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Use of Shock-Wave Heating for Faster and Safer Ablation of Tissue Volumes in High Intensity Focused Ultrasound Therapy

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Abstract. Simulation of enhanced heating of clinically relevant tissue volumes using nonlinear ultrasound waves generated by a multi-element HIFU phased array were conducted based on the combined Westervelt and bio-heat equations. A spatial spectral approach using the fast Fourier transform algorithm and a corresponding analytic solution to the bioheat equation were used to optimize temperature modeling in tissue. Localized shock-wave heating within a much larger treated tissue volume and short, single HIFU pulses within a much longer overall exposure time were accounted for in the algorithm. Separation of processes with different time and spatial scales made the calculations faster and more accurate. With the proposed method it was shown that for the same time-average power, the use of high peak power pulsing schemes that produce high-amplitude shocks at the focus result in faster tissue heating compared to harmonic, continuous-wave sonications. Nonlinear effects can significantly accelerate volumetric heating while also permitting greater spatial control to reduce the impact on surrounding tissues. Such studies can be further used to test and optimize various steering trajectories of shock-wave sonications for faster and more controlled treatment of tissue volumes.

INTRODUCTION

In high intensity focused ultrasound (HIFU) applications, reported target intensities can reach several thousands or even tens of thousands of W/cm^2. In such fields, nonlinear acoustic effects result in the formation of high-amplitude shock fronts in focal waveforms, with amplitudes that can exceed 100 MPa [1]. The presence of such shocks can lead to tissue heating and boiling within several milliseconds [2]. Even though this enhanced heating is very strong, shock fronts are highly focused and produce extreme heating effects in a very small focal volume. For single, fixed lesions, nonlinear heating thus can be utilized for rapid tissue ablation only within very small volumes before boiling occurs to limit the process. However, if the focus is steered, this localized enhancement of heating combined with thermal diffusion can be used effectively to accelerate thermal treatments over large volumes. In addition, recent experimental studies have shown that a method termed boiling histotripsy can be used to mechanically disintegrate tissue volumes with varying thermal effects by changing shock-wave parameters in the exposure [3]. In this work, numerical simulations were performed to evaluate the efficacy of using nonlinear effects to accelerate the thermal ablation of tissue volumes with the same safe exposure conditions for intervening tissues. Simulations followed the geometry of the experimental conditions of recent studies conducted with a multi-element 1.2 MHz HIFU phased array (Fig. 1a, Sonalleve V1 3.0T, Philips Healthcare, Vantaa, Finland) to generate volumetric lesions in *ex vivo* bovine tissue [4]. A pulsing scheme was combined with discrete electronic steering of the array focus over a series of targets arranged in circles with radii of 2 and 4 mm. The circles were located in a plane in the middle of the tissue

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sample, and there was a delay of 40 ms between consecutive sonications (Fig. 1b,c) [5]. An average intensity of 1.2 W/cm^2 at the array elements was kept constant while different peak intensities balanced by a duty factor were used.

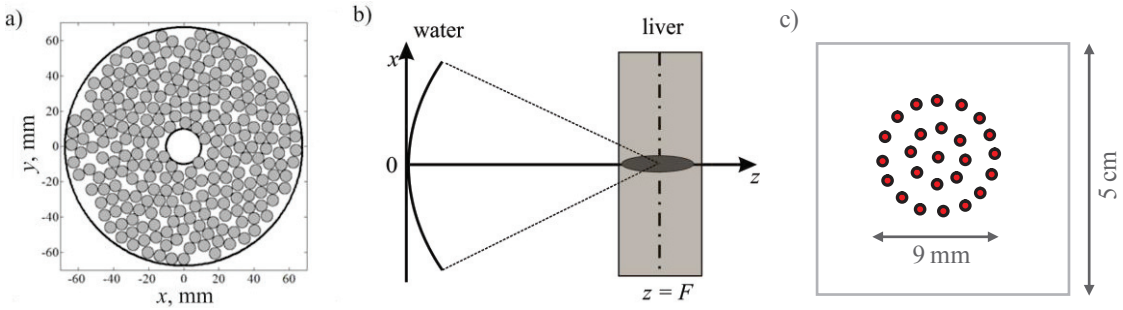

FIGURE 1. (a) Distribution of radiating elements on the surface of the therapeutic array; (b) geometry of the numerical experiment: ultrasound beam is focused within tissue layer (liver) centered at the geometric focus of the spherical shell ($z = F$); (c) Discrete trajectory of the beam's focus in the focal plane. Acoustical modeling was done both in water and in liver sample, while temperature modeling was done only in liver.

