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Heating Efficiency Improvement by Using A Spherically-Concaved Sectored Array in Focused Ultrasound Thermal Therapy

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Abstract—**Focus splitting by using sector-sectioned phased arrays is one of effective methods to increase the necrosed volume in single sonication and to reduce the total treatment time in large tumor treatment. However, the split focus contains less concentrated energy and severer focal beam distortion, which limits its usefulness in practical treatments. In this study, we proposed a new heating strategy by combining sonications of strongly-focused and split-focused patterns to increase the heating efficiency. Theoretical predictions and Ex-vivo tissue experiments showed that thermal lesions can be enlarged in dimensions after applying the proposed strategy. This may provide a useful way to solve current obstacles in low heating efficiency of split-focus sonications that attempted to shorten the total treatment time in current clinical application.**

I. Introduction

THE focused ultrasound thermal ablation technology, which appeared a half century ago, receives increasing interest recently [1,2]. The unique nature of focused ultrasound is that the ultrasonic energy can be focused into soft tissues noninvasively and induce a localized temperature elevation (>55°C) in a few seconds and can be utilized for tumor ablation.

Recently, researchers attempted to use phased array technology to split the focus or even generate multiple foci at the designated target position. The advantage is that the necrosed volume per single sonication can be enlarged, which reduce the number of the intervening "cooling time" between sonication (recognized to be the major time-consuming reason in treatment) and hence can largely reduce the total treatment time [3,4]. Nevertheless, split focusing or multiple foci technology suffers from the peak intensity averaging, which makes the individual focus less concentrated. Other obstacles including the sidelobes appears to be more apparent, and the severer focal-beam distortion problem [5]. Reasons above make the split-focus or multiple foci sonication is difficult to be clinically applied [6].

This study proposed an easy but effective heating strategy to facilitate the split focusing sonication. Hybrid use of the strongly-focused pattern and split-focused pattern were used consecutively to increase the ability of thermal lesion formation under the tissue property change. Ex-vivo experiments were conducted, and theoretical predictions and estimations were made to explain the mechanism of the improvements.

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II. Methods

A. Experimental Setup

A block diagram of the experimental setup is shown in Fig. 1. A 566-kHz PZT-4 spherical focused transducer (Four elements with quarterly-sectored, diameter = 10 cm, radius of curvature = 10 cm; components obtained from Elecerom, Taiwan, and assembled in-house) was used in this study. The four-element transducer was then driven by a four-channel phased-controllable driving system with an embedded power measurement module (UDS04PF, Advanced Surgical, Arizona, USA).

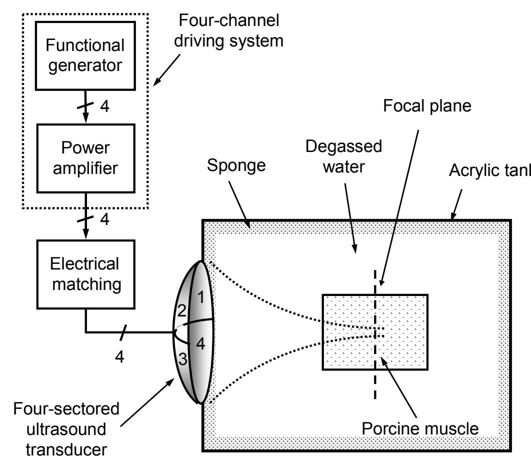


Fig. 1. Schematic diagram of the system setup.

Freshly excised porcine muscle specimens were also used in this study. All experiments were completed within 6 hours of animal death. Before sonication, the porcine muscle was kept in a vacuumed 37°C water bath for about 10 minutes. The tissue surfaces (sonication side) were cut to provide a smooth water/ tissue interface in the first part of experiment. In the second part of experiment, to make a clear comparison of the heating efficiency between the hybrid mode-0/ -2 focusing and the mode-2 focusing, original surfaces of the ex-vivo tissues were retained to introduce apparent ultrasonic wave scattering at the water/tissue surface during the sonication. The water tank was filled with deionized and degassed water, and the water temperature was also controlled at 37°C for the entire sonication. To prevent interference from ultrasound waves scattered or reflected from environments, sponges were attached to four sides of the water tank. The focal point was fixed at a depth of 5 cm beneath the ex-vivo tissues for every sonication.

