THERMAL LESION FORMATION AND DETERMINATION FOR EXTERNAL ULTRASOUND THERMAL THERAPY

Hao-Li Liu1, Yung-Yaw Chen1, Jia-Yush Yen2 and Win-Li Lin3
1Department of Electrical Engineering, 2Department of Mechanical Engineering, 3Institute of Biomedical Engineering, National Taiwan University
Taipei, Taiwan

ABSTRACT

The purpose of this paper is to investigate the relationship between the formation of the thermal lesion and the major parameters of the external ultrasound heating systems, and to propose a useful thermal lesion determination procedure, which is capable of specifying the range of a thermal lesion by temperature feedback in external ultrasound thermal therapy. This work is based on an ideal ultrasound power deposition formed by an external ultrasound heating system and the temperature distribution is calculated by the transient bioheat transfer equation. A simplified model was employed to determine the heating pattern for four most important parameters. Through the simplified power expression, the properties of a new parameter, T300, which is defined as the maximal temperature corresponding to the thermal dose of 300 minutes, is also investigated. When the target volume is large enough such that the thermal conduction effect becomes negligible, the T300 value is almost independent of the system parameters and the heating strategies, and is dominated by the blood perfusion rate with a monotonic correlation. The method enables us to use feedback information in the ultrasound heating process and to pre-determine the heating range of the thermal lesion, which will be very useful in ultrasound treatment planning.

1. INTRODUCTION

The aim of ultrasound thermal therapy [1-5] is to use high intensity, short-duration, focused ultrasound [6-8] to deliver enough energy into a specific tumor volume such that tissue necrosis is formed and the overheating of the intervening normal tissue can be avoided [2,9]. The external ultrasound heating is a non-invasive and very flexible modality for heating deep-seated tumors for its vast penetration and focusing ability. The major task in external ultrasound thermal therapy is to correctly form a thermal lesion on the targeted tumor volume. In practice, the thermal lesion cannot be visualized directly. Thermal dose distribution with a threshold value [10] is usually used to determine the effective region of thermal lesion.

The relationship between the size of the thermal lesion and the thermal dose distribution with threshold values has been studied in literatures [1-9]. Taar et al. [27] performed high intensity, focused ultrasound trail in-vivo and exercised liver sample in-vitro to investigate the thermal lesion patterns under different sonication time and heating power. It was found that the thermal lesion enlarged with increasing sonication time and heating power. The conclusion was consistent with Hutchinson and Hynynen’s [11] study for non-invasive ultrasound thermal therapy using phased arrays. Moreover, it was also found that a larger blood perfusion rate results in a smaller thermal lesion size in [2], while the shape as well as the size of the thermal lesion varies with different arrangement of external ultrasound heating systems [12].

Although there are many discussions on thermal lesion formation from the existing literatures, few studies focused on its relationship with the heating system arrangement, such as the size of the acoustic window, the focal depth, the attenuation coefficient and the size of the focal zone. These indices were found to be the major factors to form various power depositions and the associated heating patterns in external ultrasound heating systems. In addition, the determination of the sonication time and the heating power for a desired thermal lesion volume is difficult due to its complicated correlations to the above-mentioned system parameters.

The objectives of this research are to investigate the relationships between the formation of the thermal lesion and the major parameters of the external ultrasound heating systems, and to propose a procedure for thermal lesion formation and determination. Furthermore, the procedure will be shown to provide a proper and simple heating configuration for thermal therapy. In order to focus on the study to the parameters determinations in thermal lesion formation, the Specific Absorption Ratio (SAR) model is employed to approximate the absorbed power density generated by practical external ultrasound thermal therapy systems. The approach has been widely used and verified by many researchers in a number of experiments [13-15, 16,17]. The temperatures as well as the thermal dose distributions are calculated to examine the relationships between the system indices and the thermal lesion region, which is identified by a region with a threshold value of 300 minutes in thermal dose. Studies show that the heating temperature corresponding to a threshold value of thermal dose is only affected by the blood perfusion rate when the focal zone diameter is large than 2 cm. This property can be used in thermal lesion determination and consequently provides a guideline in thermal therapy design. Three design examples with different tumor volume settings are studied and both show satisfactory results on lesion determination. This paper provides a useful reference for researchers attempting to design the externally ultrasound thermal therapy system for deep-seated large tumors and offers a simple but useful clinical treatment lesion determination scheme.

