Estimation of the tissue lesion induced by a transmitter with aluminium lens

Tingbo Fan, Dong Zhang, Xiufen Gong
Institute of Acoustics, Key Laboratory of Modern Acoustics(Nanjing University), Ministry of Education, Nanjing University, Nanjing 210093, China
dzhang@nju.edu.cn

Abstract. A virtual source model is developed to describe the nonlinear acoustic field generated by a transmitter with aluminium lens. This model assumes the geometry focal length of the virtual concave transducer to be equal to the acoustic focal length of the real transducer. Thus the acoustic field in the focal area can be accurately presented by that generated by the virtual source. This model in combination with the bio-heat equation is applied to the size estimation of tissue lesion created by high intensity focused ultrasound. A transmitter with aluminium lens is used to create tissue lesions for bovine livers in vitro under three different focal acoustic intensities of 7, 13.1, 25.4 kW/cm2. The predicted tissue lesion volumes coincide well with those previously reported measured results for 7 kw/cm2, but are smaller those in the measurement for 13.1 and 25.4 kW/cm2 owing to effect of vapor bubbles.

1. Introduction
High Intensity Focused Ultrasound (HIFU) is a noninvasive treatment that delivers high intensity ultrasound energy into the targeted area of tissue within the body without damage to intervening tissue. The principle of this technique is to raise the tissue temperature to relatively high values and cause thermal coagulation and ablation of cells by using an ultrasonic focusing transducer. HIFU devices are currently under investigation as an effective treatment modality for ablating solid tumors of the prostate, liver, breast, kidney, and brain. In order to provide a focus with prescribed depth and shape in HIFU therapy, single element therapy transducers are designed using a flat piezoelectric element with a lens, a spherically curved element with concavity in the propagation direction, or a combination of transducer curvature and a lens. The first type of transmitter has been widely used in the clinical applications owing to its facile manufacture. Previously, Wang et al used a 1.6 MHz flat annular piezoelectric element and an aluminium lens as a HIFU transmitter, and three kinds of acoustic power were applied to create tissue lesions in bovine liver tissues [1]. As we know, it is highly desirable in HIFU therapy to produce lesions with well-controlled spatial characteristics. To achieve this purpose, it is important of well understanding of the acoustic field generated by the transmitter.

The Westervelt equation is usually used to describe the finite amplitude ultrasound propagation in a medium [2]. Some approximations can be employed to reduce the complexity of numerical calculation. The widely accepted Khokhlov-Zabolotaskaya-Kuznetsov (KZK) equation can be derived under paraxial approximation [3]. It can accurately describe the acoustic field generated from a transducer with half aperture angle less than 16° [4]. For strongly focused finite amplitude sound
beams, the spheroidal beam equation (SBE) is developed for describing the sound propagation [5]. Unfortunately, since the half aperture angle of this kind of transducer study is larger than 16°, the KZK equation is not suitable for describing the acoustic field. On the other hand, as the phase on the lens surface is not uniform, the SBE model cannot be directly used to describe the acoustic field. For this reason, we put forward a virtual source approach to predict the acoustic field generated from this transmitter. To examine the validity of this theoretical model, we apply the same transmitter used in the previous experimental study [1] to the numerical simulation. Three different kind of focal acoustic intensities are used in to create tissue lesions for 20s, and the predicted tissue lesion volumes are compared with the published in vitro results.

2. Methods
Figure 1 illustrates a 1.6 MHz single element transmitter (diameter \(a_2=7.5\) cm) used in the simulation, whose configuration is the same as that in the previous experiment [1]. It consists of a flat annular piezoelectric element and an aluminium lens. An aperture \((a_1=4.0\) cm) in the center of the transducer is used to mount the imaging transducer confocally to monitor therapeutic processes. OD=9.3 cm represents geometry focal length of aluminum lens and OF=11.90 cm is acoustic focal length which can be calculated using Rayleigh integral.

![Fig.1 Geometry of the transmitter used in the simulation. The transmitter consists of a flat annular piezoelectric element and an aluminium lens.](image)

Since the half aperture angle of the transducer is larger than 16°, the KZK equation is not suitable for describing the acoustic field. On the other hand, as the phase on the lens surface is not uniform, the SBE model cannot be directly used to describe the acoustic field. For this reason, we put forward a virtual source approach to predict the acoustic field generated from this transmitter. Points D and F represent the geometry focuses of the real source and virtual source respectively. The inner and outer apertures of the virtual source are \(a_{v1}=4.07\) cm and \(a_{v2}=8.09\) cm respectively, which can be calculated easily using geometric relations. The geometry focal length of the virtual concave transducer is set to be equal to the acoustic focal length of the real transducer with lens, and the phase on the virtual source is assumed to be uniform. In this way, the SBE model can be applied to predict the acoustic field generated by the virtual source. Under this hypothesis, only the acoustic field in the focal area can be approximately presented by the virtual acoustic field. The acoustic field generated by the virtual source is described using SBE model.

