An experimentally obtainable heat source due to absorption of ultrasound in biological media

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Deposition of heat as a result of loss in an ultrasonic wave may result in damage to biological tissues. The extensive use of ultrasound for diagnostic purposes during pregnancy necessitates the evaluation of thermal risk to a developing fetus during routine clinical exposures. Because of the small ultrasonic absorption coefficient in soft tissues at low megahertz frequencies, temperature elevations exceeding 1 °C are not expected from clinically employed ultrasound systems, and there is no evidence that such small temperature increases can result in deleterious effects. However, when the propagation path includes bone, which is known to be highly lossy, theoretical calculations and experimental work indicate that local heating might exceed 1 °C for realistic clinical conditions. Thus it is imperative to obtain reasonable estimates of the temperature elevation in and around fetal bone in order to assess risk. Because of a lack of measured data for the thermal and acoustic properties of fetal bone, which depend on gestational age, estimates of the temperature elevation resulting from exposure to ultrasound must be based on crude models. A measured quantity for a heat source resulting from conversion of acoustic to thermal energy in an ultrasound field is suggested. The heat source is developed from theoretical considerations, and can be used in the bioheat transfer equation to obtain better estimates of the temperature increase in fetal bone and the surrounding tissues as a result of exposure to ultrasound.

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INTRODUCTION

Ultrasound has been employed clinically to monitor the health and well being of the developing fetus for approximately the past three decades. It has been estimated that currently more than one-half of the U.S. and European neonatal population is exposed to ultrasound prior to birth. From the perspective of the safety of routine clinical use of diagnostic ultrasound, evidence of adverse biological effects have not been reported. Nevertheless, caution and continuing research are necessary.[1]

A physical mechanism by which biological effects could be produced is thermal deposition in tissues as a result of ultrasonic loss.[2] In soft tissues, a knowledge of the ultrasonic absorption coefficient allows for calculations of the temperature increase to be made from the bioheat transfer equation,[3] and assessment of thermal risk. The absorption coefficient has been measured for many soft tissues, as well as attenuation for bone.[4,5] The temperature increase in the skull of mice resulting from ultrasonic exposure has also been measured.[6] Other studies have investigated theoretically and experimentally the temperature elevation at a bone/tissue interface.[7,8] However, little is known regarding conversion of ultrasonic energy to heat in fetal bone. Bone is known to be highly lossy, and there is the potential to create a significant temperature increase in the bone and neighboring soft tissues in ultrasonic fetal exposures. Previous studies have measured the temperature elevations in fetal femurs exposed to ultrasound in excess of 1 °C at 0.5 W/cm^2 (continuous wave) for second trimester specimens.[9] It is essential to be able to estimate the temperature elevation in and around bone as a result of ultrasonic exposure in order to assess the thermal risk to a developing fetus.

The anisotropic, heterogeneous nature of bone is well known,[10] and devising experiments to determine the elastic constants is challenging. Measurements of the elastic constants in adult human and bovine cortical bone assuming a hexagonal medium and employing plane-wave techniques have been reported.[10–13] Determining the elastic constants including loss in fetal bone are complicated because the cutting and machining necessary for employing plane-wave measurement techniques is all but impossible as a result of the size, shape, and varying degrees of hardness of the bone specimens. Further the acoustic properties vary with gestational age. An experimentally obtained heat source for use in temperature increase estimations in hard fetal tissues exposed to ultrasound is proposed herein. The heat source is derived from theoretical and experimental considerations. While the "accuracy" of this heat source is limited, it provides a basis for better temperature increase calculations in fetal bone and surrounding tissues than is presently available. Experimental results from a previous study, some unpublished, are presented to support the approach.

