Thermal ablation of biological tissue by high intensity ultrasound

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Abstract. The paper discusses the effect of a series of focused high-intensity ultrasound pulses from a multi-element transducer on the biological tissue. The simulation of the ultrasound intensity field in a homogeneous medium uses the Rayleigh integral. The thermal problem modelling is based on the numerical solution of the heat equation. The advantages of processing a given volume of tissue with pulses, whose focal points over time consistently diverge from the geometric focus of the transducer, have been demonstrated. The effect of the time delay between pulses on the nature of tissue heating and the size of the thermal ablation region is analyzed. The issues of scaling for the problem of heat distribution are discussed.

1. Introduction
Cancer treatment is a priority for modern medicine. In the past decade, along with traditional surgical methods for removing tumors, high-tech methods of treatment such as gamma-knife, cryoablation or high-intensity focused ultrasound (HIFU) became more common. HIFU technology is considered one of the promising non-invasive methods for treating breast cancer. It involves the impact of a series of high-intensity ultrasonic pulses on biological tissue, leading to ablation / necrosis of the affected area [1, 2]. The tumor treatment program requires setting the parameters of each pulse, the number and the sequence of pulses in a series and the localization of focus points of individual pulses in a volume. The correct choice of parameters determines the quality of therapy, which should result in the ablation of the entire tumor volume with minimal effect on healthy tissue.

This paper presents a theoretical study of the effects of different treatment programs on a given volume of breast tissue.

2. Interaction of ultrasound with a homogeneous medium
Thermal problem solution requires determining the power of the absorbed ultrasound energy in the spatial area under consideration. In the vicinity of the focal point, the wave can be considered quasi-planar and the power of heat release is assumed to be [1]

\[ Q = 2\alpha I , \]  \hspace{1cm} (1)

where \( I \) is the intensity of ultrasound radiation in the tissue, and \( \alpha \) is the amplitude absorption coefficient.

Traditionally, the problem of determining the intensity field of ultrasonic radiation of a single pulse is solved with no reference to the thermal problem [3-6]. In the case when the influence of nonlinear
effects in the medium can be neglected, the intensity in the medium is calculated using the Rayleigh integral [1]. In this work, moderate intensities of ultrasound of 100-200 W/cm² are considered and this approximation is justified. The acoustic pressure generated by a single unit of the transducer in a given space point is

\[ p = -\frac{1}{2\pi} \frac{ka\rho u}{r} \int_{S} e^{-(\alpha + ik)r} dS, \]

where \( k \) is the wave number, \( S \) is the entire surface area of the unit, \( a \) is the sound velocity, \( \alpha \) is the absorption coefficient, \( \rho \) is the density, \( u \) is the velocity component normal to the element \( dS \) (\( u \) does not depend on \( dS \) location), \( r \) is the distance between the element \( dS \) and the considering space point.

A 128-element HIFU array produced by Sonic Concept Ltd (figure 1) with a main frequency of 2 MHz is considered. The overall pressure field of the transducer is simulated as a superposition of fields of individual units. The ultrasound wave intensity is \( I = \frac{p^2}{2a\rho} \), where \( p \) is amplitude of the pressure.

Based on equation (2), an approximation of the sound field intensity in the focal area was obtained for arbitrary point \((X, Y, Z)\) (focus position \( (X_F, Y_F, Z_F)\)):

\[ I = I_F \exp(10^{-3} \rho(z)) \exp(q(r)), \quad p(z) = -0.1z^4 + 0.2z^3 - 4.5z^2 - 3z \]

\[ q(r) = -0.5r^4 - 0.35r^2, \quad z = Z - Z_F \quad r^2 = (X - X_F)^2 + (Y - Y_F)^2 \]

Here \( X, Y, Z, X_F, Y_F, Z_F \) are in millimetres and measured from the geometric focus of the radiator with coordinates \((0,0,0)\) and the intensity \( I_{F,0} \).

