Ultrasonic absorbed dose, dose rate, and produced lesion volume

R. L. JOHNSTON and F. DUNN

Histological preparations of ultrasonically produced lesions in cat brain, at 3 and 4 MHz, have been studied microscopically. The relationship of the delivered acoustic intensity at the lesion site, the energy absorbed per unit volume of the lesion, and the lesion volume is exhibited. It is suggested that universal responses to ultrasonic exposure may exist for different tissues.

Ultrasound is becoming more widely used in medical practice as a diagnostic tool and as a therapeutic agent. Thus, dosimetry, the area providing measures of energy involving functions correlatable with graded tissue response, becomes a major concern from the points of view of effective employment of this modality and of safe operating conditions. Such concerns have been expressed strongly by all bodies recently convened to examine progress in this field, to plan future undertakings, and to advise on proposed expenditures.[1,2]

In the usual laboratory and clinical situations, investigators and practitioners are able only to provide information on the acoustic output of the exposing ultrasonic transducer. Generally, the quantity specified is the calibrated acoustic intensity [dose rate $(\text{area})^{-1}$] developed in what must always be an approximation of free field conditions. Subsequent acoustic exposure conditions of the specimen, by the same transducer operated in a similar fashion with reference to that of the calibration procedure, are extrapolated by methods which have not always received universal acceptance. However, several laboratories have been able to determine the intensity delivered to the site of interest in the specimen and the intensity-time threshold levels at which lesions (irreversible structural changes) begin to appear in the mammalian central nervous system.[3] Cat, rat, monkey, and human brain appear to respond identically [4] and existing frequency variations are relatively small.[5] Discussion has occurred with regard to the various physical mechanisms involved in the production of these lesions and with regard to the apparent lack of frequency dependence in the lower dosage region where thermal mechanisms are implicated.[6] The observed frequency variation of the threshold remains puzzling and continues to receive attention.

The relationship between delivered dosage, absorbed dose, and lesion dimensions has not as yet been investigated and this paper is an initial report of such an attempt. The study was undertaken with the view towards correlation of the acoustic intensity delivered to the site of interest in the brains of cat and rat, the ultrasonic energy absorbed within the volume of tissue irreversibly structurally altered, and the lesion volume.

The authors are at the Bioacoustics Research Laboratory, University of Illinois, Urbana, Illinois 61801, USA. Paper received 12 November 1975 and was presented before the Colloquium on ultrasound bioeffects and dosimetry, Chelsea College, London (July 22–23 1974)

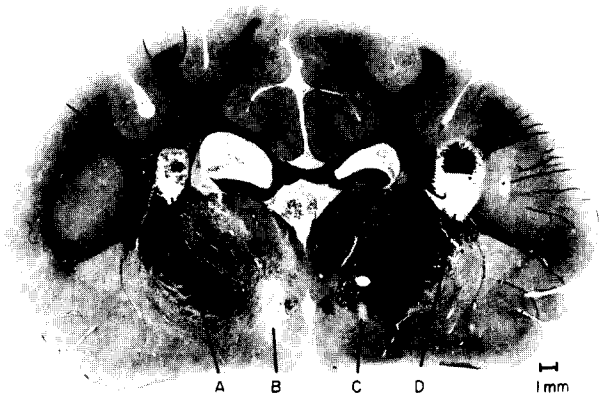

Fig.1 Ultrasonically produced suprathreshold lesions in cat brain at a frequency of 4 MHz. The figure represents the central section only for lesion B.

Lesion	Intensity ($W\ cm^{-2}$)	Time (s)
A	300	2
B	150	5
C	150	2.5
D	300	2

Suprathreshold lesions were produced in cat brain with focussed ultrasound at 3 MHz and 4 MHz, by established procedures.[3,7] The animals were sacrificed 24 h after irradiation, the brain sections were subsequently stained by the Weil method, and the histological preparations were then examined microscopically to obtain lesion dimensions. Fig.1 is typical of the histological preparation, available for this study, showing several lesions for investigation in a single specimen. Fig.2 is an enlargement of one of these lesions exhibiting its ellipsoidal character and revealing a major source of uncertainty in determining the lesion volume, viz., that the lesion edges are not uniquely identifiable, thus requiring the investigator to make judgements

on its positions and thereby introducing errors in the computed volume. The maximum uncertainty in any linear measurement is estimated to be 0.1 mm. Lesions distended by hemorrhagic involvement were not included, thus setting an upper volume limit of approximately 100 mm^3. Lesions below 0.01 mm^3 are difficult to measure due to the background of numerous histologic entities of similar size and appearance.

The lesion volumes were computed assuming the lesions to be ellipsoids of circular cross-section. Thus, the volume could be computed from measurements of the major and minor axes only. It should be noted that the direction of incidence of the ultrasonic wave, and the geometry of sectioning the tissue, insured that appearance of the lesion in section was coplanar. Further, serial 10 μ sections were prepared to permit the lateral extent of the lesion to be investigated.