2. MATERIALS AND METHODS

2.1 Specific Absorption Rate (SAR) Model

Fig. 1 shows the geometrical relationship between transducer and treatment portion in external ultrasound-heating model. The external ultrasound transducer is assumed to create an acoustic window of diameter d(0) at the origin. The targeted tumor region is at distance Zt with a diameter d(Zt). The z-axis is referred to be the depth of penetration and is vertical to the skin surface, which is located at the origin of the z-axis. The ultrasound wave is assumed to propagate in straight line, and to converge and focus on the targeted tumor region at Z = Zt, and diverge beyond this focal depth. At Z = 0 cm, the area with diameter d(0) is referred to be the acoustic window of the ultrasonic beam. The deposition of ultrasonic intensity at each depth was ... approximation in evaluating the power deposition and the thermal dose distribution to avoid over-complicated calculations.

The ultrasonic power attenuates exponentially as it propagates through the tissue. Assuming that the ultrasonic power intensity is not too large to cause wave distortions and to be absorbed by the tissue, the ultrasonic power at depth z cm, Q(z), and the associated power intensity, I(z), can be described by:

\[ Q(z) = Q(0) e^{-2\pi \mu z} \]  

(1)

\[ I(z) = \frac{Q(z)}{A(z)} \]  

(2)

where Q(0) is the total power propagating through the acoustic window, \( \mu \) is the attenuation coefficient and A(z) represents the cross-sectional area of the conical power region at depth z cm. From Fig. 1, it is clear that

\[ A(z) = \pi d(z)^2 \]  

(3)

\[ d(z) = d(z, j) = d(0) - dz, j = \frac{z}{L} \]  

(4)

where d(z) is the diameter of the conical power region at depth z cm. The acoustic attenuation coefficient \( \mu \) depends on the driving frequency, and is approximately 5Np/m at 1MHz [18].

The specific absorption rate (SAR) is defined to be the absorbed power density (q) in soft tissue, and can be calculated by:

\[ q = \frac{Q(z)}{m} \]  

(5)

where m is the mass of the tissue volume. The SAR distribution can be calculated by:

\[ SAR(z) = \int q(z') dz' \]  

(6)

where q(z) is the power density at depth z cm. The SAR distribution is usually used to determine the effective region of thermal lesion.
I(z) and acoustic is set to 2.5/5/10/15 Np/m and is the absorption coefficient. Moreover, the $d(0)$ are set to be $d(0)$ (cm)

The thermal dose (TD), in terms of equivalent minutes at 43°C, is used to estimate the necrosed tissue volume, and is calculated using the following equation

$TD = \int_0^\infty R(t) + \sum_{n=1}^n R(t) \Delta t$ (4)

where $R = 2$ for $T \geq 43°C$, $R = 4$ for $37°C < T < 43°C$, $\Delta t$ is the time step, and $t_0$ and $t_f$ represent the initial and the final times, respectively. The TD value required for total necrosis ranges from 25 to 240 minutes for brain to muscular tissues [8,24]. In this study, a value of TD = 300 minutes is chosen as the threshold for complete heat [26].