I. EXPERIMENTAL RESULTS

The temperature increase in fetal bone is a function of both acoustic loss and size, which increase with gestational age. A previous study reported temperature increases in fetal bone exposed to continuous (cw) ultrasound.[9] However, it is desirable to have a heat source obtained experimentally on which to base temperature increase calculations for more

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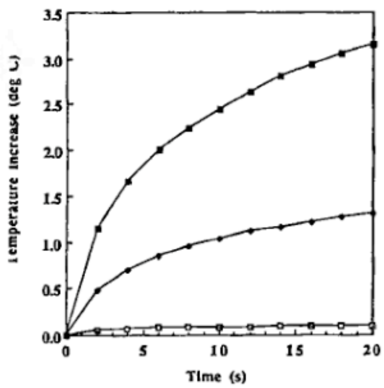

FIG. 1. Temperature elevation in fetal femurs of gestational ages □ 59 days, ◆ 83 days, and ■ 108 days, exposed to 1 W/cm² ultrasound intensity.

general shapes and sizes. The proposed source quantity can be obtained from experimental results of this previous study. The experimental procedures are detailed in Ref. 9, and are briefly summarized here. The temperature elevation and rate of temperature increase were measured *in vitro* with a single beam 1-MHz (cw) transducer with a half-power beamwidth of 1 cm in fetal femurs with gestational ages ranging from 59 to 108 days. The femur dimensions are given in Ref. 9. A thermocouple sensor was inserted through the middle of the femur diameter at the midpoint along the length, and the specimen was potted in 3% agar to minimize convective heat removal. The output of the thermocouple was amplified and sampled with an A/D converter.

The temperature elevation in fetal femurs of gestational ages 59, 83, and 108 days exposed at 1 W/cm^2 (cw) with a single beam transducer with a half-power beamwidth of 1 cm is shown in Fig. 1. The diameter and lengths of the specimens are (0.5, 11), (1.2, 24), and (3.3, 38), mm for the 59-, 83-, and 108-day specimens, respectively. (Figure 1 shows unpublished results from a previous study.[9]) The temperature elevation in the 59-day specimen has reached steady state prior to 20 s as a result of the small size, and the other two specimens achieved steady state well after 60 s. While the measurement over extended time provides an idea of the total temperature elevation, it is the information at short time that is useful for developing a heat source for theoretical calculations. The temperature increase will be affected by the bone dimensions as well as the acoustic loss and thermal properties. At short times prior to significant thermal diffusion, however, the temperature increase will be a function of the acoustic loss and thermal properties independent of the specimen size.

A quantity that is related only to ultrasonic loss independent of bone size is desired for the purpose of approximate temperature increase calculations. The initial rate of the temperature increase is significantly different for the three specimens of Fig. 1. Only the temperature increase in 2-s increments is plotted, however, the temperature was measured with a thermocouple, and sampled at greater than 500 samples/s. The slope can be accurately obtained from these data. For the specimens measured in this study, the measured rate of temperature increase in the initial 0.5 s is linear. The time derivative was determined at 0.2 s. The data in this time range was prior to the onset of diffusion, and showed little viscous heating artifacts. Further, the linearity of the data indicates that at 1 MHz, the loss in the specimens considered is not so great that large thermal gradients at the bone/agar interface are present. This is not entirely the case at 3, 5, 7, and 9 MHz. Preliminary measurements have shown that at 3 MHz the thermal gradient is observable in gestational ages beyond 100 days for a thermocouple placed in the center of the bone diameter. The temperature begins increasing at one rate, and then the rate of change increases as heat generated closer to the interface diffuses to the measurement location. However, if the thermocouple is located closer to the bone/agar interface toward the incident ultrasound beam, the thermal gradient artifact is not apparent. At 5, 7, and 9 MHz, however, the thermal gradient becomes very significant. In these cases, the measurement location must be near the bone surface. Further, it is expected that the thermal gradients would be sufficiently great that diffusion processes occur prior to 0.2 s, and the measured time derivative is decreased as a result. More work is required at higher frequencies to determine the limitations of the proposed scheme.

Because of the difficulties involved in experimentally determining the acoustic loss properties of fetal bone, an alternative is sought for use in temperature increase calculations in and around bone for fetal ultrasound exposure. An experimentally determined heat source developed from theoretical considerations is suggested herein for this purpose. For fetal bone, the experimentally determined heat source can be measured as a function of gestational age, and the temperature elevation in the bone and surrounding tissues can then be estimated using numerical or analytical methods.