The temperature rise in soft tissues can be modeled by a diffusion type equation. The Pennes bioheat transfer equation (BHTE) is used to describe the thermal effects of ultrasound in tissue [6], [7].

\[
\frac{\partial T}{\partial t} = \frac{1}{\rho_0 C_e} \nabla (k_0 \nabla T) - \frac{W_b}{\rho_0 C_e} (T - T_a) + \frac{Q}{\rho_0 C_e},
\]

where \(\rho_0\) is the ambient tissue density and \(T\) is the temperature in the tissue; the thermal conductivity and specific heat at constant pressure are \(k_0\) and \(C_e\). The second term on the right-hand side accounts for heat loss via tissue perfusion. The perfusion constant for a given tissue is \(W_b\) and \(C_b\) is specific heat of blood. \(T_a\) is the ambient temperature. The last term is heat source due to the acoustic field, which can be calculated by:
\[ Q = 2 \pi l = \frac{1}{\rho c_0} \sum_{n=1}^{N} \alpha_{n} |C_n|^2 \]  

(2)

where \( N \) is the harmonic number used in calculation, \( C_n \) is the nth harmonic complex amplitude of pressure.

Equation (1) is solved in cylindrical coordinate using the operator-splitting paradigm [8]. Constant flux boundary conditions are assumed for the edges of the computational domain to simulate the extended thermal region beyond the computational boundaries of simulations. The step sizes are set to be 0.1mm along the wave propagation direction and 0.06 mm perpendicular to the propagation direction. The concept of thermal dose (TD) developed by Saparteo and Dewey provides a quantitative description on the heating of tissue [9]. The expression of the TD can be written as:

\[ TD(x, y, z) = \int_{t_0}^{t_1} R^{(t-t_0)} dt \]  

(3)

where TD is the thermal dose in equivalent minutes at 43°C, \( t_0 \) and \( t_1 \) are the starting and ending time of the ultrasound exposure; \( R \) is 0.5 if \( T>43°C \), and 0.25 if \( T<43°C \). Results of previous studies on the effects of hyperthermia have shown that the threshold for 100% necrosis in different tissues ranges 50-240 minutes [10], and we consider 240 minutes as the threshold for lesion formation in this work.

3. Results

To examine the validity of this virtual source model, we first calculate the linear acoustic field in pure water using the virtual source model, and make a comparison with that from Rayleigh integral. In the numerical computation, the acoustic parameters for water [11] are: \( \rho=1000 \text{ kg/m}^3 \), \( c_0=1486 \text{ m/s} \), \( \alpha=0.025 \text{ Np/m/MHz}^2 \), and the acoustic nonlinearity is assumed to be zero. Figure 2 presents the axial and radial pressure profiles normalized by the peak pressure at the transducer surface, where 3a and 3b are axial and radial distributions respectively, and solid lines are calculated by Rayleigh integral, and dash lines are calculated by the virtual source model. Figures 2c and 2d compares the two-dimensional (2D) acoustic spatial distributions between Rayleigh integral and virtual source model. The good agreement of the linear acoustic field in the focal area indicates that it is possible to simulate the temperature distribution and lesion formation on the basis of the virtual source model.

![Fig. 2 The normalized pressure profiles: (a) axial profile, (b) radial profile at focal plane; The two-dimensional acoustic spatial distributions: (c) by Rayleigh integral, and (d) by virtual source model.](image)

In the previous study [1], the transmitter (Fig. 1) was used to be the HIFU source, and three different focal acoustic intensities of 7, 13.1, 25.4 kW/cm² were applied to create tissue lesions in bovine liver tissues in vitro. For further examination of the validity of the virtual source model, we calculate the thermal dose and induced tissue lesions, and make a comparison with the published
experimental results. In the numerical calculation, the values of the acoustic parameters are [11]:

\[ \rho_0 = 1000 \text{ kg/m}^3, \ c_0 = 1486 \text{ m/s}, \ \alpha = 0.025 \text{ Np/m/MHz}^2, \ \beta = 3.5, \]  
for water and \[ \rho_0 = 1214 \text{ kg/m}^3, \ c_0 = 1614 \text{ m/s}, \ \alpha = 4.3 \text{ Np/m/MHz}^{1.266}, \ \beta = 4.775, \]  
for liver tissue; the thermal properties are: \[ k_t = 0.508 \text{ W/m}^\circ\text{C}, \ C_t = 3810 \text{ J.s/m}^3/\circ\text{C}, \ W_b = 0 \]  
for bovine liver tissue in vitro. Changes in the acoustic parameters of tissue due to HIFU-induced heating are not considered in the simulation.

Figure 3 gives the calculated lesion volume created by HIFU at various focal acoustic intensities for 20s. For comparison, the experimental results (from Ref. 1) are also plotted as solid points in this figure. We can find that in Fig. 3a, the calculated result coincides well with the experimental result; however deviations are found from 15 to 20 s in Fig. 3b and from 10 to 20 s in Fig. 3c. Especially in Fig. 6c, the measured lesion volume is almost twice than the calculated volume at 20 s. The deviations probably come from the reason of boiling bubbles which enlarge the lesion volume.

