWR

Excitation	Skull		Plastic Plates	
	Ratio R	SWR	Ratio R	SWR
Single Frequency	0.276	2.37 dB	0.354	1.42 dB
Swept-Frequency	0.174	1.57 dB	0.102	0.89 dB
Random Modulation	0.135	1.20 dB	0.063	0.54 dB

over a region with the average amplitude of $p_{\rm avg}$

$$R = \frac{p_{\max} - p_{\min}}{p_{\rm avg}} \tag{1}$$

which provides a quantification of the deviation from the mean pressure. The ratio R in the region between 40 and 60 mm from the transducer face was investigated for the estimation of the effectiveness of the standing-wave suppression and evaluated from the experiments with the *ex-vivo* human skull and the plastic plates. For reference, the standing-wave ratio (SWR) between the wave node and antinode is also presented. The SWR quantifies the extent to which the wave is pure or partial standing wave [22]. These results are summarized in Table I. From the skull experiments, the standing-wave effect was reduced by 1.6 and 2 times, respectively, in ratio R with the swept-frequency and the random-frequency excitations. A similar trend was recorded in the plastic plates; the standing-wave effect is reduced by 3.4 times with the swept-frequency method, and 5.6 times with the random-frequency method in the plastic chamber situation.

IV. Discussion and Conclusion

The study was designed to demonstrate a potential method for reducing standing waves that may be induced with low-frequency transcranial ultrasound. The approach was examined at 250 kHz, due to the frequency's direct implications from recent studies in transcranial tumor ablation, sonothrombolysis, and targeted opening of the blood–brain barrier. The method, however, is expected to readily generalize to any application, where it would be advantageous to eliminate standing waves.

Experiments indicated the effect of inducing random-frequency modulations on ultrasound standing waves. Results indicate the approach's ability to inhibit standing waves both within a human skull as well as within a plastic cavity of parallel walls. The approach was found to be superior to the established swept-frequency method. The method may have application in stroke treatment, transcranial ablative therapies, and studies using ultrasound to open the blood–brain barrier. Application is further expected to translate to an assortment of situations where suppression of standing waves is desired.

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