ARCHIVES OF ACOUSTICS
9, 1-2, 29-34 (1984)

THE ULTRASONIC NONLINEARITY PARAMETER FOR BIOLOGICAL MEDIA

F. DUNN, W. K. LAW, L. A. FRIZZELL

Department of Electrical Engineering, Bioacoustics Research Laboratory, University of Illinois
(1406 West Green Street, Urbana, Illinois 61801, USA)

The nonlinearity parameter B/A of several soft tissues was measured using two independent methods. The B/A values of most soft tissues were found to be between 7 and 8, with the exception of fat which has a B/A value close to 11. It is proposed that structural hierarchy contributes to the B/A values of tissues.

1. Introduction

Ultrasound has been used extensively in the diagnosis of diseases and in therapeutic applications and its employment continues to increase. However, evidence is accumulating to indicate that ultrasonic propagation associated with biomedical applications may not always be considered linear [3, 4, 10]. The effects of the nonlinear propagation, which include harmonic generation, additional attenuation over that expected from the fundamental frequency component alone, increased heat development, and change in beam profile, can have important consequences on both the diagnostic and therapeutic applications. It is believed that detailed understanding of these nonlinear phenomena should lead to improved accuracy and increased information from procedures using diagnostic instruments. With regard to the therapeutic application, additional understanding should lead to more sophisticated control of heat deposition in the selected tissue volumes.

In order to predict accurately the effect of nonlinear propagation of ultrasound in biological media, it is necessary first to determine the degree of nonlinearity that the medium itself exhibits. Two independent methods of measuring the nonlinearity parameter in biological materials have been developed for this purpose. The first method, the finite amplitude technique, determines the nonlinearity parameter in a medium by measuring the magnitude of the second harmonic generated. This method has the potential for use in making *in vivo* measurements. The second method, the thermodynamic technique, involves determination of the change of sound speed with hydrostatic pressure and temperature. The accuracy of the thermodynamic technique is superior to that of the finite amplitude technique, though it is limited to *in vitro* measurements only. This paper is a report on the *in vitro* measurement of the nonlinearity parameter in soft tissues by both techniques. Based on the present tissue observation, and previously reported observations with tissue models, it is proposed that the B/A value (the nonlinearity parameter) for biological materials reflects structural hierarchy.

2. Methods of measurement

For a nonlinear fluid medium, the relation between p, the pressure of the liquid, and ϱ, the density, is nonlinear and can be expressed in a Taylor's series expansion of p about the point of equilibrium density and entropy (ϱ_0, s_0), [2]

$$p = p_{\varrho_0,s_0} + A\frac{(\varrho-\varrho_0)}{\varrho_0} + \frac{1}{2}B\frac{(\varrho-\varrho_0)^2}{\varrho_0^2} + \ldots; \tag{1}$$

$$A = \varrho_0\left(\frac{\partial p}{\partial \varrho}\right)_{\varrho_0,s_0};$$

$$B = \varrho_0\left(\frac{\partial^2 p}{\partial \varrho^2}\right)_{\varrho_0,s_0}.$$

From (1) and from the definition of sound speed,

$$c^2 = \left(\frac{\partial p}{\partial \varrho}\right)_{\varrho_0,s_0}, \tag{2}$$

it is possible to express the ratio of the coefficient of the quadratic term to that of the linear term, B/A, as

$$\frac{B}{A} = 2\varrho_0 c_0\left(\frac{\partial c}{\partial p}\right)_{\varrho_0,s_0}. \tag{3}$$

Equation (3) is the basis for the thermodynamic method for determining B/A, the nonlinear parameter, since ϱ_0, c_0, and $(\partial c/\partial p)_{\varrho_0,s_0}$ are quantities that can be determined experimentally. However, for experimental ease, it is desirable to transform equation (3) using thermodynamic relations and to deal with conditions of constant temperature and pressure, instead of constant entropy. The new expression [1] is

$$\frac{B}{A} = 2\varrho_0 c_0 \left(\frac{\partial c}{\partial p}\right)_{T,s} + \frac{2c_0 T\beta}{C_p}\left(\frac{\partial c}{\partial T}\right)_{p,s}, \tag{4}$$

where T is temperature in degrees Kelvin, p is the pressure, C_p is the heat capacity per unit mass at constant pressure and β is the volume coefficient of thermal expansion. For the materials of interest in this study, the second term in equation (4) is less than 5 per cent as compared to the first term so that the precision required in determining β and C_p is not very stringent. By measuring the change of sound speed with pressure and temperature, together with a knowledge of the density and sound speed and an estimation of the values for β and C_p, the parameter B/A can be determined. Details of the instrumentation and procedures of the technique are described in Ref. [9].