The computation procedure involved two further assumptions. Firstly, the sound field distribution within the lesion volume may be considered uniform. Consideration of the wavelengths employed (approximtely 0.4 mm), the linear dimensions dealt with (0.2 to 4 mm), and the geometry of the focussed ultrasonic field (approximately 1 λ) suggests that the errors so introduced are less than the uncertainties associated with the linear measurements. Secondly, it was assumed that the ultrasonic absorption coefficient of the tissue was constant during the period of exposure though recent studies show this not to be true in all cases.[8,9]

Fig.2 Enlargement of lesion B in Fig.1

However, the relatively short path of sound through the focal volume – the only portion of the path wherein significantly high intensity values are developed – determines that even the suggested tripling [8,9] of the absorption coefficient would not contribute errors as great as those of the microscopic linear measurements. With these conditions, data, and previous methods,[3,5,8] the ultrasonic intensity delivered to the lesion site and the ultrasonic energy absorbed therein were determined. Fig.3 shows the lesion volume, at 4 MHz, as a function of exposure time, with the delivered intensity as the parameter from curve-to-curve. The error bars exhibit the uncertainty in the volume where it is seen that for small lesions, for which the uncertainty in the linear measurement becomes appreciable, the uncertainty in the lesion volume becomes immoderate. Fig.4 shows the lesion volume as a function of the absorbed acoustic energy per unit volume of the

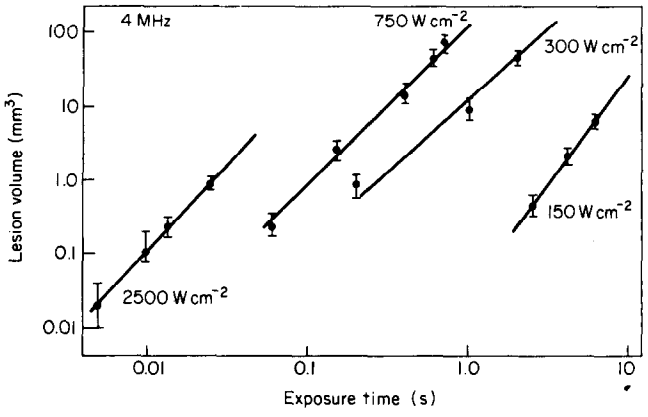

Fig.3 Ultrasonically produced lesion volume as a function of exposure time and delivered intensity at 4 MHz

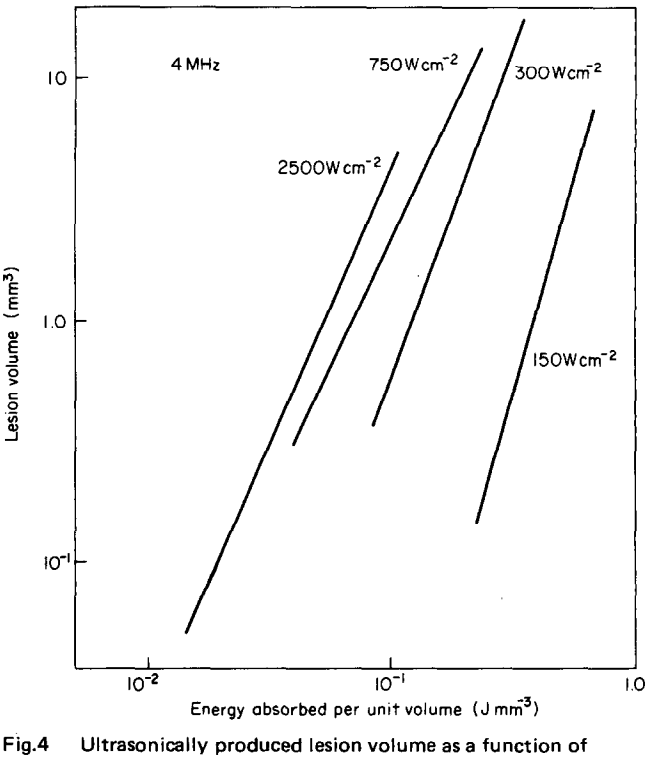

Fig.4 Ultrasonically produced lesion volume as a function of absorbed energy per unit volume of lesion and delivered intensity at 4 MHz

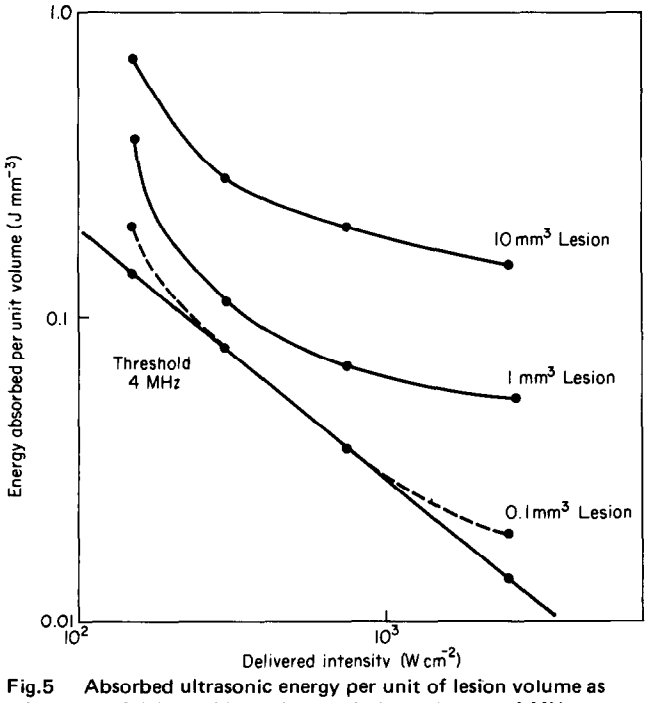

Fig.5 Absorbed ultrasonic energy per unit of lesion volume as a function of delivered intensity and lesion volume at 4 MHz. Dashed lines suggest the curves in the threshold region