The \( I_F \) value is defined as

\[ I_F = I_{F,0} \exp(10^{-6} P(Z_F)) \exp(10^{-4} Q(R_F)), \quad Q(R_F) = -0.0035R_F^4 - 4.7R_F^2 \]

\[ P(Z_F) = -0.01Z_F^4 + 1.1Z_F^3 - 65Z_F^2 - 1300Z_F, \quad R_F^2 = X_F^2 + Y_F^2 \]

The error of the approximation in the range of the intensity variation from 0 to -10 dB is within 0.5 dB in water \((a = 1515 \text{ m/s}, \rho = 1000 \text{ kg/m}^3, \alpha = 0.092 \text{ m}^{-1})\) and in a water-fat layer medium [7].

3. Simulation of the evolution of the thermal field in the tissue

The non-stationary process of tissue heating under the impact of a series of pulses of focused ultrasound with constant thermal physical parameters of the medium is described by the heat conductivity equation [8]
\[ c\rho \frac{\partial T}{\partial t} = \lambda \Delta T + Q, \quad (5) \]

where \( c \) is the heat capacity, \( \lambda \) is thermal conductivity and \( \rho \) is density of the tissue, \( T \) is the temperature, and \( t \) is the time.

We use a Cartesian coordinate system: the origin coincides with the geometric focus of the transducer, and the \( Z \) axis coincides with the axis of the radiator (figure 1b).

During the operation of each pulse in the series, the source term \( Q(X,Y,Z,t_i < t \leq t_i + \tau) \) in (5) is calculated according to (1), (3), (4) \((t_i \) is the start time of the pulse in the series, and \( \tau \) is the pulse duration).

The parameters correspond to the breast fat [9]: \( \lambda = 0.21 \text{ W/(m-K)}, \quad c = 2348 \text{ J/(kg-K)}, \quad \rho = 911 \text{ kg/m}^3 \). The absorption coefficient of ultrasound in fat tissue is assumed to be \( \alpha_{\text{ref}} = 7.253 \text{ m}^{-1} \) for the frequency \( f_{\text{ref}} = 1 \text{ MHz} \) [10]; the dependence on the frequency of the transducer \( f \) is assumed to be linear. The initial temperature value in the entire region was \( T_0 = 309.6 \text{ K} \), and the temperature at the boundaries of the region was assumed constant and equal \( T_0 \).

The numerical solution of equation (1) was performed by the finite difference method [8]. An employed scheme of predictor-corrector provides the second order of accuracy in time and space (\( \tau_{\text{step}}, h_{\text{step}} \) are time and space steps). Depending on the case, the computational grid consisted of 5-100 million nodes.

The concept of the thermal dose is used to determine the lesion area [11]. According this concept the time equivalent of the thermal dose is

\[ t_D = \sum_{i=0}^{t_{\text{fin}}} R^{T_{\text{ref}}-T_i} \Delta t, \quad (6) \]

where \( T_m \) is the temperature corresponding to the time step \( \Delta t = \tau_{\text{step}} \), \( T_{\text{ref}} = 56^\circ\text{C} \), \( t_{\text{fin}} \) is the end time, \( R = 0.5 \) for the temperature larger \( 43^\circ\text{C} \) and \( R = 0.25 \) for \( T < 43^\circ\text{C} \). We use the value \( t_{S6} = 1.76 \text{ s} \) [2] as a dose required to the lesion formation.

4. Results
The lesion area for a single pulse is limited by the intensity and duration of the pulse, the spatial distribution of the ultrasound intensity and the thermophysical parameters of the tissue [7]. The treatment of a large tumor requires using a series of pulses (treatment program). The foci of pulses have to be localized in a specific sequence within the tumor. The number of pulses \( N \), the location of the focal areas inside the tumor, the order of pulses and the time interval \( \Delta t \) between the pulses are additional parameters that, together with the parameters of a single pulse, determine the lesion zone in the biological tissue.

To analyze the impact of a series of pulses on a biological tissue, it is convenient to use dimensionless parameters:

\[ \tau_s = \frac{t_S}{t_0}, \quad B_y = \frac{NQ_y \tau}{c\rho T_0}, \quad (7) \]

Here \( t_S = N\tau + (N-1)\Delta \tau \) is the total time of ablation; \( Q_y = 2\alpha I_y \) is the specific power of the heat source in focus; and \( t_0 = cpl^2 / \lambda = 9s \) is the typical time scale for fat tissue. The typical size \( l \) is taken as 0.94 mm and is equal to the radius of the circle in the plane \( Z = 0 \), for the points where \( II/I_y = 0.5 \).

