3J5-2

A Simplified Physico-Mathematical Model toward Tumor Ablation Therapy by Microbubble Enhanced HIFU

気泡増強集束超音波による腫瘍焼灼治療のための
簡易予測モデルの提案

Shunsuke Kagami[1‡] and Tetsuya Kanagawa[2] ([1]Grad. Sch. Syst. & Inf. Eng., Univ. Tsukuba; [2]Fac. Eng., Inf. & Syst., Univ. of Tsukuba)
加賀見俊介 [1‡], 金川哲也 [2] ([1] 筑波大院シス情, [2] 筑波大シス情)

1. Introduction

Cancer treatment by High-Intensity Focused Ultrasound (HIFU) [1] is a low invasive method utilizing a thermal coagulation of tumor tissues. A Khokhlov-Zabolotskaya-Kuznetsov (KZK) equation [2] describing weakly nonlinear (i.e., finite but small amplitude) propagation of focused ultrasound in a single-phase liquid has been used as a physico-mathematical model for HIFU treatment.

Recently, it is reported that the utilization of microbubbles as an enhancer drastically improves the heating effects of HIFU [3]. Kanagawa et al. [2] has extended the KZK equation for single-phase liquid into that for bubbly liquid. In our previous work [4], thermal conduction at gas-liquid interface is introduced by utilizing the energy equation [5] for gas inside bubble and we then found that the thermal conduction strongly contributes the dissipation effect. However, the phase difference between the temperature gradient at gas-liquid interface and the average temperature of gas inside bubble [6] is neglected. Since temperature of the tumor may rise over 80 degrees in HIFU treatment [1], detailed description of these thermal effects is strongly desired for such an application.

In this study, a KZK equation is re-derived by incorporating the phase difference between the temperature gradient at gas-liquid interface and the average temperature [6].

2. Problem statement

Long-range propagation of ultrasound radiated from circular sound source placed in an initially quiescent liquid non-uniformly containing many spherical microbubbles is theoretically investigated (**Fig. 1**). The main assumptions are summarized as follows: (i) Incident frequency of ultrasound is quite lower than eigenfrequency of bubble oscillations; (ii) Wavelength is quite longer than the bubble radius; (iii) Diameter of circular sound source is sufficiently longer than the wavelength, and this leads to the assumption that wavefront is quasi-planar [2, 4]; (iv) Gas inside bubbles is only composed of non-condensable gas, hence the phase change across gas-liquid interface does not occur.

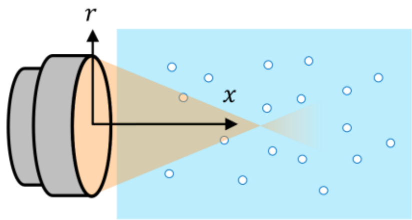

Fig. 1 Schematic of the model.

3. Basic equations

The energy equation for single-bubble describing thermal conduction at the bubble-liquid interface is used [5]:

$$\frac{\mathrm{D_G} p_\mathrm{G}^*}{\mathrm{D}t^*} = \frac{3}{R^*}\left[(\kappa-1)\lambda^* \left.\frac{\partial T_\mathrm{G}^*}{\partial r_\mathrm{G}^*}\right|_{r_\mathrm{G}^*=R^*} - \kappa p_\mathrm{G}^* \frac{\mathrm{D_G} R^*}{\mathrm{D}t^*}\right], \quad (1)$$

where t^* is the time, p^* pressure, R^* bubble radius, κ ratio of specific heats of gas, λ^* thermal conductivity of gas, T^* temperature; the subscript G denotes volume-averaged variables in gas phases, subscript 0 does the quantities in the initial uniform state at rest, and superscript * does a dimensional quantity. Temperature gradient $\partial T_\mathrm{G}^*/\partial r_\mathrm{G}^*|_{r_\mathrm{G}^*=R^*}$ in Eq. (1) is rewritten by the following model considering the phase difference between the temperature gradient at gas-liquid interface and the average temperature of gas inside bubble [6]:

$$\left.\frac{\partial T_\mathrm{G}^*}{\partial r_\mathrm{G}^*}\right|_{r_\mathrm{G}^*=R^*} = \frac{\mathrm{Re}\left(\tilde{L}_\mathrm{P}^*\right)}{\left|\tilde{L}_\mathrm{P}^*\right|^2}(T_0^* - T_\mathrm{G}^*) + \frac{\mathrm{Im}\left(\tilde{L}_\mathrm{P}^*\right)}{\omega_\mathrm{B}^*\left|\tilde{L}_\mathrm{P}^*\right|^2}\frac{\mathrm{D_G} T_\mathrm{G}^*}{\mathrm{D}t^*}, \quad (2)$$

where $\tilde{L}_\mathrm{P}^*$ is the complex number having the dimension of length [6] and ω_B^* eigenfrequency of bubble oscillation. Furthermore, the conservation laws of mas and momentum for bubbly liquids based

[1]kagami.shunsuke.sw@alumni.tsukuba.ac.jp
[2]kanagawa.tetsuya.fu@u.tsukuba.ac.jp

of two fluid-model [7], the momentum conservation for a spherical symmetric oscillating bubble in a compressible liquid, Tait equation of state for liquid, equation of state for ideal gas inside bubble, conservation equation of mass inside bubble, and balance of normal stresses at the bubble-liquid interface are also introduced (see the explicit forms in Refs. [2, 4]).

