Empirical relationships between acoustic parameters in human soft tissues

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Abstract: Previously published summaries of sound speed, density, attenuation coefficient, and nonlinearity parameter, B/A, in human soft tissues are quantitatively analyzed. A highly significant empirical linear relationship is found to hold between sound speed and density for a wide range of soft tissues, including adipose, parenchymal, muscular, and connective tissues as well as body fluids. Even higher correlations occur between nondimensional parameters describing density variations and compressibility variations. Values for the nonlinearity parameter correlate significantly with sound speed and density, while the attenuation coefficient is found not to correlate significantly with any of the other parameters considered. Implications for tissue modeling and quantitative ultrasonic imaging are discussed.

PACS numbers: 43.80.Cs, 43.80.Qf
Received: October 9, 2000 **Accepted**: November 6, 2000

Introduction

Understanding relationships between acoustic parameters of human soft tissues is important for several reasons, including scientific interest in tissue properties, accuracy in simulation of acoustic propagation in tissues, and effectiveness in design and interpretation of quantitative ultrasonic imaging methods.

Simulations of ultrasonic propagation in tissue require choices for acoustic properties such as sound speed, density, absorption, and nonlinear propagation characteristics. Previous research has resulted in simple empirical relationships between sound speed and density for compact calcified tissues [Lees et al., 1983] and a range of mammalian soft tissues [Aroyan, 1996]. These relationships are useful for tissue modeling; for example, the linear sound speed-density relationship observed by Lees et al. [1983] was used by Mast et al. [1999] to estimate the sound speed of calcified cartilage based on a density measurement. Aroyan [1996] used a similar piecewise-linear relationship to obtain three-dimensional maps of sound velocity in dolphin tissue, based on density maps estimated from computed tomography image data. To the extent possible, corresponding relationships between attenuation, nonlinearity parameter, and other acoustic parameters would also be useful for construction of tissue models.

Quantitative ultrasonic imaging methods such as diffraction tomography [Mast, 1999 and references therein] provide images of intrinsic tissue properties such as sound speed, density, compressibility, and absorption. The diagnostic efficacy and utility of such methods would be improved by a greater knowledge of the relationships between tissue parameters. For instance, if two parameters, such as sound speed and density, are highly correlated with one another for all tissue structures in the human body, measurement or imaging of both parameters will be of little diagnostic value. Analysis of correlation between tissue parameters would allow ultrasonic imaging methods to be designed for maximum diagnostic information content.

Tissue Properties

Reference sound speed, mass density, attenuation, and nonlinearity properties for a variety of human soft tissues were compiled from three secondary sources, each of which drew on many

Table 1: Sound speed, density, attenuation, and nonlinearity parameter values used for analysis. Sources: [1]Mast et al., 1997, [2]ICRU Report 61, 1998, [3]Duck, 1990.

Tissue Type	Speed (mm/μs)	Density (g/cm^3)	Atten. Coef. @ 1 MHz (dB/cm)	Nonlin. Param. (B/A)
Connective[1]	1.613	1.120	1.57	—
Muscle[1]	1.547	1.050	1.09	—
Fat[1]	1.478	0.950	0.48	—
Adipose[2]	1.450	0.950	0.29	10.0
Blood[2]	1.584	1.060	0.20	6.1
Brain[2]	1.560	1.040	0.60	7.1
Breast[2]	1.510	1.020	0.75	—
Eye: lens[2]	1.645	1.070	0.80	—
Eye: vitreous[2]	1.528	1.010	0.1	—
Kidney[2]	1.560	1.050	1.0	7.4
Liver[2]	1.595	1.060	0.50	6.6
Muscle, cardiac[2]	1.576	1.060	0.52	7.1
Muscle, skeletal[2]	1.580	1.050	0.74	6.6
Skin[2]	1.615	1.090	0.35	7.9
Fatty[2]	1.465	0.985	0.40	8.5
Non-fatty[2]	1.575	1.055	0.60	7.0
Blood cells[3]	1.627	1.093	0.28	—
Blood plasma[3]	1.543	1.027	0.069	—
Eye: cornea[3]	1.586	1.076	—	—
Spinal cord[3]	1.542	1.038	—	—
Spleen[3]	1.567	1.054	0.4	7.8
Testis[3]	1.595	1.044	0.17	—
Mean	1.561	1.043	0.54	7.5
St. Dev.	0.051	0.042	0.37	1.1

