

Acoustic propagation effects in therapeutic ultrasound

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Abstract. Accurate understanding of ultrasound-tissue interaction is important for realization of clinically useful therapeutic ultrasound methods and devices. Linear acoustic propagation in homogeneous media, including diffraction and absorption effects, provides a useful first approximation but fails to accurately model many problems of interest. Depending on the therapy regime, other important effects can include cavitation and other gas activity, inhomogeneous tissue structure, finite-amplitude propagation, temperature-dependent tissue properties, and irreversible tissue modification. For ablation of soft tissue using ultrasound, prediction of therapeutic effects requires accurate knowledge of space- and time-dependent heat deposition from acoustic absorption. In addition to perfusion losses, acoustically inhomogeneous tissue structure, even in nominally homogeneous organs such as the liver, can modify heating patterns enough to change treatment outcomes. Gas activity due to boiling and tissue property changes due to local ablation, both of which markedly affect treatment, can be approximated by appropriate modification of the initial heat deposition pattern. These issues are illustrated by simulations of ultrasound therapy and comparison with *in vivo* and *in vitro* ultrasound ablation experiments.

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INTENSE ULTRASOUND ABLATION

This paper reviews recent work concerning the effects of propagation phenomena on ultrasound thermal therapy, with emphasis on modeling of bulk ablation using intense ultrasound beams that are unfocused or weakly focused; this approach has been developed for interstitial ablation of focal tumors [1]–[3]. In one recent approach for interstitial intense ultrasound ablation [3], an ultrasound probe capable of both B-scan imaging and intense ultrasound ablation is inserted into target tissue, using a percutaneous, laparoscopic, or open-surgery approach. The probe is then used to image the target tissue, allowing user planning of an ablation procedure, and thermal ablation of a tissue volume is performed using electronic scanning and mechanical probe rotation. One probe configuration recently employed for this approach is based on an ultrasound array operating at a frequency 3.1 MHz, capable of acoustic energy densities $> 80 \text{ W/cm}^2$ at the probe surface, with active dimensions of about $2.3 \times 49 \text{ mm}^2$ [3].

Numerical modeling of interstitial ablation has been performed using numerical solution of the bio-heat transfer equation, which represents heat diffusion with an added term for perfusion losses [4]. Heat deposition associated with ultrasound absorption has been incorporated using a number of numerical propagation models, some of which have considered tissue changes induced by thermal coagulation [2, 5, 6]. Typically, cumulative thermal damage to tissue is measured using the thermal dose [7], which is defined

in units of equivalent minutes at 43°C, with damage threshold values on the order of $EM_{43} = 200$ min for cell death and $EM_{43} = 10^7$ min for complete protein denaturation and severe coagulative necrosis [6]. These values correspond to measurable transitions in the ultrasonic absorption of soft tissue [8].

For absorption caused by relaxation processes, the rate of heat deposition per unit volume is $Q = \alpha |p|^2 / (\rho c)$ [9], where α is the acoustic absorption in nepers per unit length, $|p|$ is the pressure amplitude of a time-harmonic acoustic field, and c is the speed of sound. Acoustic fields induced by ultrasound transducers can be simulated in a number of manners suitable for efficient numerical computations, including the Fresnel approximation for the fields of rectangular elements [3, 10], exact series solutions for disk radiators in unfocused [11, 12] and focused [13] configurations, and the KZK equation for approximations of finite-amplitude propagation [14, 15]. More general computations of propagation in inhomogeneous tissue for therapy modeling can be performed using three-dimensional tissue models, which can be established from image data such as cross-sectional photography or volumetric CT scans [16, 17]. For large-scale three-dimensional computations, such as those required for simulation of ultrasound therapy, a particularly useful approach is the k -space method [18, 19], which provides accurate results for relatively coarse spatial and temporal discretization. Acoustic absorption effects can be incorporated directly into any of these models, or can be applied *post hoc* in an approximate manner. The approximate approach to absorption modeling is convenient for representing changes in heat deposition due to tissue modification without further computation of the full acoustic field [6].

PHENOMENA AFFECTING ULTRASOUND ABLATION

Although numerical models of ultrasound ablation employing homogeneous media provide considerable insight, they often fail to predict the significant variability of real ablation results *in vivo*, due to factors including those described below.