The absorbed power density at the focal depth in all five cases was set to be 16W cm$^{-2}$ with heating time of 6 seconds throughout the study unless otherwise mentioned. In our simulations, such transducer power will provide a maximal temperature about 40°C during the heating process. The computation of temperature profiles is terminated at time of 600s, which is sufficient to determine the TD distribution precisely. The SAR ratio distributions along the central z-axis with the parameter settings in Table 1 are shown in Fig. 2(a). The corresponding temperature distributions at the end of heating session (at $t = 6s$) and the thermal dose distributions (at $t = 600s$) are shown in Fig. 2(b) and Fig. 2(c) respectively. The maximal thermal dose with equal absorbed power density and heating time in five cases are different, which is caused by various thermal conduction effects from different SAR distributions. It can be observed that the maximal thermal dose is smaller if the SAR distribution has a sharper profile at the focal depth. The cross-sectional areas with TD value 300 minutes in Fig. 2(c) for five cases in Table 1 are different. Their dimensions increase as $\mu_1$ (Case 1 vs. Case 2) increases and as geometrical gain (Case 1 vs. Case 3, and 5) decreases. It is also found that to deliver the same absorbed power density to heat the focal zone at z = zt and the acoustic window at z = 0 (i.e. $d(z)/d(0)$) is defined to be the Geometrical Gain (GG) for the SAR model. The corresponding temperature distribution can be then computed from the SAR(z) distributions in the following section.

2.2 Temperature and Thermal Dose Calculation

The tissue temperature response, $T$, is calculated using the well-known bio-heat transfer equation [19]:

$\rho c_\rho \frac{\partial T}{\partial t} - \nabla \cdot (\kappa \nabla T) = \rho c_\rho \gamma \rho_w(T - T_{aw}) + q$ (3)

where $c_\rho$ and $c_w$ are the specific heats of tissue and blood (both set to 3770 J kg$^{-1}$C$^{-1}$), $k$ is the thermal conductivity of tissue (0.56 W/m°C), $\gamma$ is the blood perfusion rate, and $T_{aw}$ is the arterial blood temperature.

2.3 Thermal Lesion Determination Using $T_{300}$

The focal depth $(Zt)$, focal zone diameter $(d(z))$, acoustical attenuation $(\mu_2)$ and acoustic window $(d(0))$ are set to be $5/10/15/20$ cm, $d(z)$ is set to $2/3/4/5$ cm, $\mu_2$ is set to $2.5/5/10/15$ Np/m and $d(0)$ is set to $7/10/15/20$ cm. The observed $T_{300}$ value, and the corresponding thermal dose distributions are shown in Fig. 3. From this figure, it can be observed that the size of the TD = 300 min contour increases with $\mu_2$ and $Zt$. The observed $T_{300}$...
value are found ranging from 51.1°C to 51.3°C except for the case of small d(Zt). The exception seems to be from the small focal zone diameter, which causes the value of T300 along the central z-axis easily affected by thermal conduction effect.

3.2 Effect of Different Blood Perfusion Rates and Absorbed Power Densities

Blood perfusion rate (q) is also a critical factor affecting the thermal dose distribution and the contour of T300. For illustrations, different blood perfusion rates of 0.5/2.5/10/20 kg/m3/s and d(Zt) of 0.5/1.0/1.5/2/3/4 cm were selected to depict the various conditions of human body. The corresponding T300 values in the pre-focal area on the central z-axis are shown in Fig. 4. It can be found that T300 decreased monotonically with increasing d(Zt), and converged to steady values with d(Zt) larger than 2 to 3 cm. The values of T300 with the blood perfusion rates of 0.5, 2, 5, 10, 20 kg/m3/s converged to 49.2°C, 51.2°C, 52.7°C, 53.8°C and 54.8°C, respectively. It is reasonable that higher blood perfusion rate acts as a strong heat sink, and takes the energy away faster. The result is higher temperature elevation required to achieve the thermal dose threshold of 300 minutes, which means the value of T300 is higher.

When d(Zt) is smaller than 2cm, the corneal-shape power profile at the focal depth at is narrower, and hence the value of T300 is affected by both the blood perfusion rate and thermal conduction effect. On the other hand, When the focal zone diameter d(Zt) is large enough (approximately 2 cm in diameter), the T300 is dominantly affected by the blood perfusion rate, and the thermal conduction effect can be neglected.