The finite amplitude method involves measurement of the magnitude of the second harmonic component at several distances from the sound source and then extrapolation to the source to eliminate the effect of absorption in the medium. For a medium with near linear frequency dependence of absorption, specifically $(\alpha_2 - 2\alpha_1) < 1/2$, where α_1 and α_2 are, respectively, the absorption coefficients at the fundamental and second harmonic frequencies, the magnitude of the second harmonic component, averaged over a phase sensitive receiver the same size as the source, can be written as

$$p_2(z) = p_0^2(z)\left(\frac{B}{A} + 2\right)\frac{\pi f}{2\varrho_0 c_0^3}\exp\left[-\left(\alpha_1 + \frac{\alpha_2}{2}\right)z\right]F(z), \tag{5}$$

where z is the axial distance from the sound source, f is the frequency of the fundamental, p_0 is the average source pressure at the fundamental frequency, and $F(z)$ is a correction term for the diffraction effect of the finite aperture sound source [5, 6]. Over the range of distances between one and three centimeters from the source, $F(z)$ is an exponentially decreasing function. When $p_2(z)/p_0^2(z)$ is extrapolated exponentially to the source, one may write

$$\left.\frac{p_2(z)}{p_0^2(z)}\right|_{z\to 0} = \left(\frac{B}{A} + 2\right)\frac{\pi f}{2\varrho_0 c_0^3}\left. F(z)\right|_{z\to 0}. \tag{6}$$

For a 1/2″ diameter sound source resonating at 4 MHz, $F(z)|_{z\to 0}$ is 0.91. The value of B/A can then be calculated using equation (6) when $p_2(z)/p_0^2(z)|_{z\to 0}$ and c_0 are measured. Details of the instrumentation for the finite amplitude technique and for sample preparation are described in Ref. [6].

3. Results and discussion

Results of B/A measurements in soft tissues are shown in Table 1. The finite amplitude technique was emphasized in these measurements because of the possibility of extending it to *in vivo* measurements in the future. Tissue samples were obtained from different animals for each of the measurements.

Table 1. B/A value in soft tissues measured by the thermodynamic and the finite amplitude methods

Material	Thermodynamic method	Finite amplitude method
water	5.31	5.5 ± 0.5*
beef liver	7.23, 7.0	7.7 ± 0.9**
pig fat	10.9	11.0, 11.3
beef heart		6.75, 7.4
pig muscle		7.53, 8.1
beef brain		7.6

Entries represent single measurements, except those otherwise labelled.
* Average of seven samples, ** average of five samples

It is observed that B/A values of soft tissues range from about 7 to 8, with the exception of fatty tissues, which have a B/A value of approximately 11. The variations in B/A value for samples of the same tissue type can be as high as ± 10 per cent. It is not clear whether such variation results from differences in B/A values of different specimens, or is caused by artifacts arising from tissue preparation, e.g., phase cancellation induced by inhomogeneities in the tissues, or air bubbles resulting from autolysis after excision.

The typical B/A value of a soft tissue is greater than that of a protein solution of the same dry weight content [8], and yet with the exception of fatty tissues, 70 per cent of the dry weight content of the tissues measured are proteins [7]. This observation suggests that besides the protein concentration, other factors exist to contribute to the B/A value of tissues. Based on observations reported previously [6, 8, 9], the structural hierarchy of the material being measured is believed to be one of these factors. The B/A value of blood, which has higher structural hierarchy than a simple protein solution because the hemoglobin solution is contained within a membranous enclosure, has a slightly greater B/A value than a protein solution of the same dry weight content. Whole liver, which is much more complex in structure than blood, has a correspondingly greater B/A value. Homogenization of the liver, which destroys an unspecified portion of the structure, decreases the B/A value.

4. Concluding remarks

It is felt that the knowledge of the nonlinearity of the medium provides information for better understanding of the propagation details of ultrasound in tissues. Further, this should lead to improvements of present diagnostic and therapeutic applications of ultrasound, and may actually provide information about the structure of these media not available through existing means of tissue characterization.

References

[1] R. T. Beyer, *Parameter of nonlinearity in fluids,* J. Acoust. Soc. Am., **32**, 719-721 (1960).

[2] R. T. Beyer, *Nonlinear acoustics,* Naval Ship System Command, Dept. of the Navy, 1974, 91-164.

[3] E. L. Carstensen, W. K. Law, N. D. McKay, T. G. Muir, *Demonstration of nonlinear acoustical effects at biomedical frequencies and intensities,* Ultrasound Med. Biol., **6**, 359-368 (1980).

[4] E. L. Carstensen, A. S. Becroft, W. K. Law, D. B. Barbee, *Finite amplitude effects on the thresholds for lesion production in tissue by unfocused ultrasound,* J. Acoust. Soc. Am., **70**, 302-309 (1981).

[5] W. N. Cobb, *Finite amplitude method for the determination of the acoustic nonlinearity parameter B/A,* J. Acoust. Soc. Am., **73**, 1525-1532 (1983).

[6] F. Dunn, W. K. Law, L. A. Frizzell, *Nonlinear ultrasonic wave propagation in biological materials,* IEEE Ultrasonics Symposium, 1981, 527-532.

[7] S. A. Goss, L. A. Frizzell, F. Dunn, *Dependence of the ultrasonic properties of biological tissue on constituent proteins,* J. Acoust. Soc. Am., **67**, 1041-1044 (1980).

[8] W. K. Law, L. A. Frizzell, F. Dunn, *Ultrasonic determination of the nonlinearity parameter B/A for biological media,* J. Acoust. Soc. Am., **69**, 1210-1212 (1981).

[9] W. K. Law, L. A. Frizzell, F. Dunn, *Comparison of thermodynamic and finite amplitude methods of B/A measurement in biological materials,* J. Acoust. Soc. Am., **74** (1983) (in press).

[10] T. G. Muir, E. L. Carstensen, *Prediction of nonlinear acoustical effects at biomedical frequencies and intensities,* Ultrasound Med. Biol., **6**, 345-357 (1980).