METHODS

Acoustic modeling was based on the Westervelt equation:

$$\frac{\partial^2 p}{\partial \tau \partial z} = \frac{c_0}{2}\Delta p + \frac{\beta}{2\rho_0 c_0^3}\frac{\partial^2 p^2}{\partial \tau^2} + \frac{\delta}{2c_0^3}\frac{\partial^3 p}{\partial \tau^3} + L(p). \qquad (1)$$

where $\tau = t - z/c_0$ is the retarded time, $\Delta p = \partial^2 p/\partial z^2 + \partial^2 p/\partial x^2 + \partial^2 p/\partial y^2$, parameters c_0, β, ρ_0 and δ are the ambient sound speed, nonlinearity coefficient, density, and thermoviscous absorption of the propagation medium, respectively; the operator $L(p)$ accounts for the linear power-law absorption in tissue. The Westervelt equation was solved using a previously developed finite-difference algorithm. Parameters of the numerical scheme were: longitudinal step $dz = 0.075$ mm, transversal steps $dx = dy = 0.025$ mm, and the maximum number of harmonics was limited to 800. The values of the physical constants in Eq. (1) were representative of typical conditions in water and in liver at room temperature (20°C): $\rho_0 = 998$kg/m^3, $c_0 = 1485$ m/s, $\beta = 3.5$, $\delta = 4.33\cdot10^{-6}$ m^2/s for water and $\rho_0 = 1050$ kg/m^3, $c_0 = 1580$ m/s, $\beta = 4.0$ for liver. The absorption coefficient in liver was taken to be 8.4 m^{-1} at 1.2 MHz and to follow a linear power law with frequency.

Shown in Fig.2 are waveforms at the focus of the array for three different peak intensities at the array elements: $I_0 = 1.2$, 4, and 8 W/cm^3. These output levels correspond to a quasilinear sonication (a), the regime in which a shock front has just started to form (b), and a sonication with a fully developed shock front (amplitude 95 MPa), which was expected to produce a strong enhancement of heat deposition [2].

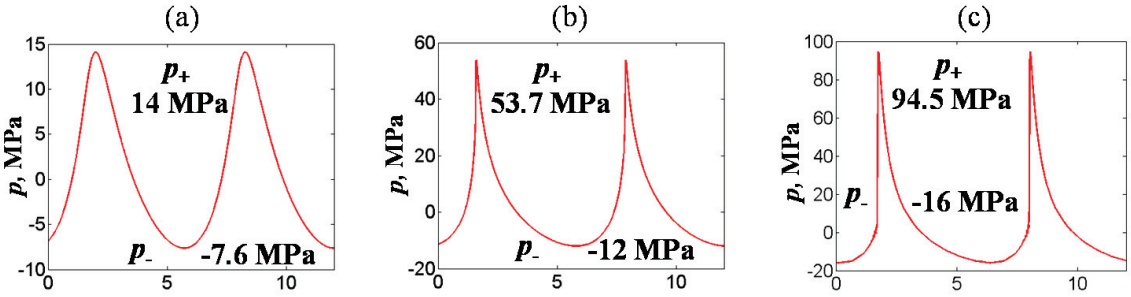

FIGURE 2. Modeling results for non-linear acoustic pressure waveforms of different intensities at the focus. Heating time is in inverse proportion to the intensity, to keep the absorbed heat equal in all three cases. (a) $I_0 = 1.2$ W/cm^3, $T_{heat} = 40$ ms, the wave is quasilinear, (b) $I_0 = 4$ W/cm^3, $T_{heat} = 12$ ms, beginning of shock-front formation can be seen, peak pressure reaches about 50 MPa (c) $I_0 = 8$ W/cm^3, $T_{heat} = 6$ ms, developed shock front of 95 MPa.