The absorbed power density is also an important factor for T300 values. With constant heating time (6s in our examples), higher power intensity setting provides a higher temperature elevation, which results in higher peak values in thermal dose distributions and bigger thermal lesions. Fig. 5(a) and Fig. 5(b) show the relationships between T300 and different values of absorbed power density with constant heating time, different blood perfusion rates, and d(Zt) of 0.5 cm and 2 cm respectively. The value of T300 decreased monotonically with increasing absorbed power density as shown in Fig. 5(a), while the T300 values showed no apparent changes as the absorbed power intensity varied in Fig. 5(b). The difference between Fig. 5(a) and 5(b) is from the size of d(Zt). Similar to the conclusion above, the conduction effect is strong when d(Zt) is small, while the blood perfusion rate becomes dominant when d(Zt) is large enough.

The corresponding thermal dose distributions with the power density of 18 and 38 W/cm3 and the blood perfusion rates of 0.5 and 20 kg/m3/s are shown in Fig. 5(c) with d(Zt) of 0.5 cm and in Fig. 5(d) with d(Zt) of 2cm. It was found that the thermal dose distributions changed when the absorbed power density or blood perfusion are different. The absorbed power density had a greater influence to the thermal dose distributions than the blood perfusion rate. We also found that with smaller d(Zt) and smaller power density, diameter of the induced necrosis volume decreases and T300 increases from the thermal conduction effect.

3.3 Effect of Different Heating Rates

In real thermal therapies, different heating strategies are usually determined heuristically. The heating strategy in our paper is referred to the determination of heating power level and heating time. Even for constant energy settings (i.e., constant product of heating power and heating time), different heating temperature patterns and thermal lesions are usually formed. In this section, the values of T300 under different heating strategies are discussed and listed in Table 2. It is found that T300 values maintain consistent results under different heating strategies with the same blood perfusion rate.

3.4 Thermal Lesion Determination Procedure

According to the above analysis, it is concluded that the value of T300 is only determined by the blood perfusion rate when d(Zt) is larger than 2 cm. The property can be used to perform thermal lesion coverage determination by controlling the temperature of the selected target points to reach the proper T300 value. To determine the thermal lesion dimension, at first, two target points on the heating volume’s boundary are set, one is ahead and the other is behind. Next, it is only to design the heating pattern, which can deliver the same absorbed power density level onto these two target points and heat until reach the value of T300. The thermal lesion determination procedure is as follows:

1. Determine zt and d(Zt) to completely cover the target tumor. Moreover, according to the transducer and the driving frequency, the m and d(0) and be also determined. Here, the treatment volume must be larger than 2cm in diameter to be eligible for our approach.
2. The front and rear boundaries of the target volume along the central z-axis are defined as the front target and rear target points.
3. Apply the simplified SAR model to roughly estimate the power deposition. Note that since the selected pair (z, d(0)) is not unique, therefore, a suitable z and d(0) should be determined to offer enough geometrical gain (GG). A GG value larger than 10 is suggested to prevent the thermal lesion extension problem.
4. With the given blood perfusion of the tissue, determine the value of T300 according to Fig. 6.
5. Choose a heating power of the ultrasound thermal therapy system, which can offer the maximal absorbed power density over 20W/cm3 (according to the result shown in Fig. 5(b)).

Table 2. T300 under different heating strategies and different blood perfusion rates (2.5 and 10 kg m-3 s-1).

<table>
<thead>
<tr>
<th>Case</th>
<th>q (W/cm3)</th>
<th>Heating time (s)</th>
<th>Wb (kg/m3 s)</th>
<th>T300 (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>5</td>
<td>2</td>
<td>51.1</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>10</td>
<td>2</td>
<td>51.1</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>15</td>
<td>2</td>
<td>51.0</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>5</td>
<td>5</td>
<td>52.5</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>15</td>
<td>5</td>
<td>52.5</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>15</td>
<td>5</td>
<td>52.6</td>
</tr>
<tr>
<td>7</td>
<td>20</td>
<td>5</td>
<td>10</td>
<td>53.6</td>
</tr>
<tr>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>53.6</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>15</td>
<td>10</td>
<td>53.5</td>
</tr>
</tbody>
</table>

Fig. 5 Relationship between T300 and the absorbed power density at focal depth when the blood perfusion rate is varied from 0.5 to 20 kg/m3/s and d(Zt) is set to (a) 0.5 cm and (b) 2 cm. (c) and (d) depict the respective thermal lesions under different absorbed power density (18 and 38 W/cm3) and blood perfusion (0.5 and 20 kg/m3/s) under d(Zt) is set to (c) 0.5 cm and (d) 2 cm.

