criterion for all subjects). According to the model, the mean signal threshold for a notch width of 0.0 should be equal to the sum of the noise spectrum level (45 dB), 10 log(ERB) (24.9 dB), and K (-0.7 dB), i.e., 69.2 dB. The obtained mean value was 68.5 dB (standard deviation 2.0 dB). This is in reasonable agreement, but confirms the tendency of the roex(p) model to overestimate thresholds for a notch width of 0.0 (Glasberg *et al.*, 1984). Notice that, because of the variability of the threshold for a notch width of 0.0, filter ERBs estimated indirectly from critical ratios would be considerably more variable than those estimated directly; the standard deviation would be about 150 Hz instead of 32 Hz.

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In vivo B/A determination in a mammalian organ

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Investigations of the ultrasonic nonlinearity parameter B/A have been restricted previously to *in vitro* preparations. The parameter B/A has now been determined *in vivo* in cat liver and found to have the same value as *in vitro* determinations. The finite amplitude method was used, with a substitutional procedure to improve accuracy.

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INTRODUCTION

The extensive use of ultrasound in medical diagnosis and therapy has increased the need for better understanding of ultrasonic wave propagation in biological media. The assumption of the linear state equation of biological media, while analytically simple and practically appealing, may introduce significant error in describing ultrasonic propagation in biological media.[1–3] Details of the acoustic nonlinearity of biological media, in addition to providing significant information for accurate modeling of ultrasonic propagation, provide for improved treatment planning of ultrasonic therapeutic applications, for correct interpretation of medical diagnostic information results, and provides a parameter for tissue characterization. For all these cases, it is important to determine the nonlinearity parameter B/A in different tissues and for different tissue states.

Much work has been done on the *in vitro* determination of B/A in a few mammalian tissues[4–7] and it has been found that B/A ranges from 6.5 to 11. Since a major medical application of the B/A values will be for *in vivo* applications, it is considered essential to have available *in vivo* values, or at least to know the relation of *in vitro* measurements to *in vivo* applications. That is, it is presently not known how the vascular system influences the B/A value. In this letter, a set of results of *in vivo* and *in vitro* B/A values in cat liver is presented.

I. MEASUREMENT METHOD

The finite amplitude method was employed and modified for the *in vivo* B/A determination. The technique has been described in detail previously.[8,9] The method evaluates the magnitude of B/A by measuring second harmonic generation as a function of distance from the source, as

$$\frac{B}{A}+2=\frac{P_2(x)}{xP_1^2(0)\ \mathrm{DIFF}\ (x)}\frac{2\rho_0 c_0^3}{\pi f}e^{(\alpha_1+\alpha_2/2)x},$$

where x is the axial distance between the receiving transducer and the sound transmitter, $P_2(x)$ is the second harmonic acoustic pressure averaged over the surface of the receiving transducer, $P_1(0)$ is the fundamental acoustic pressure output of the transmitter, DIFF(x) is the diffraction correction that is a function of the geometry of the transmitter and the receiver, ρ_0 is the equilibrium density of the medium, and c_0 is the infinitesimal wave velocity. Figure 1

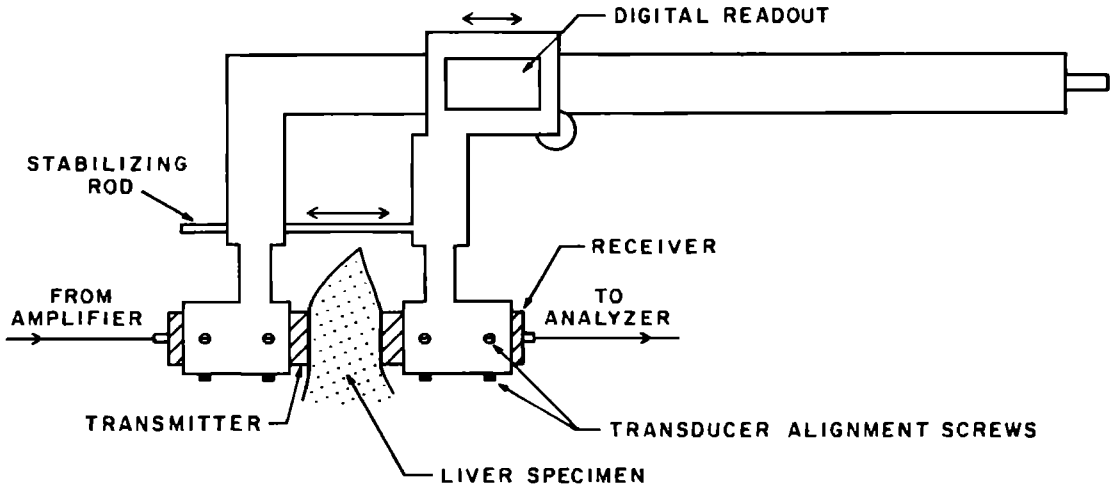

FIG. 1. Transducer-caliper assembly used in *in vivo B/A* measurement. The digital readout gives the separation distance between the transmitter and the receiver.