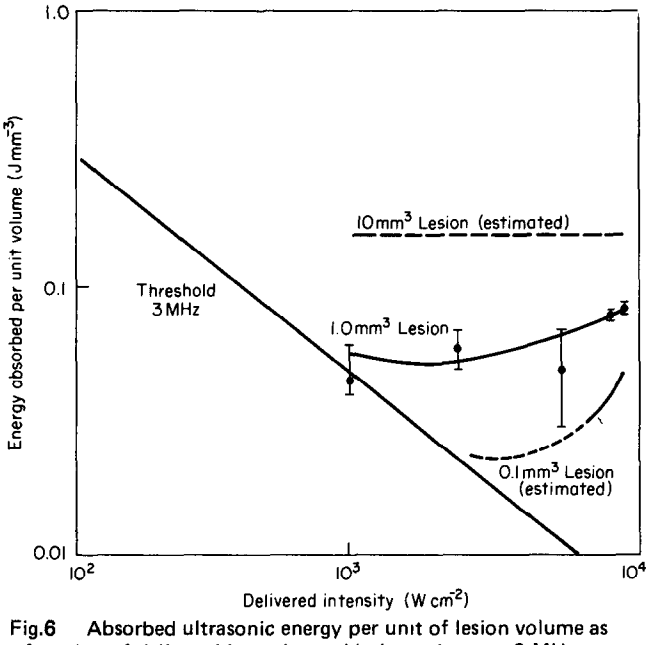

Fig.6 Absorbed ultrasonic energy per unit of lesion volume as a function of delivered intensity and lesion volume at 3 MHz. Dashed lines are estimates

lesion, with the delivered intensity as the parameter from curve-to-curve. Fig.5 shows the energy absorbed per unit volume of the lesion as a function the delivered intensity, with the lesion volume being the parameter from curve-to-curve. The dashed lines suggest the shape of these curves in the threshold region. Fig.6 shows similar results for 3 MHz. However, as much less data are currently available at this frequency, some estimates are included. Fig.7 shows the data of Figs. 5 and 6 plotted together, wherein it is 'suggested' that a universal set of curves may exist for the energy absorbed per unit volume of lesion versus the delivered intensity. Note that the slight differences in thresholds, as a function of frequency, will produce some differences in any such set of universal curves.

In these studies, both the gray and white matter of the cat

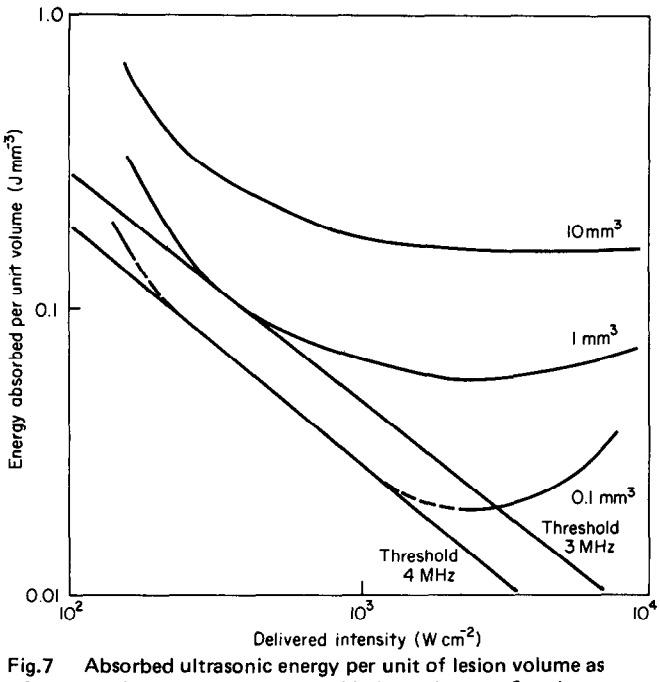

Fig.7 Absorbed ultrasonic energy per unit of lesion volume as a function of delivered intensity and lesion volume at 3 and 4 MHz

brain were treated, yielding identical results. With this observation, and the implications of Fig.7, it is interesting to speculate that these results may be universal for other tissues as well. The authors, asks investigators in this field to treat their data, with tissues other than those of the CNS, in a fashion similar to that described herein so that the important question of the universal behaviour of biological structures submitted to ultrasonic exposure may be resolved shortly.

Acknowledgement

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