4. Results

All the dependent variables are expanded in power series, e.g., the expansion of T_G^* is

$$\frac{T_G^*}{T_{G0}^*} = 1 + \epsilon T_{G1} + \epsilon^2 T_{G2} + \cdots, \tag{3}$$

where $\epsilon\ (\ll 1)$ is a typical nondimensional (finite but small) amplitude of the ultrasound. As in the same manners of Refs. [2, 4], we can derive the KZK equation in terms of temperature T_{G1}:

$$\frac{\partial}{\partial \tau}\left(\frac{\partial T_{G1}}{\partial \xi} + \Pi_1 T_{G1}\frac{\partial T_{G1}}{\partial \tau} + \Pi_{21}\frac{\partial^2 T_{G1}}{\partial \tau^2} + \Pi_{22} T_{G1} + \Pi_3 \frac{\partial^3 T_{G1}}{\partial \tau^3}\right) = \frac{\Gamma^2}{2\zeta}\frac{\partial}{\partial \zeta}\left(\zeta\frac{\partial T_{G1}}{\partial \zeta}\right), \tag{4}$$

via a variables transform as retarded time expression,

$$\tau = t - (1 + \Pi_0)x,\ \xi = \epsilon x,\ \zeta = \sqrt{\epsilon}\Gamma r, \tag{5}$$

where Γ is the quantity of $O(1)$ representing the size of focusing of ultrasound. The right-hand side of Eq. (4) represents the focusing along the radial direction. The term with coefficient Π_0, Π_1 and Π_3 represent the advection, nonlinearity and dispersion effects, respectively, both Π_{21} and Π_{22} the dissipation effects. Advection coefficient Π_0 and dissipation coefficient Π_{22} are

$$\Pi_0 = \frac{(1-\alpha_0)U^{*2}}{6\alpha_0 c_{L0}^{*2}}\left[\frac{\omega_B^{2*} R_0^{*2}}{\omega^{*2} L^{*2}} - \frac{3(\gamma_e - \kappa)p_{G0}^*}{\rho_{L0}^* U^{*2}}\right] - \frac{2L^{*2}}{3\alpha_0 R_0^{*2}}\left(\frac{\mu_{e0}^*}{\rho_{L0}^* U^* L^*}\right)^2 - \frac{3(\kappa-1)^2[\alpha_0(1-\alpha_0)+\beta_1]\lambda^*}{2\beta_1\alpha_0(1-\alpha_0)\rho_{L0}^* U^{*2} R_0^* \epsilon}\frac{\mathrm{Im}(\tilde{L}_P^*)T_0^*}{\omega_B^*|\tilde{L}_P^*|^2} \tag{6}$$

$$\Pi_{22} = \frac{3(\kappa-1)^2[\alpha_0(1-\alpha_0)+\beta_1]\lambda^*}{2\beta_1\alpha_0(1-\alpha_0)\rho_{L0}^* U^{*2}\omega^* R_0^* \epsilon}\frac{\mathrm{Re}(\tilde{L}_P^*)T_0^*}{|\tilde{L}_P^*|^2}, \tag{7}$$

where L^*, U^*, ω^* are typical wavelength, wave speed, incident frequency of the ultrasound, α void fraction, c_{L0}^* wave speed in pure water, γ_e and μ_e^* are effective polytropic exponent and viscosity [6]. The last term of advection coefficient Π_0 (Eq. (6)) arises from the imaginary part of Eq. (2), hence the phase difference between the temperature gradient and the average temperature affects the advection effect.

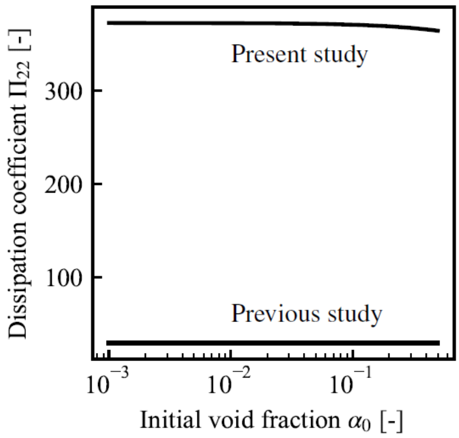

Fig. 2 Dissipation coefficient Π_{22} versus the initial void fraction α_0 for the normal condition of air–water system in our previous study [4] and present study.

Dissipation coefficient Π_{22} arises from the thermal conduction at gas-liquid interface (the real part of Eq. (2)). **Fig. 2** shows the dependence of Π_{22} on α_0 in our previous study [4] and present study, and then we found that thermal conduction more strongly affects the dissipation effect in this study.

5. Summary

We have derived a KZK equation for a nonlinear propagation of focused ultrasound in bubbly liquids incorporating the thermal conduction at the gas-liquid interface by Eq. (1). Temperature gradient term in Eq. (1) is rewritten by Eq. (2) considering the phase difference between the temperature gradient at gas-liquid interface and the average temperature of gas inside bubble. As a result, the phase difference affects the advection effect and the thermal conduction more strongly affects the dissipation effect than in our previous work [3].

Acknowledgment

This work was partially supported by JSPS KAKENHI (18K03942) and Casio Science Promotion Foundation.

References

1. Kennedy et al.: Br. J. Radiol. **76** (2003), 590.
2. Kanagawa: J. Acoust. Soc. Am. **137** (2015), 2642.
3. Chen et al.: Int. J. Hyperthermia. **34** (2018), 1311.
4. Kagami & Kanagawa: Jpn. J. Multiph. Flow. **35** (2021), 346.
5. Prosperetti: J. Fluid Mech. **222** (1991), 587.
6. Sugiyama et al.: Trans. JSME Ser. B. **71** (2001), 1011.
7. Egashira et al.: Fluid Dyn. Res. **34** (2004), 317.