Thermal Lesion Development in Bubble-Mediated HIFU: Modeling

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Abstract. Fast heat deposition during high-intensity focused ultrasound (HIFU) therapy is often accompanied by acoustic cavitation. *In vivo* and *in vitro* experiments have shown that with cavitation the heating rate is greatly enhanced and HIFU efficacy can be favorably improved. However uncontrolled cavitation usually results in irregular lesions and other undesirable effects. This work studies the interaction between the ultrasound pressure, cavitation and temperature field in a medium containing cavitation bubbles, with size distribution estimated by stability criteria and number density estimated from empirical observations. Treating the bubbly mixture as an effective medium with effective sound speed and attenuation coefficient determined from bubble dynamics, iterative computations on acoustic propagation and subsequent cavitation and thermal effects can be performed. The thermal lesion development is then simulated in a tissue-like medium exposed to 1-MHz HIFU in CW with MPa pressure amplitudes, and compared with experiment.

Keywords: HIFU, cavitation, effective medium, thermal lesion, nonlinear bubble dynamics.
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INTRODUCTION

Acoustic cavitation is often the result of the application of high-intensity ultrasound in biological structures. Characterized by the efficient and highly nonlinear conversion of acoustic energy to mechanical motion, cavitation brings both undesirable and desirable effects to ultrasound therapy. Cavitation bubbles formed in the propagation path scatter and absorb much of the delivered energy before it reaches the target area, which induce tissue damage in unwanted areas [1, 2]. On the other hand, bubbles greatly enhance the heating effects from HIFU in the focal zone [3], which is attractive to therapeutic procedures requiring efficient large-scale energy deposition. Recent studies [4, 5] indicate that bubble-assisted HIFU therapy protocols can be designed, provided cavitation works effectively in and only in target areas. To understand more about the bubble-mediated HIFU we present here a tractable effective medium model for including the effect of bubbles on both the acoustic and thermal fields.

PHYSICAL CONSIDERATIONS

We employ the Westervelt nonlinear wave equation to model the acoustic pressure propagation in an homogeneous, absorptive tissue [6]. Once the pressure field is

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known, the heat source from sound absorption can be calculated and the Pennes bio-heat equation [7] can be solved for the temperature field. The result thermal dose TD_{43} can be calculated [8] and by defining lesions with TD_{43} greater than 240min the thermal lesion development can be simulated. The presence of acoustic cavitation however, introduces significant complexities. It is generally intractable to account for bubble effects by a linear summation of contributions from individual bubbles. Instead we consider the multi-scale structure of cavitation activity in HIFU. The time scale for bubble oscillations is 10^{-6} s, whereas that for bubble field dynamics is 10^{-3} s and the thermal time scale is 1 s. The relevant spatial scale for individual bubbles is 10^{-6} m, while the acoustic wave length and size of the cavitation field are on the order of 10^{-3} m. This well-separated multi-scale feature makes it possible to treat the bubbly mixture as an effective medium and compute the acoustic propagation in this medium with averaged acoustic parameters, essentially the effective speed of sound and the effective attenuation coefficient, which are obtained from bubble dynamics.

For cavitation bubbles in HIFU, small ones will dissolve away under surface tension; bubbles surviving surface tension will grow by rectified diffusion until reaching diffusion equilibrium or breaking upon shape instability. The remnants from broken bubbles can serve as new cavitation nuclei. The medium properties, including surface tension, viscosity, dissolved gas content, compressibility, and the bubble dynamics including dissolution, rectified diffusion, break-up, together have placed stability boundaries for possible size distributions (for details see ref.[9]). For 1-MHz MPa HIFU, the allowed initial radius of cavitation bubbles is of order 0.1-1μm. The rectified diffusion growth rate is extremely large for 0.1μm bubble and considerably smaller for bubbles near 1μm. We further let the bubble initial size be 1 μm averaged over the bubble field dynamics time scale. Taking these considerations into account, we compute the time averaged sound speed and attenuation for a HIFU bubbly medium containing 1 μm bubbles at number density $n=5\ mm^{-3}$. The number density is chosen to be on the order of optimal bubble enhanced heating effect estimations [10].