Most simulations of ultrasound propagation for therapy modeling have assumed tissue structure either to be uniform [6, 20] or composed of uniform layers [21]. However, the inhomogeneous structure of real tissue, which causes distortion of ultrasound beams known to cause significant aberration in ultrasound imaging [22], is equally relevant to ultrasound therapy. In a common noninvasive HIFU configuration, a highly focused ultrasound beam propagates through the abdominal wall to ablate tissue in the abdominal cavity, such as a liver tumor [23, 24]. Measurements [22] and simulations [25] have indicated that propagation through the abdominal wall can cause random fluctuations on the order of 3 dB (rms) in the transmitted amplitude, due both to scattering and inhomogeneous absorption. A 3 dB change in amplitude, which corresponds to a factor of two in heat deposition, causes the time required for local tissue ablation to be correspondingly changed by a factor of two, large enough to significantly change ablation results for a given treatment plan.

Inhomogeneous tissue structure can also affect ablation results within nominally homogeneous organs such as the liver. An example from an interstitial ablation experiment performed *in vivo* in porcine liver is shown in Fig. 1 (a). In this case, anomalously severe and deep ablation occurred distal to a large blood vessel. A plausible explanation for this

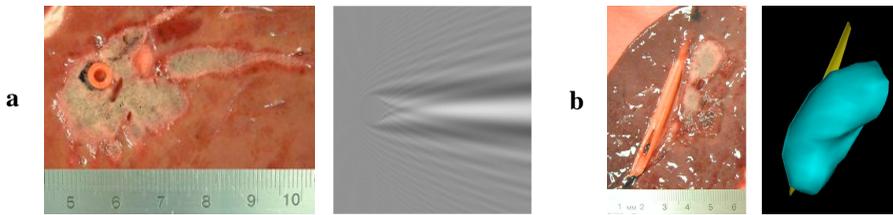


FIGURE 1. Example effects of blood vessels on ultrasound bulk ablation. (a) Acoustic effects of a large blood vessel on interstitial bulk ablation: cross section of a thermal lesion created *in vivo* with a rotationally scanned 3 mm, 3.1 MHz array, showing anomalously large ablation distal to the vessel, and simulated total squared pressure amplitude for a 3.1 MHz plane wave scattered by a 3 mm blood-mimicking cylinder in a liver-mimicking background. (b) Cooling effects: cross section of a thermal lesion from an *in vivo* interstitial, rotationally scanned exposure and surface rendering of lesion from multiple cross sections.

result is acoustic focusing caused by the difference in sound speed between blood and liver parenchyma. This possibility is illustrated here by a computation performed using the exact solution for scattering from a fluid cylinder [26], with the liver background was modeled as a fluid with sound speed 1595 m/s and the blood vessel modeled as a cylinder with sound speed 1580 m/s. The simulated acoustic field image in Figure 1(a) shows substantial focusing, resulting in over a 50% increase in peak heat deposition, consistent with the increased lesioning shown. This result is opposite to the typical alterations in heating patterns associated with cooling effects caused by large vessels, illustrated in Fig. 1 (b) by a thermal lesion induced interstitially in porcine liver *in vivo*. In the vicinity of large blood vessels, tissue ablation can be substantially reduced due to local cooling effects [3, 20].

For the intense ultrasound beams employed in bulk ablation, finite-amplitude propagation has a nonzero effect, due to both waveform steepening (generation of higher harmonics) and inertial cavitation. For a recent ultrasound bulk ablation configuration [3], a typical acoustic pressure amplitude is about 1.5 MPa at the transducer surface for a frequency of about 3 MHz; a test computation has shown that acoustic nonlinearity has a small effect on heat deposition compared to other phenomena described here [27]. The importance of inertial cavitation can be assessed using the mechanical index (MI) [28], which for the same configuration has a maximum value of 0.866, substantially less than the maximum value of 1.9 generally recognized as safe for diagnostic ultrasound.

Particularly severe effects on ultrasound ablation are caused by changes to tissue acoustic properties that result from thermal coagulation. These include increases in tissue absorption that have been quantified by measurements [8] and gas activity due to tissue boiling, which has been observed to alter positions and extents of HIFU lesions [29, 30]. Effects of ablation on tissue absorption have been incorporated into numerical models, in correspondence with measurements [8], using both stepwise-discontinuous [2] and piecewise-linear [5, 6] dependence of absorption on thermal dose. The effects of tissue boiling, which include both strong shadowing and increased local absorption, can limit the achievable depth of ultrasound ablation. This effect has been modeled for single HIFU lesions by redistributing the thermal energy originally deposited in