In order to compare the heating efficiency between these two protocols, two sets of experiments were performed, i.e., purely mode-2 focusing and hybrid mode-0 and -2 focusing. The first protocol (mode-2 focusing) was to sonicate the ex-vivo tissues by driving the four elements with 180° of phase difference between adjacent elements (That is, 0°, 180°, 0°, 180° for element 1 to 4; this was also defined as mode-2 focusing [7]. The second protocol (hybrid mode-0/ -2 focusing) is to in-phase sonicate the tissues (that is, 0°, 0°, 0°, 0° for element 1 to 4; this was defined as mode-0 focusing) with a following mode-2 sonications. In the first sonication protocol, sonication time with 70s, 90s, or 110s under the acoustic power 40W were used; In the second sonication protocol, 20s was set for mode-0 sonication with the following 50s, 70s, or 90s of mode-2 sonication, and the acoustic power of 40 W were also employed. The design of the given parameters was to provide identical acoustic energy (i.e., 2800, 3600, and 4400 joules respectively) between the two protocols.

The specimens were dissected to evaluate the shapes and sizes of the induced lesions. To make the dissection process easier, the sonicated specimens were stored into a -20℃ refrigerator for 30 min. and partially thawed before dissection. The necrosed regions were easily distinguished on the basis of their color: white confined regions compared with the surrounding fresh-red color. The lesion width and length were defined as the dimensions of the lesions along radial and axial directions. The mean and standard deviation values of the lesion length / width were used to perform statistical evaluations. Statistical significance was assessed using the Student's *t*-test, with a probability value of $P < 0.05$ considered to be indicative of a significant difference.

B. Theoretical Prediction

Theoretical estimations of the thermal dynamics and lesion estimations were also performed in this study to provide analogous predictions in in-vivo conditions. To calculate the ultrasonic pressure field, the transducer was modeled as a grid of point sources. Then, the Rayleigh-Sommerfeld integral was used to sum up the contribution of each point source, r', to the point of the field at r [8]. The integral is given as:

$$p(x,y,z) = \frac{i\rho\, ck}{2\pi} \int_S \frac{ue^{-(\alpha+ik)\cdot(r-r')}}{r-r'} dS \tag{1}$$

where ρ = tissue density (1050 kg m-3), c = the speed of sound (1500 m s-1), k = the wave number ($2\pi/\lambda$, where λ is the wave length), u = the complex surface velocity of the source, and α = attenuation (4.1 Np/m/MHz). In an attenuated medium, the absorbed power deposition, q, for the desired volume is given as Arditi et al. [11]:

$$q = \frac{\alpha p^2}{\rho\, c} \tag{2}$$

The computations of the acoustic pressure and the resulting absorbed power deposition are performed with a source grid size of λ/6. Without loss of generality, nonlinear, refraction and scattering effects are not included.

The tissue temperature response, *T*, can be calculated using the well-known bio-heat transfer equation [9]:

$$\rho\; c_t \frac{\partial T}{\partial t} = k\nabla^2 T - w_b c_b (T - T_{ar}) + q \tag{3}$$

where c_t and c_b are the specific heats of tissue and blood (both set to be 3770 J/kg/°C), k is the thermal conductivity (0.56 W/m/°C), w_b is the blood perfusion rate (0 - 20 Kg/m^3/s in simulation), and T_{ar} is the arterial blood temperature (37 °C). This equation is solved using a numerical finite difference method, with all boundary and initial conditions set to 37 °C. The time step and the grid spacing in the x-, y- and z-directions are 50 ms, 0.5 mm, 0.5 mm and 1 mm, respectively.

The thermal dose (TD), in terms of equivalent minutes at 43°C, was used to estimate the necrosed tissue volume as follows [10] (TD = 240 min. is regarded as measure of tissue necrosis [10]):

$$TD = \int_{t_0}^{t_f} R^{(T-43)} dt \approx \sum_{t_0}^{t_f} R^{(T-43)} \Delta t \tag{4}$$

III. Results

The difference of the lesion formation between mode-2 and hybrid mode-0/ -2 sonications were presented first. Figure 2 demonstrates typical comparisons between two heating protocols. Four thermal lesions were made, where two were created by mode-2 focusing (sonicate time = 90s, acoustic power = 40W) solely and another two created by combining mode-0 (sonicated first, sonicate time = 20s, acoustic power = 40W) and mode-2 focusing (sonicated right after the mode-0 focusing, sonicate time =70s, acoustic power = 40W). Lesions created by combination of mode-0/ -2 focusing can be found to have wider and better-confined necrosed region for every slides with different depths. The created lesions were also found to be longer (see Fig. 2(d)) and penetrated deeper.

