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Improved Heating Efficiency with High-Intensity Focused Ultrasound using a New Ultrasound Source Excitation

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Abstract— **High-Intensity Focused Ultrasound (HIFU) is quickly becoming one of the best methods to thermally ablate tissue noninvasively. Unlike RF or Laser ablation, the tissue can be destroyed without inserting any probes into the body minimizing the risk of secondary complications such as infections. In this study, the heating efficiency of HIFU sources is improved by altering the excitation of the ultrasound source to take advantage of nonlinear propagation. For ultrasound, the phase velocity of the ultrasound wave depends on the amplitude of the wave resulting in the generation of higher harmonics. These higher harmonics are more efficiently converted into heat in the body due to the frequency dependence of the ultrasound absorption in tissue. In our study, the generation of the higher harmonics by nonlinear propagation is enhanced by transmitting an ultrasound wave with both the fundamental and a higher harmonic component included. Computer simulations demonstrated up to a 300% increase in temperature increase compared to transmitting at only the fundamental for the same acoustic power transmitted by the source.**

I. Introduction

THERAPEUTIC ultrasound has shown great potential for improving many aspects of medical care in recent years. For example, the thermal ablation of tissue by High-Intensity Focused Ultrasound (HIFU) has been used effectively to treat both cancer and uterine fibroids [1, 2] in clinical settings [3]. In addition, HIFU thermal ablation has shown potential for many other applications including the ablation of cardiac tissue [4-7], the treatment of ocular tumors [8-10], the ablation of nerves to treat spasticity and pain [11], the healing of skin grafts [12], perform hemostasis [13-15], occlude blood vessels for tissue necrosis [16], and heat regulated gene therapy [17]. Unlike other technologies to thermally coagulate tissue, such as RF and Laser ablation, HIFU is completely noninvasive reducing the risk of secondary complications such as infection.

In this study, we developed an entirely new method for improving the heating rate of an ultrasound source that takes advantage of nonlinear propagation. It has long been recognized that the harmonics generated by nonlinear propagation increase the heating of the tissue [18, 19], but we have found no designs where the excitation of the ultrasound source was modified to enhance the nonlinear propagation and subsequently the generation of the higher harmonics. Unlike increasing the source power to improve the heating rates, which increases the risk of tissue burns near the surface of the transducer, using the harmonics generated by nonlinear propagation results in a smaller "hot spot" size and better spatial control of the ablation process.

In our study, we propose transmitting sound at both the fundamental and the 2nd harmonic with the phase of the 2nd harmonic designed to enhance nonlinear propagation effects. While many other investigators have attempted to improve the effectiveness and efficiency of therapeutic ultrasound by altering the source design or excitation [10, 20-23], our approach is unique in that we attempt to directly enhance the heating from nonlinear propagation. We begin by giving a qualitative theoretical justification for our proposed method. We then find the optimal phase of the 2nd harmonic in computer simulations and determine the increase in heating efficiency.

II. Theoretical Justification

Nonlinear propagation of acoustic waves is due to the pressure dependence of sound speed [24]. As a result, the portions of the acoustic cycle at higher pressures will propagate faster than the portions at lower pressures. For plane waves, this means an initially sinusoidal wave will develop a saw-tooth shape as the wave propagates as illustrated in Figure 1. As the wave distorts, energy is transferred out of the fundamental and into the harmonics. Ultimately, a shock wave will form when the peak compressional and peak rarefactional pressures overtake each other and the amplitude of the wave will become independent of the source amplitude. The coupling of energy into the higher harmonics results in increased heating efficiency due to the frequency dependence of tissue absorption.

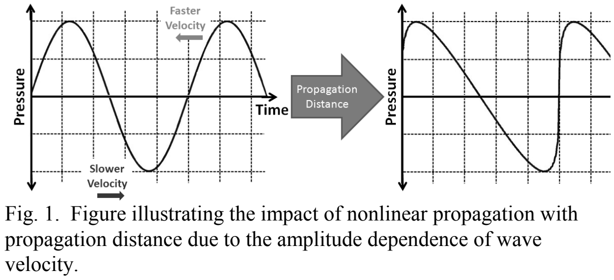

Fig. 1. Figure illustrating the impact of nonlinear propagation with propagation distance due to the amplitude dependence of wave velocity.

Since the generation of the higher harmonics and the subsequent increase in heating is greatest when a shock is formed we hypothesized that heating can be enhanced by

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enhancing shock formation. In this study, this possibility was investigated by simulating the temperature increase in tissue when transmitting at the fundamental and the 2nd harmonic. Transmitting at the fundamental and 2nd harmonic generates an approximate saw-tooth wave when the ratio of the amplitude of the second harmonic, p_2, to the fundamental, p_1, is approximately ½. In order to obtain this ratio, the amplitude of the second harmonic needs to be scaled at the source by $\left|p_2/p_1\right| = 0.25 \cdot \exp\left(d\alpha f_o\right)$ where d is the distance to the focal region from the aperture plane in cm, α is the attenuation along the propagation path in Np/cm-MHz, and f_o is the frequency of the fundamental in MHz. The factor 0.25 results from the frequency dependence of the focusing gain for the transducer.