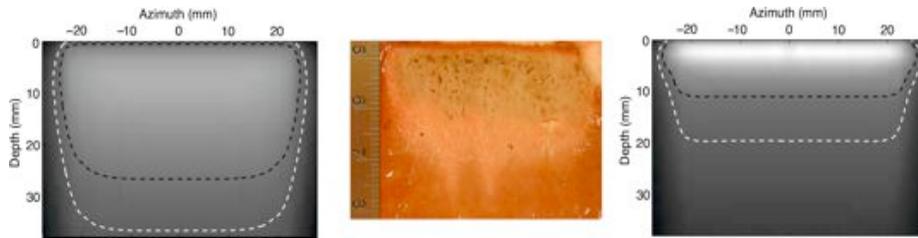


FIGURE 2. Effect of boiling and thermal dose dependent attenuation for a lesion created in *ex vivo* porcine liver tissue by a 3 mm, 3.1 MHz array. Left: simulation without boiling and dose-dependent attenuation modeling. The simulated thermal dose is shown on a logarithmic gray scale with superimposed contours at $EM_{43}=200$ and 10^7 equivalent minutes. Center: *In vitro* lesion. Right: simulated thermal dose with boiling and dose-dependent attenuation modeling.

the distal half-space into a small spherical region centered at the location of initial tissue boiling [31]. For simulation of bulk tissue ablation, in which boiling effects are not necessarily localized at a focal point, the thermal energy deposited within the region shadowed by all boiling locations has been taken to be redistributed around each of the boiling locations [6]. These tissue modification effects can substantially effect ultrasound bulk ablation, as illustrated by Fig. 2. The two simulated thermal dose maps shown were obtained by identical methods except for modeling of boiling and thermal dose-dependent attenuation, which results in much better agreement with the experimental result for the depth, overall shape, and rate of thermal ablation.

In summary, modeling of therapeutic ultrasound requires consideration of an array of potential complicating effects. For interstitial bulk ablation, the most important effects include the thermal and acoustic effects of natural tissue inhomogeneities as well as tissue changes caused by the therapy itself. Other therapy regimes can require different considerations for accurate modeling, such as explicit treatment of finite-amplitude propagation and inertial cavitation. For any form of ultrasound therapy, it is likely that natural variations of tissue properties and structure will limit the predictive accuracy of simulations. Thus, methods for accurate monitoring and assessment of ultrasound ablation effects could increase the clinical viability of therapeutic ultrasound.

REFERENCES

1. R. Chopra, M. J. Bronskill, and F. S. Foster, "Feasibility of linear arrays for interstitial ultrasound thermal therapy," *Med. Phys.* **27**, 1281–1286 (2000).
2. C. Lafon, F. Prat, J. Y. Chapelon, F. Gorry, J. Margonari, Y. Theillere, and D. Cathignol, "Cylindrical thermal coagulation necrosis using an interstitial applicator with a plane ultrasonic transducer: *in vitro* and *in vivo* experiments versus computer simulations," *Int. J. Hyperthermia* **16**:508–522 (2000).
3. I. R. S. Makin, T. D. Mast, W. Faidi, M. M. Runk, P. G. Barthe, and M. H. Slayton, "Miniaturized ultrasound arrays for interstitial ablation and imaging," *Ultras. Med. Biol.*, in press (2005).
4. H. H. Pennes, "Analysis of tissue and arterial blood temperatures in the resting human forearm," *J. Appl. Physiol.* **1**, 93–122 (1948).
5. P. D. Tyreus and C. J. Diederich, "Theoretical model of internally cooled interstitial ultrasound applicators for thermal therapy," *Phys. Med. Biol.* **47**:1073–1089 (2002).
6. T. D. Mast, I. R. S. Makin, W. Faidi, M. M. Runk, P. G. Barthe, and M. H. Slayton, "Bulk ablation of