illustrates the measurement system. The 3-MHz gated cw signal, 10 μs on and 1 ms off, is amplified and fed to the transmitter. Both transmitter and receiver are calibrated at the frequencies of 3 and 6 MHz at 30 °C. An HP 8557 A spectrum analyzer was used in the determination of both the fundamental and the second harmonic ultrasonic pressure amplitudes. Here, α_1 and α_2, the absorption coefficients of the fundamental and second harmonic components, respectively, can be calculated from

$$\alpha_i = -\frac{1}{x}\ln\frac{P_i(x)}{P_i(0)\ \mathrm{DIFF}_i(x)} \quad (i=1,2)\,.$$

The following method was employed to determine the speed of sound c_0. The transmitted signal was fed into one channel of a Tektronix 2445 oscilloscope and the received signal into the other channel. The oscilloscope was operated in the delay mode and, by aligning the leading edges of the two signals, the delay time could be obtained directly from the screen digital readout. The system was calibrated against degassed, distilled water, for which the speed of ultrasound is known, to determine the inherent delay of the system.

A special caliper–transducer assembly was fabricated to provide convenient *in vivo* measurement[10] (see Fig. 1). The two transducers are adjusted to be acoustically coaxial in the transmitting medium, viz., saline. A digital readout gives the separation distance of the two transducers.

Cats of 6 to 9 lb were injected i.p. with sodium pentobarbital (Nembutal, Abott Laboratories) at the dose of 0.3 ml/lb body weight. The liver was exteriorized so that the caliper assembly could be positioned about the specimen to be examined. The body fluid on the liver surface served as the acoustic coupling fluid. The velocity, attenuation, and second harmonic ultrasound pressure amplitude were measured without moving the transducers from their original positioning and the *in vivo B/A* value was calculated from these measurements.

The cat was sacrificed by injecting T-61 euthanasia solution. The blood in the liver was partially drained by a cut in the liver near the observation point. During all these operations, the relative position of the transducer assembly with respect to the liver specimen was maintained unchanged. Determination of the *in vitro B/A* value followed. Although the *B/A* determination procedure was the same herein, for both the *in vivo* and *in vitro* states of specimens, some earlier reports described a slightly different procedure in which the specimens and the transducers were submerged in saline.[5–7]

II. RESULTS

Table I shows the results of *in vivo* and *in vitro B/A* values measured in five cats, as described above. It is seen that blood circulation and blood content seem not to contribute to the tissue *B/A*, within the experimental error. Although the uncertainty of the absolute determination of *B/A* is estimated to be 8%,[7] it should be much less for the relative measurement. The *in vitro B/A* values of cat liver from this study, and those of mammalian liver from other studies, are given in Table II for completeness.

III. DISCUSSION

These preliminary results are a first reporting of the relation of *in vivo* and *in vitro B/A* values of a mammalian organ. The finding of a lack of significant difference of *in vivo* and *in vitro B/A* values in cat liver may not necessarily mean that similar results will obtain for other organs of the cat or

TABLE I. The *B/A* values of cat liver.

Cat #	*In vivo*	*In vitro*	$\Delta(B/A)$
1	6.9	6.9	0
2	7.0	6.9	+0.1
3	6.5	6.4	+0.1
4	6.6	6.6	0
5	7.0	6.9	+0.1

TABLE II. Comparison of *in vitro B/A* with literature values.

Animals	Cat liver (this study)	Beef liver Ref. 7	Dog liver Ref. 5	Human Ref. 6
B/A	6.9, 6.9 6.6, 6.8 6.4	7.5, 7.9 6.2, 8.0	7.6, 7.9	7.6, 6.54

for different pathological conditions of cat liver. Indeed, assumptions should not be extended even to normal liver of other animals, as supported by the entries of Table II. However, it is implied that blood circulation in the normal cat liver has little influence upon the *B/A* value. More studies are needed to draw more general conclusions. Should the results hold in more complete studies, it may suggest that *B/A* values obtained *in vitro* are sufficient for treatment planning and for interpretation of diagnostic results.

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