Before preceding it is critical to mention that it is not possible to transmit at both the fundamental and the second harmonic using traditional piezoelectric elements because they only emit sound at the odd harmonics. While some have begun to develop Capacitive Micromachined Ultrasonic Transducers (cMUT's) for therapy applications which would allow the transmission of multiple harmonics [25], piezoelectric transducers are still the standard. Therefore, some type of array arrangement is needed if both the fundamental and harmonic are to be present in the transmitted signal. For focused sources, it may be possible to implement some type of annular array, but the design of such an array is beyond the scope of the present study. Currently, we only hope to demonstrate that transmitting at the second harmonic will dramatically improve the efficiency of the ultrasound therapy source. This preliminary study will also lay the ground work for future studies such as transmitting at the fundamental and the 3rd harmonic (approximate square wave) which could be done using current piezoelectric elements.

III. Simulation Parameters and Results

A. Simulation Parameters

The simulations were conducted by appropriately modifying code which calculates the nonlinear pressure wave for spherically focused sources by solving the KZK equation. The code was originally written and supplied by Joshua Soneson at the United Stated Food and Drug Administration (HIFU_Simulator_v1.0, US FDA, October 2008). The modifications allowed for both the fundamental and the second harmonic (magnitude and phase relative to the fundamental) to be specified in the aperture plane of the transducer while the original code only allowed for the amplitude of the fundamental to be specified.

The ultrasound therapy source used in the simulations was a spherically focused source with a diameter of 5 cm and a focal length of 7.5 cm (f-number of 1.5) operating at a frequency of 1 MHz. The total average acoustic power per acoustic cycle emitted by the transducer was varied from 10 to 1000 W. The tissue medium in the simulations had an attenuation of 0.5 dB/cm-MHz, a sound speed of 1540 m/s, a density of 1000 kg/m^3, and a nonlinear parameter ($\beta = 1 + B/2A$) of 3.5. While it is true that some tissues have a larger nonlinear parameter [24], we maintained the same value as water in these preliminary simulations. The calculations for most of the acoustic powers (10-500 W) used a grid size of 50 points per wavelength in both the axial and radial directions while the grid size was increased to 75 points per wavelength for the acoustic powers of 750 and 1000 W. The number of harmonics included in the simulations was 1024 for power levels from 10 to 250 W while the number of harmonics for power levels greater than 250 was increased to 2048 in order to account for the increased distortion.

For the purpose of calculating the temperature, the heat capacity of the tissue was 4180 J/kg-K, the thermal conductivity was 0.6 W/m-K, and the perfusion rate was 20 kg/m^3-K. The bioheat transfer equation was then solved using the finite element code written and supplied by Joshua Soneson at the United Stated Food and Drug Administration (HIFU_Simulator_v1.0, US FDA, October 2008). The maximum temperature in the field, which always occurred in the focal zone, after 0.5 seconds of continuous sonication was then recorded. A short exposure time was selected so that only heating rates would be compared in this initial set of simulations. The short exposure time also reduced the computational load required for each data point. Also, in the simulations, the phase of the second harmonic relative to the fundamental that resulted in the maximum temperature increase was determined for each power level.

B. Simulation Results

The percent increase in temperature following the 0.5 second exposure relative to a source transmitting at only the fundamental with the same acoustic power level is shown in Figure 2.

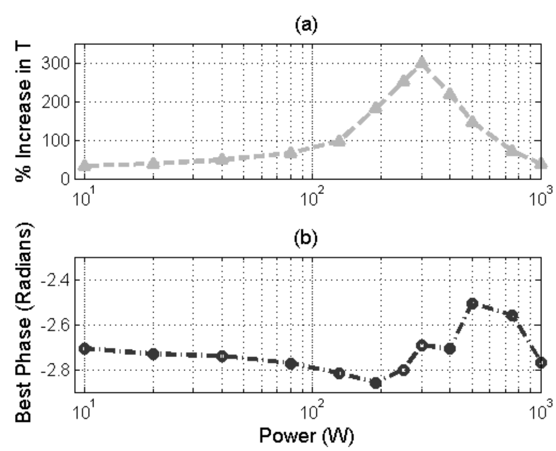

Fig. 2. Percent increase in temperature, (a), and corresponding optimal phase for the second harmonic at the source, (b), for each acoustic power level.

Notice that the percent increase in temperature is ~300% when the time-average acoustic power over a single cycle is 300 W indicating a dramatic increase in source efficiency. The optimal phase of the second harmonic relative to the fundamental is -2.7 rad at this peak with only a minimal dependence on acoustic power.

Before proceeding, it is important to clarify that decrease in source efficiency for power levels greater than 300 W (Figure 2a) does not correspond to a decrease in temperature increase. The temperature continues to increase as the source power is increased. However, the temperature increase when transmitting only at the fundamental begins to increase dramatically for power levels greater than 300 W. As a result, the percent increase when transmitting at both the fundamental and the second harmonic relative to a source transmitting at only the fundamental drops.