previously published measurements. Reference values for fat, muscle, and connective tissue were obtained from Mast et al. [1997], which summarized data from Goss et al. [1978; 1980b], and Woodard and White [1986]. Attenuation coefficients reported there were extrapolated to 1 MHz values assuming linear frequency dependence. Reference values for nine soft tissue types (adipose tissue, whole blood, brain, breast, liver, skeletal muscle, skin, “average” fatty soft tissue, and “average” non-fatty soft tissue), as well as for four specific tissues (kidney, cardiac muscle, eye—lens, and eye—vitreous), were taken from ICRU Report 61 [1998]. For the latter four tissues, values used here are means of the upper and lower limits presented in the report.

Parameters for five additional human soft tissues, not addressed in the above summaries, were compiled from values given by Duck [1990]. In all cases, only values measured on human tissues were employed. Sound speed values employed were only those measured at body temperature (37° C) or *in vivo*. When more than one listed sound speed measurement met those criteria, all available values for adult human tissue were averaged; when ranges were given, means of the upper and lower limits were taken. Density values were taken to be the mean of mass density ranges given by Duck. Attenuation coefficients, when necessary, were extrapolated to 1 MHz assuming a linear dependence of attenuation on ultrasonic frequency.

The compiled sound speed, density, attenuation, and nonlinearity parameter data are listed in Table I.

In addition to the four acoustic properties listed in Table I, two other parameters of particular interest are the compressibility variation γ_κ and the density variation γ_ρ, defined as

$$\gamma_\kappa \equiv \frac{\rho_0 c_0^2}{\rho c^2} - 1, \quad \gamma_\rho \equiv 1 - \frac{\rho_0}{\rho}, \tag{1}$$

where c and ρ are local values of sound speed and density, and c_0 and ρ_0 are reference values, taken here to be the mean sound speed and density values from Table I. These parameters are

 1529-7853/00/1(1)/37/6/$17.00

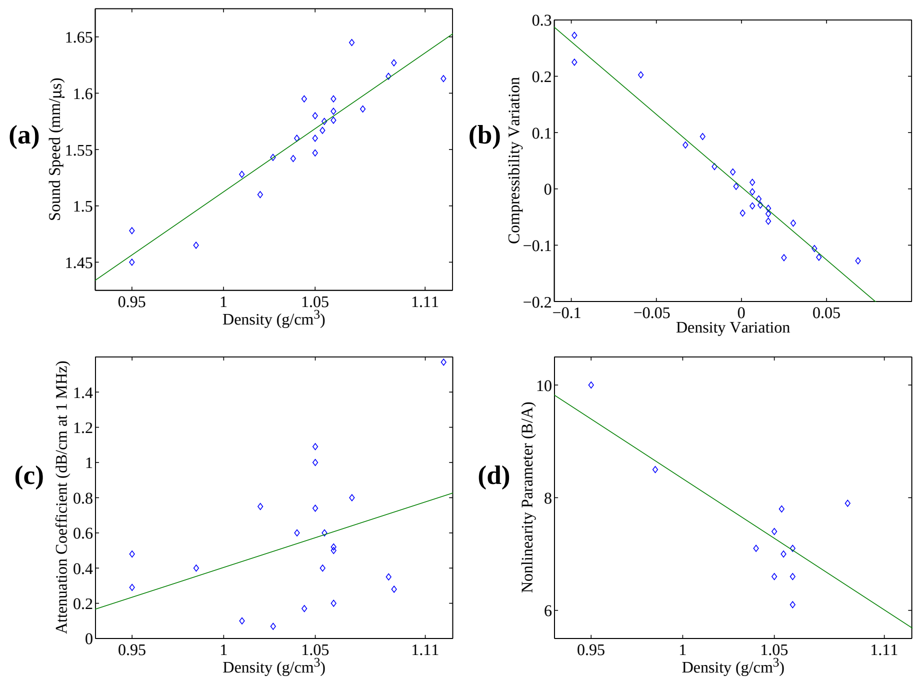

Figure 1: Pairs of acoustic properties for human soft tissues, plotted with corresponding lines of best fit.