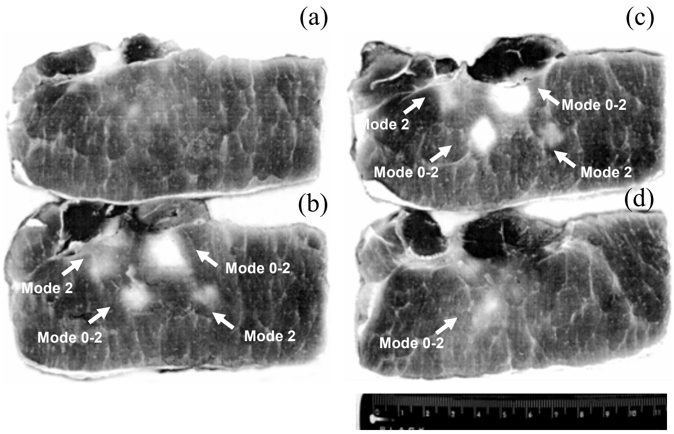
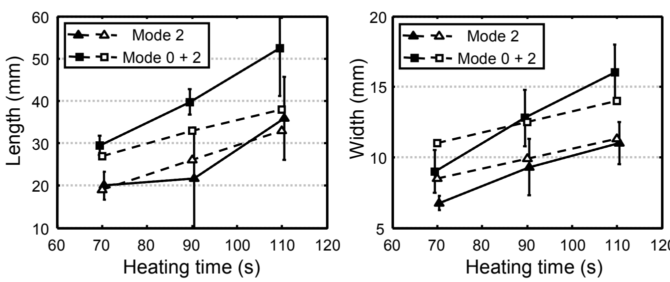


Fig. 2. Comparison of the necrosed regions in cross-section view between mode-2 sonication (acoustic power = 40W, sonication time = 90s) and hybrid mode -0/ -2 sonication (acoustic power = 40W, sonication time = 20s and 70s respectively): (a) surface; (b) 3-cm in depth; (c) 5-cm in depth ; (d) 7-cm in depth.



(a) (b)

Fig. 3. Experimental (solid lines) and theoretical (dashed lines) comparison of the (a) necrosed lesion length and (b) necrosed lesion width between mode-2 sonications (acoustic power = 40W, sonication time = 70/90/110s) and hybrid mode -0/ -2 sonications (acoustic power = 40W, sonication time = 20s and 50/70/90s respectively).

Figure 3 shows the statistical comparisons of the lesion length and width between the mode-2 focusing and hybrid mode-0 and -2 focusing (see the solid lines). In average, the lesion length of the induced lesions by hybrid mode-0 and -2 focusing were 10 to 15 mm longer than mode-2 focusing for all sonication times; about 2 - 5 mm larger lesion width can also be found. The data shown in Figure 3 all had significant difference statistically ($P < 0.05$).

Theoretical predictions of the lesion dimensions were also provided for comparison with the experimental results. The simulations results for the same heating conditions in Fig. 3 were superimposed in the same figure (denoted as dashed lines; w_b was set to zero in Equ. (3)). The simulation provide agreeable prediction that lesions created by hybrid mode-0 / -2 focusing can have larger dimension both in lesion length and width. The simulation were shown to provide similar width difference (3 mm in simulation compared with the 2 - 5 mm in experiments) to experimental measurements; in lesion length, simulation can still provide reasonable predictions, but the differences tend to be underestimated (6 – 9 mm in simulations compared with the 10 – 15 mm in experiments).

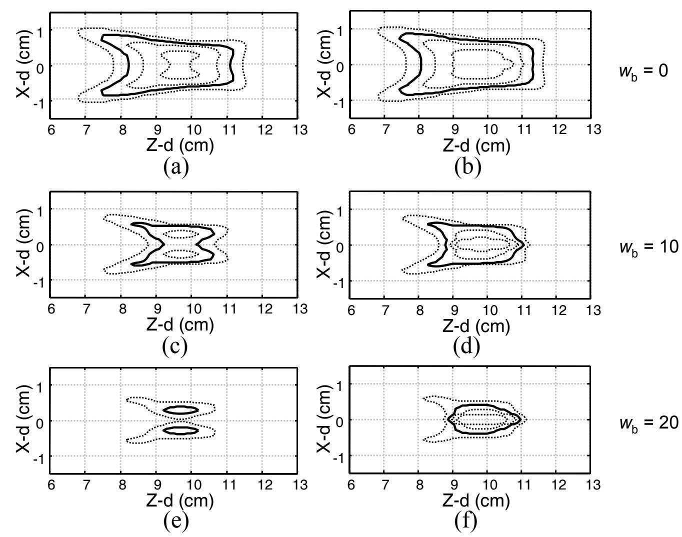
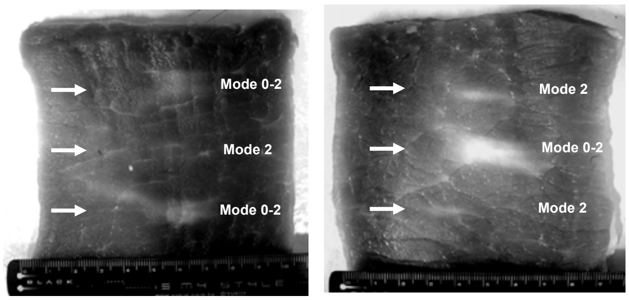


Fig. 4. Comparison of estimated thermal dose distributions with blood perfusion rate 0/ 10/ 20 kg/m3/s between mode-2 sonications (left column, acoustic power = 40W, sonication time = 90s) and hybrid mode -0/ -2 sonications (right column, acoustic power = 40W, sonication time = 20s and 70s respectively). Contours with TD = 100, 240 (in bold), 1000, and 10000 min. were drawn.