The resonant frequency for a 1 μm bubble is approximately 3MHz, which is greater than the HIFU frequency; this enables us to employ Wood's equation [11] for the sound speed *c* of the bubbly mixture with time averaged void fraction given by $n<4\pi R^3/3>$ where R is the time dependent bubble radius. The primary mechanisms by which an oscillating bubble dissipates incident acoustic energy are viscous damping and acoustic radiation. Having obtained the dissipation powers from bubble motions R(t), we calculate the extinction cross section σ_{ext} [12], which characterizes the total energy removal from the incident beam by one single bubble. The effective attenuation coefficient of the bubbly mixture can be obtained from the summation of the attenuation from medium and bubbles $\alpha_{eff}=\alpha_m+n\sigma_{ext}$. Both calculation of the effective sound speed and attenuation are based upon bubble dynamics and thus both are pressure-dependent.

As the surrounding temperature increases during the HIFU insonation, there will be increasingly strong effects on the bubble dynamics. Assuming tissue properties respond to temperature elevation similarly as water, the surface tension and viscosity will decrease while vapor pressure increases when medium temperature increases. Consequently the effective medium parameters computed via the bubble dynamics become temperature dependent, which will be included in the current model.

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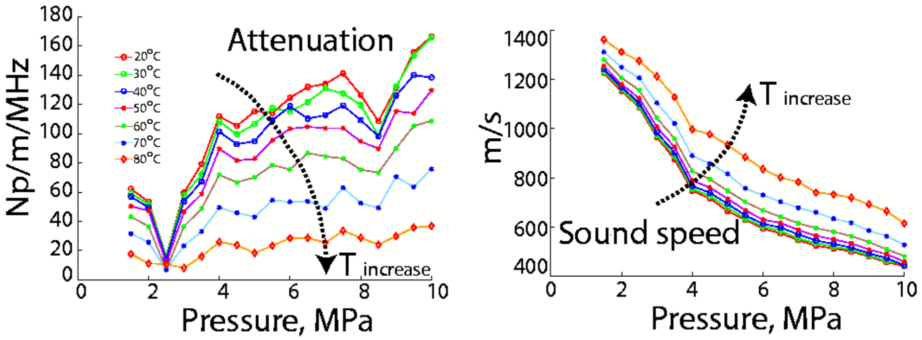

Figure 1. The effective attenuation coefficient and the effective sound speed for local pressure amplitudes ranging from 1.5 to 10 MPa and for temperatures from 20 ºC to 80 ºC.

Figure 1 shows that the effective bubbly medium attenuation increases strongly, while the effective sound speed decreases strongly with increasing pressure amplitude. We note that the local minimum at 2.3MPa for α_{eff} is the result of single bubble nonlinear behavior. It will be smoothed by the uncertainties in initial bubble sizes and their paths to equilibrium in most clinical conditions. The bubbly medium attenuation approaches the original medium attenuation as the temperature increases, while the sound speed remains well below the normal value.

SIMULATION, RESULTS AND DISCUSSION

With pressure-temperature dependent effective medium c and α_{eff} at hand, we compute HIFU propagation and the resulting temperature field in the presence of bubbles by solving the coupled Westervelt and Pennes equations. The calculation was constructed on a finite-difference time-domain (FDTD) scheme [6] in 2-D axi-symmetric cylindrical coordinates assuming quasi-steady field parameters. Since the pressure, temperature and effective medium parameters interact with each other and evolve with time, the computation was performed in an iterative fashion. In spatial locations where the pressure exceeded the cavitation threshold, effective values for c and α_{eff} were computed and used. The acoustic propagation was then re-calculated using effective parameters and the cavitation fields were re-allocated in space according to the new pressure fields. The pressure, cavitation and temperature fields were calculated every 100ms in the first second and then every 1s until 5s. This was done in order to mimic the experimentally observed phenomena that cavitation fields migrated very fast initially and tended to be stabilized later [13]. The cavitation threshold and the bubble population density in the cavitation zones, however, were kept constant in all computations. The thermal dose and lesion areas were calculated every second through the entire simulation time.

