Frequency dependence of thresholds for ultrasonic production of thermal lesions in tissue

R. M. Lerner and E. L. Carstensen
Department of Electrical Engineering, University of Rochester, Rochester, New York 14627

F. Dunn
Bioacoustics Research Laboratory, University of Illinois, Urbana, Illinois 61801
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The ultrasonic intensity threshold for producing lesions in mammalian brain tissue is not a strong function of frequency (over the range of 1–10 MHz) for exposures longer than 1 sec. A model is presented to explain this apparent lack of frequency dependence. It is assumed that the maximum temperature developed in the lesion volume for a given pulse duration is determined (1) by the absorption coefficient of that tissue, and (2) by the distribution of the acoustic intensity over the treated volume (sharpness of the beam). The former is observed experimentally to be nearly linearly dependent upon frequency in the range 1–10 MHz, and the latter, for a good lens, is related inversely to frequency. Temperature calculations which account for heat loss by diffusion as well as the frequency dependence for the beam geometry and the absorption coefficient are presented. These lead to nearly frequency independent curves for threshold dosages beyond 1-sec exposure, giving credence to the suggestion that thermal processes may be predominant for such exposures.

Subject Classification: 16.4.

INTRODUCTION

The use of the focused ultrasound to produce structural changes in brain tissue (lesions) has been studied over a broad range of single pulse exposures (20 000 W/cm^2 for 3×10^{-4} sec to 50 W/cm^2 for 3×10^2 sec) by several investigators.[1–3] The data are conveniently presented as a dosage curve of acoustic intensity versus pulse duration for threshold lesions (Fig. 1). For pulse durations less than 40 msec, the lesions are attributed to a cavitation mechanism and an expected increase in threshold intensity with an increase in frequency is observed.[1] Lesions produced for pulse durations on the order of 1 sec and greater are attributed to a thermal mechanism.[1–4] Since the acoustic absorption coefficient in mammalian tissue exhibits a nearly linear frequency dependence over the 1–10 MHz range,[5] intuitively it might be expected that a strong frequency dependence of threshold acoustic intensity would be exhibited for thermal lesions. However, the data for 1–6 MHz, shown in Fig. 1, do not show such a frequency dependence.

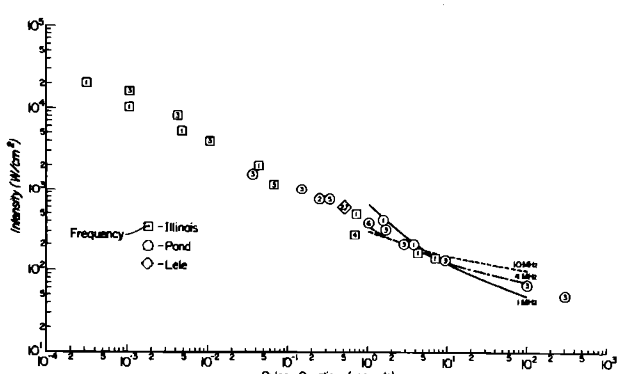

FIG. 1. Thresholds for ultrasonic focal brain lesions. Data points are observed threshold: □ Ref. 1, ○ Ref. 2, ◇ Ref. 3. Curves are thresholds predicted for the source used at the University of Illinois: ——— 1 MHz, — — — — 4 MHz, - - - - 10 MHz.

A model is presented here to explain the apparent lack of frequency dependence observed for 1- to 100-sec pulse durations. Qualitatively, it is argued that the lack of frequency dependence over the 1–10 MHz range for thermal lesions is a result of a fortuitous combination of an increase in absorption coefficient with a concommitant decrease in the focal volume, as frequency is increased. It is found that for a given pulse duration, a range of frequencies exists such that the increase in heat generation due to increased frequency (via absorption coefficient) is compensated by increased heat loss due to diffusion and, therefore, the intensity to produce a given temperature increase is not strongly frequency dependent.