II. AN EQUIVALENT HEAT SOURCE

An experimentally obtainable quantity for use in approximate temperature increase calculations can be determined by investigating an analytical solution of the bioheat transfer equation. A form of the bioheat transfer equation commonly employed in predicting the temperature elevation in tissues as a result of exposure to ultrasound is[3]

$$\frac{\partial T(\overline{\mathbf{r}},t)}{\partial t}=\kappa\nabla^2 T(\overline{\mathbf{r}},t)-\frac{T(\overline{\mathbf{r}},t)}{\tau}+\frac{q_v(\overline{\mathbf{r}},t)}{\rho C_p}, \tag{1}$$

where T is the temperature elevation, $\overline{\mathbf{r}}$ is the spatial coordinate, t is time, κ is the thermal diffusivity, τ is the perfusion time constant, $q_v(\overline{\mathbf{r}},t)$ is the rate of heat production per unit volume, ρ is the density, and C_p is the specific heat. The heat deposition in bone due to power loss is related to the acoustic particle velocity $\overline{\mathbf{v}}$ and the stress tensor $\overline{\overline{\mathbf{T}}}$ by $q_v(\overline{\mathbf{r}})=-\frac{1}{2}\nabla\cdot\Re e[\overline{\mathbf{v}}\cdot\overline{\overline{\mathbf{T}}}]$.[14] In general, though, $\overline{\mathbf{v}}$ and $\overline{\overline{\mathbf{T}}}$ are unknown for fetal bone.

In the absence of perfusion, and at short times such that heat conduction is negligible, Eq. (1) becomes

$$\left.\frac{\partial T(\overline{\mathbf{r}},t)}{\partial t}\right|_{t\to 0}=\frac{q_v(\overline{\mathbf{r}},t)}{\rho C_p}. \tag{2}$$

Without a specific knowledge of the acoustic properties of fetal bone, Eq. (2) suggests an experimental method for determining a heat source for ultrasonic absorption in fetal bone. Let the source function to the bioheat transfer equation be written as

$$\frac{q_v(\overline{\mathbf{r}},t)}{\rho C_p}=\frac{q_{v_0}f(\overline{\mathbf{r}})F(t)}{\rho C_p}=Q_0F(t)f(\overline{\mathbf{r}}), \tag{3}$$

where Q_0(°C/s) is the rate of the temperature increase, q_{v0} is the volumetric rate of energy deposition, and $f(\overline{\mathbf{r}})$ and $F(t)$ are the spatial and temporal variations of $q_v(\overline{\mathbf{r}},t) = q_{v_0}F(t)f(\overline{\mathbf{r}})$, respectively. The intensity of a focused transducer in a fluid or soft tissue is reasonably well approximated in the focal region by a Gaussian function with radial and axial beam parameters β_r and β_z. Then, in an infinite, homogenous absorbing medium $f(\overline{\mathbf{r}})=f(x,y,z) =e^{-(x^2+y^2)/\beta_r-z^2/\beta_z}$, and the resulting temperature increase is[15]

$$T(\overline{\mathbf{r}},t)=Q_0\int_{\substack{\text{source}\\ \text{duration}}}d\theta\ F(\theta)\int_{\text{source}}d\overline{\mathbf{r}}'\ f(\overline{\mathbf{r}}')G(\overline{\mathbf{r}},\overline{\mathbf{r}}',t,\theta), \tag{4}$$

where the Green's function $G(\overline{\mathbf{r}},\overline{\mathbf{r}}',t,\theta)$ is

$$G(\overline{\mathbf{r}}-\overline{\mathbf{r}}',t-\theta)=\frac{e^{-(t-\theta)/\tau}e^{-|\overline{\mathbf{r}}-\overline{\mathbf{r}}'|^2/4\kappa(t-\theta)}}{[4\pi\kappa(t-\theta)]^{3/2}}. \tag{5}$$