- soft tissue with intense ultrasound: modeling and experiments," *J. Acoust. Soc. Am.* **118**, 2715–2724 (2005).
7. S. A. Sapareto and W. C. Dewey, "Thermal dose determination in cancer therapy," *Int. J. Radiat. Oncol. Biol. Phys.* **10**, 787–800 (1984).
 8. C. A. Damianou, N. T. Sanghvi, F. J. Fry, and R. Maass-Moreno, "Dependence of ultrasonic attenuation and absorption in dog soft tissues on temperature and thermal dose," *J. Acoust. Soc. Am.* **102**, 628–634 (1997).
 9. W. L. Nyborg, "Heat generation by ultrasound in a relaxing medium," *J. Acoust. Soc. Am.* **70**, 310–312 (1981).
 10. A. Freedman, "Sound field of a rectangular piston," *J. Acoust. Soc. Am.* **32**, 197–209 (1960).
 11. T. Hasegawa, N. Inoue, and K. Matsuzawa, "Fresnel diffraction: Some extensions of the theory," *J. Acoust. Soc. Am.* **75**, 1048–1051 (1984).
 12. T. D. Mast and F. Yu, "Simplified expansions for radiation from a baffled circular piston," *J. Acoust. Soc. Am.*, submitted (2005).
 13. T. Hasegawa, N. Inoue, and K. Matsuzawa, "A new theory for the radiation from a concave piston source," *J. Acoust. Soc. Am.* **82**, 706–708 (1987).
 14. E. A. Zabolotskaya and R. V. Khokhlov, "Quasi-plane waves in the non-linear acoustics of confined beams," *Sov. Phys. Acoust.* **15**, 35–40 (1969).
 15. V. P. Kuznetsov, "Equation of nonlinear acoustics," *Sov. Phys. Acoust.* **16**, 467–470 (1970).
 16. J. L. Aroyan, "Three-dimensional modeling of hearing in *Delphinus delphis*," *J. Acoust. Soc. Am.* **110**, 3305–3318 (2001).
 17. T. D. Mast, "Two- and three-dimensional simulations of ultrasonic propagation through human breast tissue," *Acoust. Res. Lett. Online* **3**, 53–58 (2002).
 18. N. N. Bojarski, "The k -space formulation of the scattering problem in the time domain: an improved single propagator formulation," *J. Acoust. Soc. Am.* **77**, 826–831 (1985).
 19. T. D. Mast, L. P. Souriau, D.-L. Liu, M. Tabei, A. I. Nachman, and R. C. Waag, "A k -space method for large-scale models of wave propagation in tissue," *IEEE Trans. Ultrason., Ferroelectr., Freq. Contr.* **48**, 341–354 (2001).
 20. F. P. Curra, P. D. Mourad, V. A. Khoklova, R. O. Cleveland, and L. A. Crum, "Numerical simulations of heating patterns and tissue temperature response due to high-intensity focused ultrasound," *IEEE Trans. Ultrason., Ferroelectr., Freq. Contr.* **47**, 1077–1089 (1999).
 21. I. M. Hallaj, R. O. Cleveland, and K. Hynynen, "Simulations of the thermo-acoustic lens effect during focused ultrasound surgery," *J. Acoust. Soc. Am.* **109**, 2245–2253 (2001).
 22. L. M. Hinkelman, T. D. Mast, L. A. Metlay, and R. C. Waag, "The effect of abdominal wall morphology on ultrasonic pulse distortion. Part I: Measurements." *J. Acoust. Soc. Am.* **104**:3635–3649 (1998).
 23. G. R. ter Haar, D. Sinnett, and I. Rivens, "High-intensity-focused ultrasound: a surgical technique for the treatment of discrete liver tumors," *Phys. Med. Biol.* **34**, 1743–1750 (1989).
 24. F. Wu, W.-Z. Chen, J. Bai, J.-Z. Zou, Z.-L. Wang, H. Zhu, and Z.-B. Wang, "Pathological changes in human malignant carcinoma treated with high-intensity focused ultrasound," *Ultras. Med. Biol.* **27**, 1099–1106 (2001).
 25. T. D. Mast, L. M. Hinkelman, M. J. Orr, V. W. Sparrow, and R. C. Waag, "Simulation of ultrasonic propagation through the abdominal wall," *J. Acoust. Soc. Am.* **102**, 1177–1190 (1997).
 26. P. M. Morse and K. U. Ingard, *Theoretical Acoustics* (McGraw-Hill, New York, 1968), Ch. 8.
 27. T. D. Mast, I. R. S. Makin, and W. Faidi, "Acoustic field modeling in therapeutic ultrasound," *Proceedings of the 17th International Symposium on Nonlinear Acoustics* (American Institute of Physics, 2005);
 28. R. E. Apfel and C. K. Holland, "Gauging the likelihood of cavitation from short-pulse, low duty cycle diagnostic ultrasound," *Ultrasound Med Biol.* **17**, 179–185 (1991).
 29. N. A. Watkin, G. R. ter Haar, and I. Rivens, "The intensity dependence of the site of maximal energy deposition in focused ultrasound surgery," *Ultras. Med. Biol.* **22**, 483–491 (1996).
 30. W.-S. Chen, C. Lafon, T. J. Matula, S. Vaezy, and L. A. Crum, "Mechanisms of lesion formation in high intensity focused ultrasound therapy," *Acoust. Res. Lett. Online* **4**, 41–46 (2003).
 31. P. M. Meaney, M. D. Cahill, and G. R. ter Haar, "The intensity dependence of lesion position shift during focused ultrasound surgery," *Ultras. Med. Biol.* **26**, 441–450 (2000).