I. TEMPERATURE PREDICTIONS

Calculations for predicting the temperature increment due to focused ultrasound in mammalian tissue are based on a model which assumes an infinite medium with internal heat generation. The infinite medium assumption is reasonable for the pulse durations under consideration (1–100 sec) since diffusion of heat to the specimen surfaces is insignificant when the focal region is located several millimeters from a surface. Because of the focused ultrasonic transducers traditionally employed, actual acoustic intensity profiles have cylindrical symmetry. The temperature at the center of an ideal cylindrical source of heat in an infinite medium of like thermal properties is given by (Fig. 2)[6]:

$$T(r=0, z=0, t)$$
$$=\frac{\dot{q}}{\rho c}\int_0^t [1-\exp(-A^2/4Dt')]\,\mathrm{erf}\left(\frac{B}{(4Dt)^{\frac{1}{2}}}\right)dt', \quad (1)$$

where $2A$ and $2B$ are, respectively, the diameter and length of the cylindrical heat source; $\dot{q}$ is the time rate of heat generation per unit volume; and ρ, c, and D are, respectively, the density, heat capacity, and thermal diffusivity of the medium. The heat generation rate $\dot{q}$ at the center of focus is related to acoustic intensity by[3,7]

$$\dot{q}=2\alpha I, \quad (2)$$

where α is the sound-pressure absorption coefficient and I is the ultrasonic intensity. The axial variation of the intensity of sound in a plane wave is

$$I(z)=I_0\exp(-2\alpha z), \quad (3)$$

where z is the coordinate along the direction of propagation. Since the axial dimension B of the acoustic intensity distribution is small by comparison with α^{-1}, i.e., $2\alpha B \ll 1$, the variation in intensity along the length of the focal region due to absorption has been neglected in the calculations.[8]

The intensity distribution of the field of a focused acoustic transducer does not correspond to the discrete heat source idealized in Fig. 2. Instead, the intensity varies continuously both in axial and radial directions as shown in Figs. 3(a) and 3(b). For the purposes of calculation, each of these profiles was approximated by superposition of a sum of ten cylindrical sources of the form of Fig. 2, as illustrated in Figs. 3(a) and 3(b). For example, the smallest cylinder for the beam of Fig. 3 is 0.1 mm in diameter and 0.18 mm long. The largest is 0.78 mm in diameter and 1.7 mm long. The size of the focal region varies inversely with frequency. From axial and lateral profiles determined experimentally over the frequency range of interest, empirical expressions for the factors A and B of Eq. 1 can be taken to be of the form

$$A=C_1/f^n,$$
$$B=C_2/f^m,$$

where C_1 and C_2 are constants. Single values of n and m have been found adequate to describe the frequency dependence of each of the component cylinders in the composite beam. The absorption coefficient can be

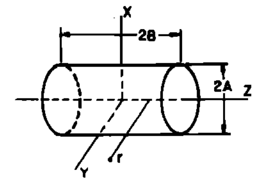

FIG. 2. Model of cylindrical heat sources used in the calculations.

described by the relation

$$\alpha=0.1f,$$

where f is the frequency in megahertz and α is in nepers/cm. This expression is in approximate agreement with the data summarized by Goldman and Hueter.[5] Substituting the frequency dependence of A, B, and α in Eq. 1 leads to the following expression for the temperature developed in the lesion per unit intensity as a function of frequency:

$$\frac{T(0,0,t)}{I_0}=\frac{2(0.1f)}{\rho c}\int_0^t \{1-\exp[-(C_1/f^n)^2/4Dt']\}$$
$$\times\mathrm{erf}[(C_2/f^m)/(4Dt')^{\frac{1}{2}}]dt', \quad (4)$$

I_0 is the intensity at the center of the focal region, i.e., the center of coordinate system used in the calculations. Expression 4 predicts the frequency dependence for $T(0,0,t)/I_0$ for a given set of constants C_1, C_2 which correspond to a given component cylinder. If, by a method similar to that of Pond,[2] the intensity profile is approximated as the summation of ten cylinders of different size (with equal heat generation per unit volume), then Eq. 4 must be evaluated for all ten cylinders and the results summed and multiplied by $\frac{1}{10}$ to obtain the temperature for the actual intensity