At the beam maximum $r=0$, the spatial variables can be integrated to yield

$$T(0,t)=Q_0\int_0^t d\theta\ F(\theta)e^{-(t-\theta)/\tau}\times\frac{1}{1+4\kappa(t-\theta)/\beta_r}\frac{1}{[1+4\kappa(t-\theta)/\beta_z]^{1/2}}. \tag{6}$$

If the material characteristics ρ and C_p, and heat source $q_{v_0}(Q_0 = q_{v_0}/\rho C_p)$ are known, the temperature at the beam maximum can be calculated from Eq. (6). In the case of ultrasonic absorption in soft tissue, q_{v_0}, and hence Q_0, is proportional to the acoustic intensity. This is the case in fetal bone as well.[9] The proportionality constant is determined experimentally for soft tissues by the transient thermoelectric or pulse decay methods.[16–18] The situation is considerably more complex in fetal bone because the elastic properties are unknown. The constant Q_0 is comprised of thermal constants as well as quantities characterizing the conversion of acoustic energy to heat. For soft tissues, these quantities can be separated as $q_{v_0}/\rho C_p = Q_0 = 2\alpha I_0/\rho C_p$, where α is the acoustic absorption coefficient, and I_0 is the acoustic intensity at the beam maximum. However, as seen from Eq. (6) this is not necessary for determining the temperature in this example. If Q_0 can be determined experimentally, the temperature can be calculated from Eq. (6).

Let the absorbing media be exposed to a unit step continuous sinusoidal ultrasonic exposure. Then $F(t)=U(t)$ in Eq. (6), where $U(t)$ is the unit step function. The temperature increase at $r=0$ is then given by

$$T(0,t)=Q_0\int_0^t d\theta\ e^{-(t-\theta)/\tau}\times\frac{1}{1+4\kappa(t-\theta)/\beta_r}\frac{1}{(1+4\kappa(t-\theta)/\beta_z)^{1/2}}. \tag{7}$$

For the case of soft tissues, the ultrasonic absorption coefficient is determined by the transient thermoelectric method from the derivative of Eq. (7), prior to thermal conduction,[19] and perfusion is absent. Measurements of the ultrasonic absorption coefficient in soft tissue are typically performed *in vitro* ($\tau\rightarrow\infty$), then

$$\frac{\partial T}{\partial t}=Q_0\left(\frac{1}{1+4\kappa t/\beta_r}\frac{1}{(1+4\kappa t/\beta_z)^{1/2}}\right). \tag{8}$$

The relationship between the temperature and Q_0 is then $\partial T/\partial t|_{t\rightarrow 0}=Q_0$. For soft tissues $\partial T/\partial t|_{t\rightarrow 0}=2\alpha I_0/\rho C_p$. The acoustic absorption coefficient in soft tissue is then obtained by measuring $\partial T/\partial t|_{t\rightarrow 0}$, together with a knowledge of the density and specific heat of the tissue, as well as the acoustic intensity. However, by experimentally determining $Q_0=\partial T/\partial t|_{t\rightarrow 0}$, the temperature increase can be computed without a specific knowledge of the acoustic loss properties of the medium. It is, however, necessary to know or estimate κ, and τ if the medium is perfused, as well as the spatial variation of the source in order to calculate the temperature elevation.

For illustrative purposes, an infinite homogeneous medium was considered above for the temperature elevation. In practice when measuring $\partial T/\partial t|_{t\rightarrow 0}$, the absorbing medium is finite. However, at short times such that heat diffusion is negligible, the time derivative of the temperature is simply related to the source as in Eq. (2), independent of the extent of the media. Similarly, for inhomogeneous media, as in the experimental procedure for measuring the rate of temperature increase in fetal bone, the source is related to the time derivative of the temperature by Eq. (2) at short times when diffusion is negligible, independent of the media inhomogeneities.