IV. Discussion

Our simulation results indicated a clear increase in heating rate efficiency when transmitting at both the fundamental and the second harmonic when the time-average acoustic power over a single cycle was 300 W. In order to understand the reason for this peak, we looked at the ratio of the various harmonics to the fundamental for the different acoustic power levels (Figure 3).

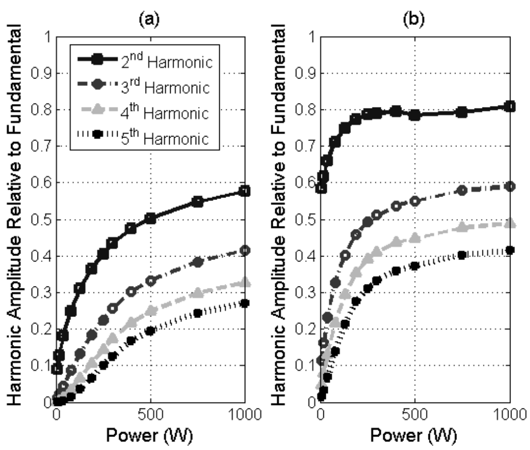

Fig. 3. Ratio of harmonic amplitudes to the amplitude of the fundamental for each acoustic power when transmitting at (a) only the fundamental and (b) the fundamental and the second harmonic at optimal phase.

Notice that the optimal improvement in efficiency (i.e., 300%) which occurs at a time-average acoustic power over a single cycle of 300 W corresponds to when the amplitudes of the higher harmonics relative to the fundamental begin to saturate. This saturation results from the formation of a shock wave in the focal region as is illustrated by the time domain waveforms shown in Figure 4. A shock wave has not yet formed when transmitting only at the fundamental and as a result, the amplitudes of the harmonics relative to the fundamental have not yet saturated (Figure 3a). The shock wave appears sooner when transmitting at both the fundamental and the 2^{nd} harmonic because the negative peak is closer in time to the positive peak at the source (Figure 4a). As a result, the positive peak will overtake the negative peak sooner as the wave propagates to the focal zone. Also, since the increased heating is due to shock formation, it was confined to a smaller region, as shown in Figure 5, than the heating produced when transmitting only at the fundamental (-3 dB "hot spot" volume of 1.9 mm^3 as compared to 17.6 mm^3).

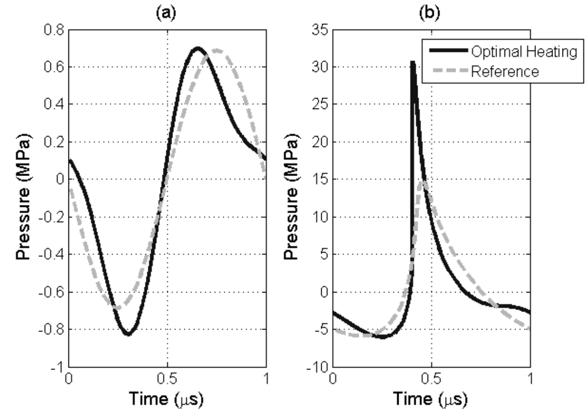

Fig. 4. Time domain waveforms at (a) aperture plane and (b) location of maximum acoustic intensity in the focal zone when transmitting at only the fundamental (Reference), and when transmitting at both the fundamental and the second harmonic when the phase of the second harmonic is optimized for maximum heating for a source power of 300 W.

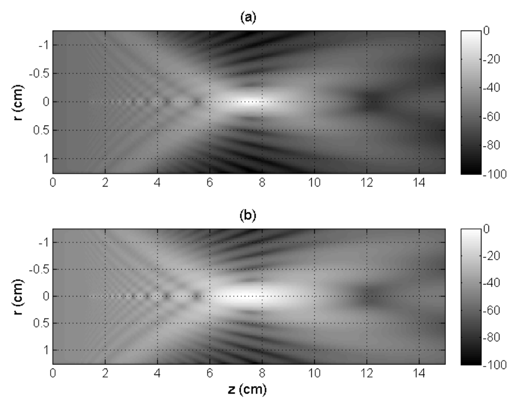

Fig. 5. A spatial map of the temperature increase in dB relative to the maximum temperature increase illustrating the size of the "hot spot" when (a) transmitting at both the fundamental and (b) when transmitting only at the fundamental for a time-average acoustic power over a single cycle of 300 W.

Therefore, transmitting at both the fundamental and the second harmonic provides better spatial control over the ablation procedure than transmitting only at the fundamental for the same acoustic power.

V. Conclusions

In this study, we demonstrated that the heating efficiency of a high-intensity focused ultrasound source can be improved by over 300% by designing the excitation to enhance nonlinear propagation. Specifically, we showed that when transmitting at both the fundamental and the second harmonic, a shock wave can be formed in the focal region that would not normally occur in the absence of the second harmonic. This shock wave dramatically increases tissue heating. It is critical that the 2^{nd} harmonic have the correct phase otherwise, the second harmonic could delay rather than enhance shock wave formation. The observed increase in efficiency can be translated to lower acoustic powers in HIFU applications by operating the transducer in pulsed mode and selecting the appropriate duty cycle.

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