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Basic Physico-Mathematical Model toward an Application of Microbubble-Enhanced HIFU Treatment: An Effect of Thermophysical Property on Nonlinearity of Ultrasound

気泡援用 HIFU 治療応用を目指した基礎理論モデル：
超音波の非線形性への熱物性の寄与

Shunsuke Kagami[1‡] and Tetsuya Kanagawa[2] ([1]Coll. Eng. Syst., Univ. of Tsukuba; [2]Fac. Eng., Inf. & Syst., Univ. of Tsukuba)
加賀見俊介 [1‡], 金川哲也 [2] ([1] 筑波大工シス, [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 ultrasound for a single-phase liquid has been utilized as a well-known physico-mathematical model for HIFU treatment. Recently, it is widely known that the utilization of microbubbles as an enhancer drastically improves the efficiency of HIFU treatment [3].

Recently, our group has extended the KZK equation for single-phase liquid into that for bubbly liquid [2]. Thermal effects such as a thermal conduction, however, were neglected and the temperature rise could not be discussed. Since temperature of the tumor may rise over 80 degrees in HIFU treatment [1], consideration of the temperature rise and thermal effects is strongly desired toward such an application.

In this study, a KZK equation is re-derived to discuss the temperature rise by incorporating thermal effects such as thermal conduction [4, 5]. As a result, the thermal effects contribute strongly the dissipation effect. Furthermore, as an important result, the nonlinearity of ultrasound is also affected by a thermophysical property.

2. Problem statement

Long-range propagation of ultrasound radiated from circular sound source placed in an initially quiescent liquid uniformly containing many 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]; (iv) Gas inside bubbles is only composed of non-condensable gas, hence the phase change across gas-liquid interface does not occur; (v) Viscosity for bubbly liquids is considered by using the initial void fraction and the viscous coefficient of liquid phase.

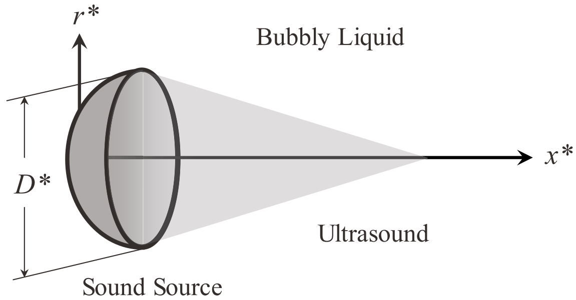

Fig. 1 Schematic of the model.

3. Basic equations

We introduce an energy conservation equation incorporating a thermal conduction at the bubble-liquid interface [4, 5]:

$$\frac{\mathrm{D}}{\mathrm{D}t^*}(p_\mathrm{G}^* R^{*3\gamma}) = 3(\gamma-1)\lambda_\mathrm{G}^* R^{*3\gamma-1}\frac{T_\mathrm{G0}^*-T_\mathrm{G}^*}{\sqrt{2\pi D_\mathrm{G}^*/\omega_\mathrm{B}^*}}, \quad (1)$$

where t^* is the time, p^* pressure, R^* bubble radius, γ ratio of specific heats in the gas phase, λ_G^* thermal conductivity in the gas phase, T^* temperature, D_G^* thermal diffusivity in the gas phase, ω_B^* eigenfrequency of single bubble oscillations; 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.

The Keller equation [6] for bubble dynamics as spherical symmetric oscillations in a compressible liquid is used (shown only important terms):

$$\rho_\mathrm{L0}^*\left[R^*\frac{\mathrm{D}R^*}{\mathrm{D}t^*}+\frac{3}{2}\left(\frac{\mathrm{D}R^*}{\mathrm{D}t^*}\right)^2\right] = P^* + \frac{R^*}{c_\mathrm{L0}^*}\frac{\mathrm{D}}{\mathrm{D}t^*}(p_\mathrm{L}^*+P^*), \quad (2)$$

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

where ρ^* is the density, P^* surface-averaged liquid pressure at gas-liquid interface, c_{L0}^* sound speed in pure water; the subscript L denotes volume-averaged variables in liquid phases. Furthermore, the conservation laws of mass, momentum, and number density of bubbles, 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 Ref. [7]).

4. Results

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

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

where ϵ ($\ll 1$) is a typical nondimensional (finite but small) amplitude of the ultrasound. As in the same manner of Ref. [3], we can derive the KZK equation in terms of temperature rise (i.e., T_{G1}):

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

via a variables transform as retarded time expression,

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

where Γ is the quantity of $O(1)$ representing the size of focusing of the ultrasound. The right-hand side of Eq. (4) represents the focusing along the radial direction. Noting that unknown variable in our previous paper was the variation of bubble radius (not temperature).

As dissipation term in Eq. (4), both terms with coefficient Π_{21} and Π_{22} are appeared; $\Pi_{22} T_{G1}$ is newly discovered term and its coefficient Π_{22} is

$$\Pi_{22} = \frac{3(\gamma - 1)^2 T_{G0}^* L^{*2} \omega^{*3} \lambda_G^*}{2\alpha_0(1 - \alpha_0)\rho_{L0}^* R_0^* \sqrt{2\pi D_G^*/\omega_B^*}\,\epsilon}, \qquad (6)$$

where L^* and ω^* are typical wavelength and incident frequency of the ultrasound, respectively, and α is the void fraction. Two dissipation coefficients, Π_{21} is owing to viscosity of bubbly liquids and liquid compressibility and Π_{22} is to thermal conduction (Eq. (6)). **Table 1** estimates an example of ratio of each (three) dissipation factor for a normal condition of air-water system. Clearly, the thermal conductivity strongly affects the dissipation.

The term with coefficient Π_1 represents a nonlinearity. Since the explicit form of Π_1 is quite complex, **Fig. 2** shows the dependence of Π_1 on R_0 for three cases of the ratio of specific heats γ.

Table 1 An estimation of three dissipation factors, viscosity of bubbly liquids, compressibility of liquid, and conductivity of gas inside bubble.

Factor of dissipation	Ratio [%]
Viscosity	0.38
Compressibility	3.20
Conductivity	96.42

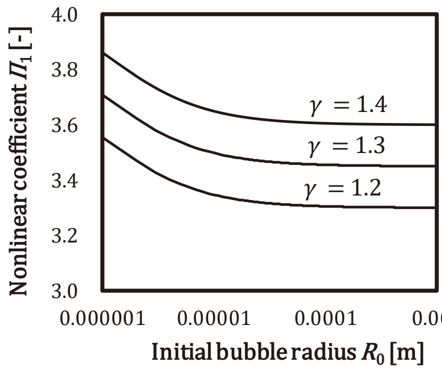

Fig. 2 Nonlinear coefficient Π_1 versus R_0 for $\gamma = 1.4$, 1.3, and 1.2 for $\alpha_0 = 0.05$, $\sqrt{\epsilon} = 0.15$, and a normal condition of air-water system.

5. Summary

We have derived a KZK equation for a nonlinear propagation of ultrasound for bubbly liquids describing the temperature rise by incorporating the thermal conduction at the gas-liquid interface. As a result, thermal conductivity of gas inside bubble strongly affects the dissipation of ultrasound. Furthermore, the ratio of specific heats, i.e., thermophysical property of gas inside bubble affects the nonlinearity of ultrasound.

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