The difference of the resulting thermal lesion dimensions for in-vivo tissue conditions was examined by using the theoretical simulations. To perform this, wider range of blood perfusion rate (0, 10, and 20 $Kg/m^3/s$) was assumed in the simulations. A specific simulation case was demonstrated in Fig. 4 (heating time =90s in mode-2 focusing, and 20/ 90s respectively in hybrid mode-0/ -2 focusing, acoustic power = 40W for both cases). Simulation results demonstrated that the lesion dimensions (represented by the thermal dose 240 min. contours in the figure) can be significantly reduced with increasing blood perfusion rate when employing mode-2 focusing (left column in Fig. 4) rather than those induced by the hybrid mode-0/ -2 focusing (right column in Fig. 4). The TD = 240 min. contour diminished rapidly at the center part of lesions in mode-0 focusing due to the lack of direct energy deposition along the central axis. In the contrary, in mode-0/ -2 focusing, the heat dissipations by blood perfusion rate were less due to the advantage of rapid temperature build-up.

Figure 5 shows experiments by using tissue samples without cutting a fresh surface at the sonication side to increase the difficulty of the ultrasonic wave transmission. Two samples were used for experiments, and six sonications were made (Three for mode-2 focusing and three for combined mode-0/ -2 focusing; sonication time = 90s and 20s/ 70s, respectively; acoustic power = 40W). Results showed that the expected lesions can be generated by using the hybrid mode-0/-2 focusing, whereas the lesions in mode-2 focusing were smaller, less controllable, or even unable to be generated.



(a) (b)

Fig. 5. Experimental comparison of sonicating tissues with rough and unpeeled surfaces between mode-2 focusing (acoustic power = 40W, sonication time = 70s) and hybrid mode-0/ -2 focusing (acoustic power =40W, sonication time =20 and 50s respectively)

IV. Discussion

The heating strategy of hybrid mode-0 / -2 focusing has been shown to be able to increase the heating efficiency when comparing with the mode-2 focusing at the basis of the same applied acoustic energy (i.e., acoustic power × sonication time). In the single mode-2 focusing sonication, the temperature buildup relied on the power deposition contributed from the split focus. The intensity for each focus was spatially averaged, which caused the temperature elevation follow a lower gradient of the temperature increase (see Fig. 4). The uncertainly of the treatment were, therefore, increased and could be affected by biological properties such as blood perfusion rate (see Fig. 4) or variation caused by tissue inhomogeneity (see Fig. 5). On the contrary, in the proposed sonicated strategy, a strongly focused mode-0 focusing were employed to build up sufficient temperature elevation along the central axis first, followed by –lesion expansion in the radial direction by using the split-focused mode-2 focusing. This was shown to increase the possibility of successful necrosed lesion formation.

This study employed linear theoretical models to estimate the ultrasound pressure distribution, power deposition, and the thermal lesion formation. The linear theory showed the difference between mode-2 focusing and the proposed hybrid mode-0 / -2 focusing can be predicted, including the heating efficiency improvement and lesion dimension enlargement. The results, however, also showed that the linear-model prediction is conservative while comparing with the experimental results (see Fig. 3). In Gertner et al. [12], the heating tissue apparently increased in the attenuation coefficient. Moreover, there are reports showing that the blood perfusion rate can be fluctuated [13]. These all supported that linear theory made a more conservative prediction than considering the tissue property change during heating, and the nonlinear tissue property change may be necessary if accurate prediction need to be made.

V. Conclusion

This study demonstrated a novel strategy to perform a more efficient heating by sonicating the hybrid focal beam patterns created by a four-sectored spherical transducer. The dimension of the produced thermal lesions was experimentally and numerically demonstrated that can be increased compared with the traditional multiple focal patterns, and was also numerically demonstrated to have higher efficiency of necrosed region formation even in highly-perfused conditions. The proposed strategy may provide a useful way to solve current obstacles in low heating efficiency of multiple focal-pattern sonications that attempted to shorten the total treatment time in current clinical application.

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