Figure 2 summarizes the results of one simulation in which the cavitation threshold was set to 1.7MPa and the HIFU focal pressure amplitude was 2.5MPa. Asymmetric “tadpole” shaped lesions can be identified (A1-A5) as early as 1s after HIFU begins (no boiling was induced in these simulations). Within the first second, active cavitation fields migrated towards the transducer and shielded acoustic energy from

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further penetration, which can be inferred from the fact that less cavitation activity was seen in the focal region within the first second (B1-B10). The observation of local sound speed (C1) and attenuation (C2) yielded a similar conclusion, in that the position of largest attenuation and lowest sound speed (signature of active cavitation) moves from the HIFU focal zone to the prefocal zone. We simulated the lesions under the same conditions but without the local pressure and/or temperature dependences on sound speed and attenuation in E and F. A comparison of the results (lesions A5,E,F) to a typical lesion observed in experiments (lesion D) qualitatively showed that simulations with both pressure and temperature effects match experiment somewhat better. Neglecting both effects under-predicts the resulting lesioned area, while neglecting only temperature dependences results in a slight over-prediction of the lesion size.

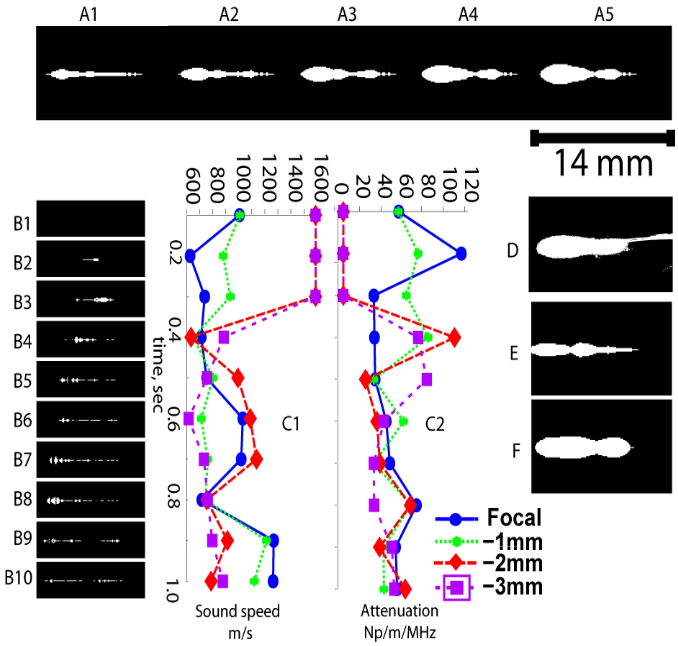

Figure 2. A1-A5 are computed lesions from 1 to 5 sec in 1sec increments; B1-B10 are the computed cavitation zones (pressure amplitude exceeds threshold) from 0.1 to 1 sec in 0.1 sec increments; C1 and C2 show sound speed and attenuation versus time at the HIFU focus, -1,-2 and -3 mm pre-focal; D is a binarized-photo of a typical lesion obtained in experiments. Lesions E and F are computed results neglecting the local pressure/temperature, and the local temperature only, respectively.

SUMMARY AND OUTLOOK

Based upon interactive bubble dynamics in an evolving pressure and temperature field, we have constructed a numerical model that can compute bubble-enhanced temperature profiles given HIFU transducer conditions and acoustic inputs. The ultrasound propagation and absorption are considered in an effective bubble medium whose acoustic properties are controlled by the pressure-temperature dependent

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bubble dynamics in a tissue-like medium, taking into account cavitation mechanisms of nucleation, dissolution, rectified diffusion and shape instability. The model may be a starting point for treatment planning and dosimetric simulations when cavitation is present during therapy.

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