convenient for scattering analyses. For example, the far-field pattern of fixed-frequency acoustic scattering from a fluid medium, under the Born approximation, is described by the equation [Morse and Ingard, 1968]

$$\Phi(\mathbf{I}-\mathbf{O}) = \frac{k^2}{4\pi}\int_V \Big(\gamma_\kappa(\mathbf{r}_0) + \gamma_\rho(\mathbf{r}_0)\,\cos\vartheta\Big)\, e^{i(\mathbf{I}-\mathbf{O})\cdot\mathbf{r}_0}\, dV_0, \tag{2}$$

where **I** and **O** are vectors with magnitudes equal to the wavenumber k and directions equal to the propagation direction of the incident wave and the measurement direction of the scattered wave, respectively, and ϑ is the angle between the vectors **I** and **O**. Many quantitative acoustic imaging methods have been devised to separately map γ_κ and γ_ρ or closely related quantities [*e.g.*, Devaney, 1985; Witten et al., 1988; Mensah and Lefebvre, 1997].

Empirical Relationships

In order to quantitatively analyze relationships between the four abovementioned parameters for human soft tissues, linear regression analysis was performed on all of the summary data listed in Table I. A regression between the nondimensional compressibility variation γ_κ and density variation γ_ρ was also performed. In each case, linear relationships of the form

$$y = (mx + b) \pm \sigma \tag{3}$$

were obtained, where m is the slope, b is the intercept, and the standard deviation σ is computed from the difference between the measured parameters and the line of least-squares fit. To assess the significance of each correlation, the Pearson correlation coefficient r (bounded between -1 and 1) and the corresponding p-values (*i.e.*, the probability of a correlation coefficient with magnitude equal to or greater than r occurring by chance [Bevington, 1969]) were also computed. A typical significance criterion is, for instance, $p < 0.05$.

Values from Table I are plotted in Fig 1 for four parameter pairs, together with the corresponding least-squares linear fit from Eq. (3). The correlation coefficients and p-values in Table I, as well as the corresponding plots in Fig. 1, provide clear indications of correlations

Table 2: Results of least-squares linear regressions between acoustic properties of human soft tissue.

Acoustic Properties	Slope m	Intercept b	Correlation Coefficient	St. Dev. σ	p-value
(c, ρ)	1.12	0.391	0.917	0.0203	2.03×10^{-9}
(α, ρ)	3.38	−2.98	0.393	0.341	0.0869
$(B/A, \rho)$	−21.18	29.52	−0.771	0.687	5.47×10^{-3}
(α, c)	1.50	−1.80	0.214	0.362	0.364
$(B/A, c)$	−16.58	33.28	−0.795	0.654	3.44×10^{-3}
$(\alpha, B/A)$	−0.0563	0.929	−0.271	0.216	0.421
$(\gamma_\kappa, \gamma_\rho)$	−2.58	0.00313	−0.972	0.0260	5.61×10^{-14}

between acoustic properties of human soft tissues. As seen in Fig. 1(a), sound speed and density are closely correlated for human soft tissues ($r = 0.9168$, $p = 2.03 \times 10^{-9}$). The corresponding nondimensional parameters γ_κ and γ_ρ are correlated even more closely ($r = 0.9715$, $p = 5.61 \times 10^{-14}$). The nonlinearity parameter B/A correlates significantly with the sound speed and density ($p = 3.44 \times 10^{-3}$ and 5.47×10^{-3}, respectively) but not with the attenuation coefficient ($p = 0.421$). The attenuation coefficient does not correlate highly with any of the other parameters considered, although its correlation with mass density might be considered marginally significant ($p = 0.0869$).