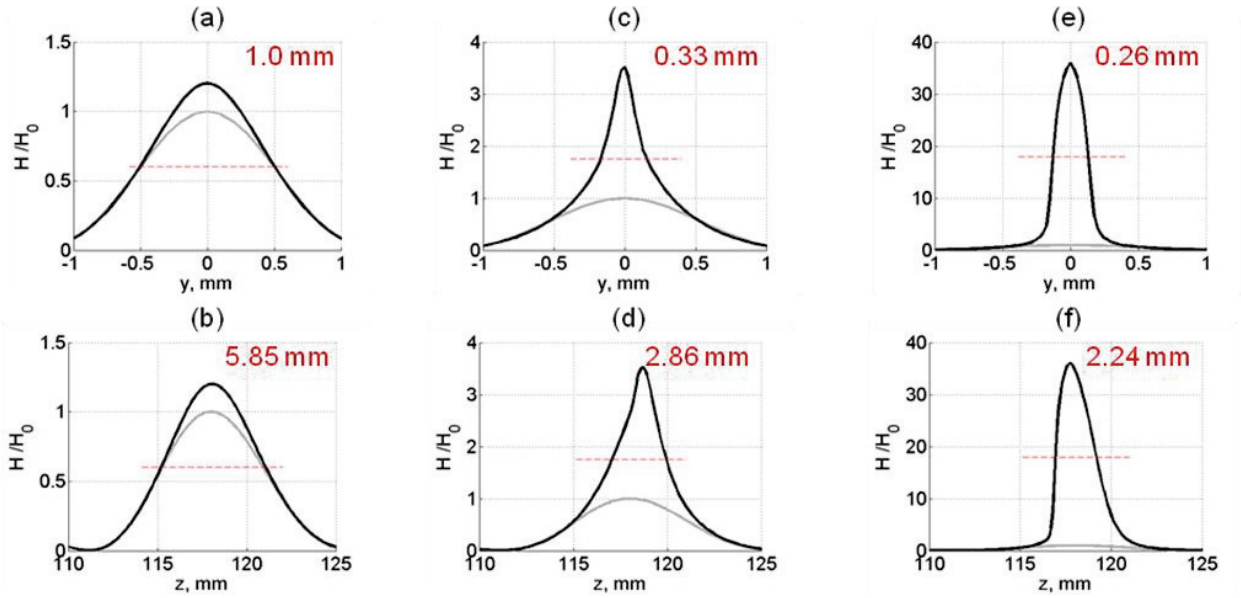

FIGURE 3. Spatial distribution of heat deposition in tissue (black line) H, normalized to the maximum of heat deposition of a harmonic wave (grey curve) $H_0 = 4.8*10^8$ W/m^3 in the case of 1.2 W/cm^3 and proportional in case of higher intensities. The distance in z axis is measured from the transducer. The red dashed lines shows the width for which the diameter of non-linear distributions is calculated and red numbers on each graph indicate the value of this diameter. For the harmonic wave the focal diameter is 1.15 mm and the axial dimension is 5.85 mm. (a,b) focal and axial distributions for the 1.2 W/cm^3 intensity waves; (c,d) the same for the 4 W/cm^3 intensity waves; (e,f) the same for the 8 W/cm^3 intensity waves.

Temperature modeling in tissue was conducted using a bioheat equation:

$$\frac{\partial T}{\partial t} = \chi \Delta T + \frac{Q}{c_v}, \tag{2}$$

where $T(t,\vec{r})$ is the temperature rise, t – time, $\chi = 1.93\times10^{-7}$ m^2/s – thermal diffusivity, $c_v = 3.06\times10^6$ J×m^{-3} °C^{-1} – specific heat capacity per unit volume, $Q(t,\vec{r})$ – heat deposition caused by HIFU (Fig. 3).