In practice the rate of temperature increase in the bone is measured *in vitro* at the spatial maximum of a single beam ultrasound field incident on the bone.[9] If the amplitude of the incident field is such that no significant nonlinear harmonics are generated, the rate of temperature increase at short times will be proportional to intensity. This is expected since linear equations of motion then apply. The measured heat source is then $(1/I_0)(\partial T/\partial t)|_{t\rightarrow 0}$, where I_0 is the incident intensity in the fluid. Experimental procedures for obtaining $(1/I_0)(\partial T/\partial t)|_{t\rightarrow 0}$ in fetal bone have been previously reported.[9] Experimental results of $(1/I_0)(\partial T/\partial t)|_{t\rightarrow 0}$ at 1 MHz as a function of gestational age are shown in Fig. 2. The heat source used in calculations then would be the incident intensity multiplied by the measured quantity $(1/I_0)(\partial T/\partial t)|_{t\rightarrow 0}$. In a complex, inhomogeneous, layered medium consisting of bone, muscle, and fat, numerical or analytical solutions of the temperature elevation resulting from ultrasound exposure would be pursued employing the

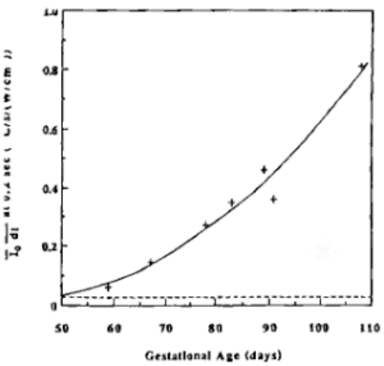

FIG. 2. Time derivative of the temperature, normalized to the incident intensity, versus the gestational age of fetal femur specimens. The solid curve is a quadratic least squares fit to the measured data. The dashed line is the value obtained for soft tissue with an absorption coefficient of 0.05 cm^{-1}. (See Ref. 9.)

bioheat transfer equation. The heat source term in the soft tissues is $Q_0 = 2\alpha I/\rho C_p$, and in the fetal bone $I((1/I_0)(\partial T/\partial t)|_{t\to 0})_{\text{measured}}$.

By measuring the heat source suggested above in fetal bone, approximate numerical or analytical temperature elevation calculations based on an experimentally determined heat source can be made. However, given the current state of knowledge of the thermal and acoustic properties, other estimates are required for the calculations. First, the thermal diffusivity and perfusion in fetal bone as a function of gestational age are currently unknown. One estimate is to use the thermal diffusivity of the surrounding soft tissues, which is assumed to be nearly that of water. In this case, the free-space Green's function can be employed and the temperature increase estimated as in Eq. (4). In the early stages of bone ossification, e.g., prior to 90 days gestational age, this is a reasonable estimate. However, beyond this gestational age, a worst case estimate can be employed by assuming the thermal diffusivity of adult bone. For this case, a finite-element or finite-difference approach might be employed for calculating the temperature elevation using the experimentally determined heat source.

In characterizing fetal bone, the experimentally determined heat source is measured only at the spatial maximum of a single beam ultrasound field, and the spatial variation of the source is unknown. The heat source as a function of position is determined from the acoustic field, however, the acoustic field inside the bone is unknown. Estimates of the acoustic field inside the bone might be made using simple approximations, for example, an isotropic medium. Alternatively, the measured heat source can be employed with the spatial distribution of the incident ultrasound beam. Measurements at 1 MHz indicate this to be a reasonable approximation for gestational ages prior to 90 days.[20] Preliminary experiments at higher frequencies (5, 7, and 9 MHz) indicate that this would result in an estimated heat source volume greater than the actual situation, and further studies are required.

The ultrasonic absorption coefficient can be measured directly for soft tissues. Hence, lumping the acoustic and thermal properties of the medium together in the quantity Q_0 is unnecessary. However, characterizing ultrasonic losses in bone presents a formidable problem. In this case, the quantity Q_0, which can be measured directly, is useful for numerical and analytical calculations of the temperature increase in fetal bone and surrounding tissues. By measuring this quantity as a function of frequency and gestational age, more reliable temperature elevation estimates can be obtained for clinically employed ultrasound fields than might be obtained by assuming that some fraction of the ultrasound field is absorbed for a given gestational age.

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