Previous studies indicated that boiling is approached when tissue temperature reaches up to 100°C, and millimeter-sized boiling bubbles are observed [12][13]. HIFU-induced boiling is the responsible for distortion of lesion shape which changes to drop-shape, and results in rapid growth from the focus towards the transducer. Simulated results indicated that tissue temperature in focal region rises up to 100°C in 1.82, 0.41, and 0.07 s for the used focal acoustic intensities of 7.0, 13.1, and 25.4 kW/cm² in this work. The divergence between measured and simulated volume mainly comes from the boiling reason. For relative large intensity, the focal temperature rises up to boiling point more quickly and thus impact on lesion volume is more serious.

4. Conclusions

In this paper, a virtual source model is proposed to predict the nonlinear acoustic field generated from a transmitter with aluminum lens. The geometry focal length of the virtual concave transducer is set to be equal to the acoustic focal length of the real transducer. As a result, the acoustic field in the focal area can be presented by that generated by the virtual source. Since the acoustic power concentrates mostly in focal region and the induced temperature rise during HIFU treatment depends on the focal heat deposition; the deviations of near and far field acoustic distributions does not impact the temperature rise distribution in HIFU therapy prediction, this theoretical model can be applied to the tissue lesion predictions in HIFU treatment. For examine its validity, the linear acoustic field in focal region calculated from this model is in good agreement with that obtained by Rayleigh integral. Further, we extend this model to predict the nonlinear acoustic field and the induced tissue lesion generated by the transmitter with aluminum lens. The lesion volume acquired from simulation coincides well with that acquired from experiment at relative low focal acoustic intensity; however, with the increment of focal acoustic intensity, the divergence between experiment and calculation becomes more obvious owing to the effect of boiling bubbles. Also it should be noted that the further complete model should consider the behavior of temperature effects on tissue physical parameters.

5. Acknowledgements
This work is supported by the National Basic Research Program 973 (Grant No. 2010CB732600) from Ministry of Science and Technology, China, and the National Natural Science Foundation of China (10774071 and 10974093).

References
[1] Z. B. Wang, J. Bai, F. Q. Li, Y. H. Du, S. Wen, K. Hu, G. H. Xu, P. Ma, N. G. Yin, W. Z. Chen, F. Wu and R. Feng, “Study of a “biological focal region” of high-intensity focused ultrasound,” Ultrasound Med. Biol., vol. 29, pp. 749-754, May, 2003.
[2] P. J. Westervelt, “Parametric acoustic array,” J. Acoust. Soc. Am., vol. 35, pp. 535-537, Apr., 1963.
[3] S. I. Aanonsen, T. Barkve, J. N. Tjøtta and S. Tjøtta, “Distortion and harmonic generation in the nearfield of a finite amplitude sound beam,” J. Acoust. Soc. Am., vol. 75, pp. 749-768, Mar., 1984.
[4] T. S. Hart and M. F. Hamilton, “Nonlinear effects in focused sound beams,” J. Acoust. Soc. Am., vol. 84, pp. 1488-1496, Oct., 1988.
[5] T. Kamakura, T. Ishiwata, K. Matsuda, “Model equation for strongly focused finite-amplitude sound beams,” J. Acoust. Soc. Am., vol. 107, pp. 3035-3046, Jun., 2000.
[6] H. Pennes, “Analysis of tissue and arterial blood temperature in the resting human forearm,” J. Appl. Phys., vol. 1, pp. 93-122, Aug., 1948.
[7] M. C. Kolios, A. E. Worthington, M. D. Sherar and J. W. Hunt, “Experimental evaluation of two simple thermal models using transient temperature analysis”, Phys. Med. Biol., vol. 43, pp. 3325-3340, Nov., 1998.
[8] Y. Jing and R. O. Cleveland, “Modeling the propagation of nonlinear three-dimensional acoustic beams in inhomogeneous media,” J. Acoust. Soc. Am., vol. 122, pp. 1352-1364, Sep. 2007.
[9] S. A. Sapareto and W. C. Dewey, “Thermal dose determination in cancer therapy,” Int. J. Radiat. Oncol. Biol. Phys., vol. 10, pp. 787-800, Jun. 1984.
[10] N. J. McDannold, R. L. King, F. A. Jolesz and K. H. Hynynen, “Usefulness of MR imaging-derived thermometry and dosimetry in determining the threshold for tissue damage induced by thermal surgery in rabbits,” Radiology, vol. 216, pp. 517-523, Aug. 2000.
[11] F. A. Duck, Physical properties of tissue. New York: Academic Press, 1990.
[12] T. D. Khokhlova, M. S. Canney, D. Lee, K. I. Marro, L. A. Crum, V. A. Khokhlova and M. R. Bailey, “Magnetic resonance imaging of boiling induced by high intensity focused ultrasound,” J. Acoust. Soc. Am., vol. 125, pp.2420-2431, Apr., 2009.
[13] V. A. Khokhlova, M. R. Bailey, J. A. Reed, B. W. Cunitz, P. J. Kaczkowski and L. A. Crum, “Effects of nonlinear propagation, cavitation, and boiling in lesion formation by high intensity focused ultrasound in a gel phantom,” J. Acoust. Soc. Am., vol. 119, pp. 1834-1848, Mar. 2006.