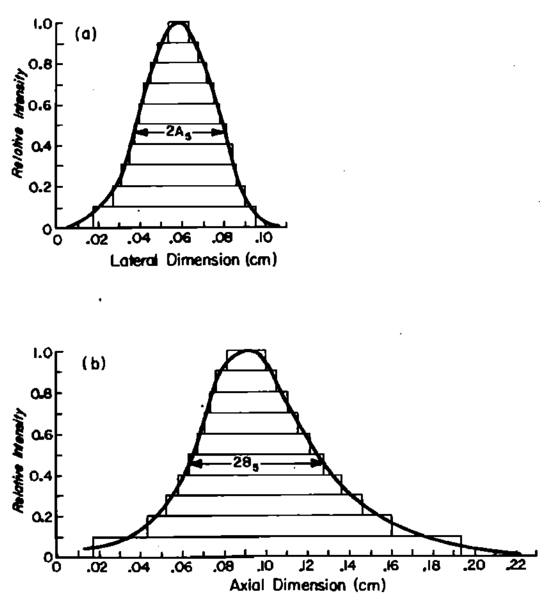

FIG. 3. Intensity profiles for 9-MHz transducer used at the University of Illinois. The actual profile is approximated as a superposition of a series of cylinders of length 2B and diameter 2A: (a) Lateral profile; (b) axial profile.

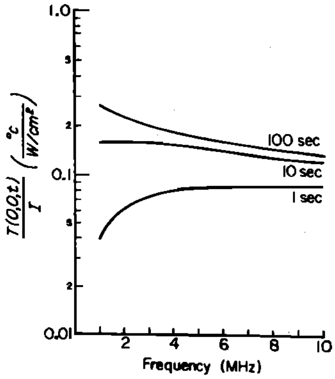

FIG. 4. Temperature/intensity versus frequency as predicted for 1-, 10-, and 100-sec exposures.

profile. This procedure was used to calculate the temperature rise (at the center of the focal region) in tissue as a function of frequency for a transducer employed at the University of Illinois, Urbana (characterized in Fig. 3). The results, presented in Fig. 4 for 1-, 10-, and 100-sec single pulse durations, do not predict a strong frequency dependence for heating of the tissue by the ultrasound. The slight variations in intensities required to produce a given temperature rise may not be discernible from the scatter in Fig. 1.

II. THRESHOLD FOR FOCAL LESIONS

Moritz and Henriques,[9] and Linke *et al.*,[10] have reported studies of the temperature time relation for thermal damage to pig and human skin, and other mammalian tissues. In experiments where a heated disk was placed against the skin, it was found that a temperature of 70°C was required to produce irreversible damage in 1-sec whereas 10 sec at 58°C, and 100 sec at 52°C were required to produce the same endpoint (initial temperature, 37°C). Although the conditions of their experiments (surface heating) were somewhat different from the condition described here (volume heating), their data may be used along with the results of the calculations shown in Fig. 4 to make an approximation of the threshold dosage (I,t) to produce irreversible damage to tissue by ultrasound. These approximations are shown by the curves in Fig. 1 for 1, 4, and 10 MHz.

It is not clear how exposures should be compared in the two kinds of experiments when the exposure times are of the order of a few seconds or less. In this case rise and fall times are a significant part of the total exposure. In these calculations we have simply equated exposure time to heating time. It is apparent, however, that a more sophisticated approach would be required to assess the contribution of heat for exposure times less than 1 sec.

III. DISCUSSION

The temperature increment produced in tissue by absorption of focused ultrasound (1–10 MHz) is essentially independent of frequency for single pulse durations of 1 to 100 sec because of the frequency dependence of both the absorption coefficient in the tissue and the focal region geometry. Further, when the temperature–time relationship for threshold lesions is considered, a remarkably good agreement emerges between predicted and observed threshold values for ultrasonic lesions produced by exposure times greater than one second (Fig. 1). The theoretical considerations leading to these predictions are based entirely upon the effects of heat, viz., the heat production by absorption of ultrasound in the tissue and the diffusion of heat away from the region of production. These considerations support the view that at threshold intensities for exposure times in excess of one second, the destruction of tissue is dominated by thermal processes.

ACKNOWLEDGMENTS

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