6. Start heating the target volume using the determined power distribution. Turn off the heating power when the temperature at the front target point reaches T300. Note that the treatment time will be shorter if the heating power chose in step 6 is larger.

7. Finally, the cumulative thermal dose distribution will roughly fit the target volume.
At second, a case of small tumor (d(0)<2 cm) is shown with a cylindrical type treatment region of 1 cm in width, 1 cm in thickness and 7.5 cm in depth. The rest of the parameters are the same as the above case. The heating times on 2 W/cm² and 32 W/cm² are 62.7s and 3.8s, and the respective thermal lesions are formed and shown in Fig. 7(a) and 7(b). It indicates that, since the heating volume is not large enough, the temperature on the target points are strongly affected, and the thermal lesions cannot be correctly determined. The third case shows a cylindrical type treatment region with 3-cm wide, 3-cm thickness and 7-cm depth was assumed. In order to show the effect of the acoustic window d(0) on the coverage of the thermal lesion, d(0) is set to be 10 cm and 14 cm, which provides geometrical gains of 11.1 and 21.8 respectively. The maximal absorbed power densities are both set to be 16 W/cm² and other parameter settings are identical to above cases. The SAR ratio distributions are shown in Fig. 6(a). In order to fit the reference point reached the set T₃₀₀ value, and the heating time on 2 W/cm² and 32 W/cm² were 5.26s and 3.2s, and the r-z thermal dose distributions are shown in Fig. 6(a) and 6(b). The contours with 1, 10, 100 and 300 minutes were plotted using real lines, and the regions enclosed by the dashed lines represent the region with the absorbed power densities larger than the power at the front and the rear target points. From Fig. 6, it shows that the thermal lesion coverage generated by different heating strategies is different. Thermal lesion formed by lower power density is smaller, which is due to the thermal conduct effect under the longer treatment time. However, the effect is not very significant to the central portion of the heating volume and the thermal lesion regions in both cases are pretty good results.

Different combination of heating strategies.


REFERENCES


INSTRUCTIONS TO AUTHORS

PUBLICATION POLICY
Theoretical and experimental records which lead to fundamental principles, or the research to development, fabrication and application of advanced technique on Biomedical Engineering will constitute the content of each issue. Only unpublished original contributions will be considered for publication. Manuscripts should be prepared in the form of full-length papers, short communication, review articles or letters to the editor. A short communication is a brief (max. 2 typewritten pages) but complete description of an investigation which will not be included in a later paper. It should be as completely documented regarding both literature and experimental procedures as a full-length paper.

MANUSCRIPT PREPARATION
1. Three copies should be provided, in double-spaced typing, on pages of uniform size (letter or A4), with a wide margin at both sides. The title should be concise and reflect the contents unambiguously. The name(s) and affiliation(s) of the author(s) should follow the title.

2. Manuscripts from countries in which there is no associate editor may be sent directly to the Editor. Professor Cheng-Yi Wang, Institute of Biomedical Engineering, College of Medicine, National Taiwan University, Taipei, Taiwan.

3. All papers should be written in English. Clear, concise and correct English usage is expected.

4. Full-length papers and review articles should be provided with an abstract of about 200-500 words, reporting concisely on the objectives and conclusions of the paper. They should be divided into sections and subsections, and should have a short introduction stating the reason for the work and proper references citing literatures on the subject. The first paragraph of a short communication or a letter to the Editor should serve the same purpose, but a separate section is not required.

5. SI (Standard International) units must be used in the text, tables, and figures of all manuscripts submitted to the Journal.