As shown in Fig. 3, spatial distributions of heat deposition become very narrow for individual shock-wave sonications (Fig. 3c) as compared to the quasi-linear case (Fig. 3a), about four times smaller in the lateral direction and about twice shorter in the axial direction. The dimensions of the heat deposition focal zone vary from 5.85 mm to 2.25 mm axially and from 1 mm to 0.25 mm laterally. To obtain adequate results in the time-domain modeling, the peak should contain at least 10 grid points. For the full 3D modeling space of the size of the tissue sample it leads to very high memory requirements and long computation of each time step. Simulations were optimized in the following way. First, the effect of a sonication in a single focus was computed in time domain on a fine grid, which covered only the focal volume until the diffused temperature distribution was broad enough to be transferred on a sparser grid that covered the full tissue sample. Second, volumetric modeling was conducted at the sparser grid in a spatial-frequency domain where an analytic solution is available [6]. Based on the linearity of the bioheat equation, the temperature distribution calculated at the first step was added to the current temperature distribution in tissue at each steering position of the focus with the time delay equal to the heating and diffusion time of the sonication in a single focus.

This way, the solutions can be obtained with large time steps at the moments, when pulse sonications stopped and at other times when HIFU was off. The spatial grid step was 0.025 mm for the *x* and *y* axes (focal plane), 0.1 mm for *z* axis (axial) plane for the fine grid and 0.05, 0.2 mm correspondingly for the sparse grid. Simulations were performed for 12 seconds of sonication with steering of the focus every 40 ms and 12 repetitions of the complete sonication trajectory, which started from the center and spiraled outward.

RESULTS

The lowest-intensity continuous wave protocol (40 ms pulses, 1.2 W/cm^3) resulted in a temperature rise of 7^{o}C for a single-focus sonication and 27^{o}C at the center of the treated volume after the complete exposure lasting 12 seconds. For the remaining two protocols it required 9 and 5 seconds, correspondingly, to reach the same temperature at the center of the volume. Maximum achieved temperatures at the end of treatment were 40^{o}C and 64^{o}C. In a single focus the temperature rise was 19^{o}C and 200^{o}C, which shows strong enhancement of heating for shock-wave irradiation. Shown in Fig.4 are the final temperature distributions in the tissue sample. It is seen that with the increase of the initial peak intensity and formation of a shock front at the focus, not only the temperature rises effectively faster, but also the boundary between treated and untreated tissue becomes more clearly defined.

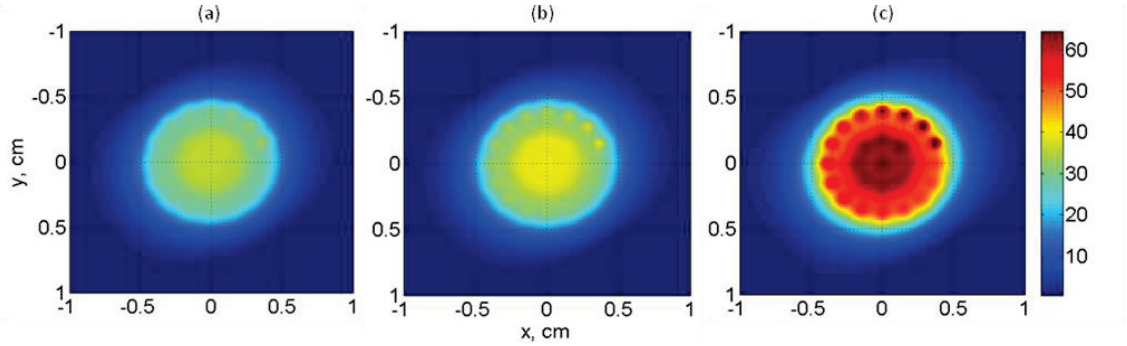

FIGURE 4. Temperature rise maps in the focal plane after 12 seconds of sonication for protocols with the same time-average power but different peak intensity at the array elements of 1.2 W/cm^2 (a), 4 W/cm^2 (b) and 8 W/cm^2 (c).

CONCLUSION

A computational method that allows fast calculations of the bioheat equation containing significantly different time- and spatial scales was developed to simulate heating of clinically relevant tissue volumes. HIFU irradiations in three different nonlinear regimes were considered. It was shown that with the same time-average power, the use of pulsing schemes with high peak power and corresponding high amplitude shocks at the focus lead to certain clinical advantages as compared to harmonic continuous wave sonications: faster heating of the desired volume and therefore lesser heat diffusion to the surrounding tissues. In addition, a relative decrease of the nearfield heating occurs, because nonlinear enhancement of heating is localized only at the focus.

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