A series of 31 HIFU pulses is considered. Each pulse was characterized by an intensity field approximated by (3), (4). The parameters of tissue processing programs are given in table 1. The ultrasonic pulses are collected in series with the time delay \( \Delta t \) between pulses. Total processing time for cases 1 and 2 is \( t_5 = 62 \text{ s} \), for case 3 it is 77 s, and for case 4 it is 32 s. Focal point locations in the transverse plane \((Z = 0)\) are presented in figure 2 for two considering programs “from” and “toward”
the center. The physical time range is 310 s and the space step between focal points along the X axis is \( h_x = 2 \text{ mm} \).

**Table 1.** Parameters of the tissue processing program.

| N  | \( I_{F0} \), W/cm\(^2\) | \( \tau \), s | \( \Delta \tau \), s | Program | \( \lambda \), W/(mK) | \( \tau_S \) | \( B_yS \) |
|----|----------------|-------------|--------------|--------|----------------|----------|----------|
| 1  | 100            | 2           | 0            | From the center | 0.21     | 6.89     | 2.72     |
| 2  | 100            | 2           | 0            | Toward the center | 0.21     | 6.89     | 2.72     |
| 3  | 100            | 2           | 0.5          | From the center | 0.21     | 8.56     | 2.72     |
| 4  | 200            | 1           | 0            | From the center | 0.42     | 6.89     | 2.72     |

**Figure 2.** Focal point locations for programs “from” (a) and “toward” (b) the center. The numbers correspond to the number of the pulse in the series.

The evolution of temperature and thermal doze in the central point is shown in figure 3. The first pulse in the program “from the center” provides the same temperature effect as the single pulse, but consequent pulses around the center point result in the additional temperature increase due to heat conductivity. In the second program ("toward the center") central point is the last in the series and previous pulses produce the temperature distribution that reduces the heat loss from the center. This leads to a significant increase in temperature and thermal doze in the center, much more than in the first case (program “from the center”). Despite the fact, that in both cases the total absorbed energy is the same (about 86 J), the difference in the results is obvious.

The process of thermal conductivity leads to a faster cooling of the central region at times \( t/t_0 < 15 \) for case 3 in the presence of a time delay between pulses. The thermal dose accumulated by the tissue is significantly lower with respect to that observed for case 1.

In terms of heat distribution, cases 1 and 4 are similar. For them, both the dimensionless parameters \( \tau_S \) and \( B_yS \), and the program of processing (figure 3a) coincide. However, the amount of heat dose received by the tissue is sufficiently different (figure 3b).

**Figure 4** shows the size of the lesion area based on the concept of thermal dose (6). For the calculation cases 1, 2 and 4, characterized by the same dimensionless parameters (7), the lesion area is different in both the \( XY \) and \( ZX \) planes. In the \( XY \) plane, the affected area is close to symmetrical with respect to the \( Z \) axis. For case 2 (program “toward the center”), there are areas of undamaged tissue in the peripheral areas (figure 4 a,b). For case 3 with a delay between pulses, such areas are visible in the \( ZX \) section (figure 4 c,d). A higher coefficient of thermal conductivity in case 4 leads to an increase in the lesion area (figure 4 e,f). Thus, despite the equal value of the absorbed energy of the ultrasonic radiation, the tissue damage areas are different for all the considered cases.
5. Conclusion
The model describing the biological tissue heating by series of intense ultrasound pulses has been developed. The model was employed for the analysis of the problem of lesion area formation under HIFU procedure. The simulation data for fat tissue have demonstrated significant influence of the type of processing program and the value of time delay between pulses on the shape of lesion area. For the considered range of parameters, implementation of so-called “to the center” program (that means location of focal spots of starting pulses in the periphery of processing area and final spot in the
center) leads to undamaged zones which is acceptable for therapy procedure. The same effect is observed for the presence of significant time delay between pulses. The evolution of the temperature field within the tissue may be described by two scaling parameters that characterize the total absorbed energy and processing time.

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