Discussion

An obvious question is the physical cause of the empirical linear relationships shown here to exist between acoustic parameters in human soft tissues. These relationships are not physically fundamental to propagation in fluid or solid media. The most likely causes of the nearly linear relationship between sound speed and density are the relative proportions of tissue constituents such as proteins, lipids, and water. Since the bulk acoustic properties of tissue are fairly well-characterized by mixture laws [Apfel, 1986; Sehgal et al., 1986; Hachiya and Ohtsuke, 1994], it seems reasonable to conclude that the present empirical linear relationships relate straightforwardly to tissue composition. Proteins such as collagen have a sound speed and density higher than water [Goss and Dunn, 1980], so that tissues with higher concentrations of collagen and other proteins have relatively higher density and sound speed [O'Brien, 1977; Goss et al., 1980a; Olerud et al., 1990]. Similarly, lipids have lower sound speeds and density than water, so that tissues with greater fat content have relatively lower sound speeds and densities.

For the limited data set available, the present study shows that the nonlinearity parameter B/A is significantly correlated with the sound speed and density of tissue. This relationship is consistent with previous results showing that the nonlinearity parameter can also be predicted using mixture laws [Apfel, 1986; Sehgal et al., 1986]. The weakly linear (marginally significant) relationship between attenuation coefficient and density found here is also consistent with a previous study, which showed that in canine skin and wound tissue the correlation between attenuation coefficient and collagen content was substantially smaller than the correlation between sound speed and collagen content [Olerud et al., 1990].

In modeling soft tissues, one may be concerned with point-to-point variations within tissues, as well as bulk properties of individual tissue types. The present study does not present direct evidence that the acoustic properties considered are linearly related except as bulk properties. However, any local variations in soft tissue properties are likely to be primarily caused by local variations in tissue composition, which should cause corresponding sound speed and density variations similar to those for bulk tissue. Likewise, acoustic parameters of other soft tissues, such as malignant tumors, may be expected to follow similar empirical relationships.

The results presented here should be useful for computational modeling of acoustic propagation in human soft tissues. For example, Borup et al. [1992] obtained model maps of tissue structure by processing two-dimensional x-ray computed tomography and magnetic resonance images of a human torsos, assigning values of a sound speed contrast function based on an assumed linear relationship to the image gray level. The empirical linear relationships between the parameters presented here in Table II could be employed to assign density variations, nonlinearity parameter variations, and absorption values consistent with those sound speed variations, thus resulting in a more realistic model.

In addition, sound speed can be difficult to measure accurately for certain small or fragile tissue structures, such as the thin septa that separate fat lobules within adipose tissue. However, density of any tissue structure can easily be determined *in vitro* using Archimedes' principle. The empirical relationships given here, like those presented by Lees et al. [1983] for calcified tissues, allow estimates of sound speed to be obtained from measurements of density.

Finally, the present results have implications for development of quantitative ultrasonic imaging methods. First, inversions yielding acoustic parameters such as the sound speed variation $c^2/c_0^2 - 1$ (which is nearly equal to $\gamma_\kappa + \gamma_\rho$) [*e.g.*, Borup et al., 1992; Mast, 1999] or the reflectivity function $\gamma_\kappa - \gamma_\rho$ [*e.g.*, Norton and Linzer, 1980; Mensah and Lefebvre, 1997] can be employed to obtain maps of more intuitive quantities such as the density and compressibility. Second, the results suggest that for human soft tissues little additional information may be gained by techniques that independently image density variations and compressibility variations. The high correlation coefficient found here between γ_κ and γ_ρ implies that separate images of compressibility and density variations in soft tissue should be expected to be highly correlated. Similarly, separate images of sound speed and density may provide little additional information compared to either individual image. This conclusion is consistent with experimental results in which sound speed and density images of excised breast cross sections have been found to be qualitatively similar and significantly correlated [Yang et al., 1991].

Additional information for quantitative images could come in several forms. One possibility is quantitative imaging of the nonlinear parameter B/A [*e.g.*, Cain, 1986; Burov et al., 1994]; however, the significant correlations found here between nonlinearity parameter, sound speed, and mass density suggest that images of the nonlinearity parameter may provide limited additional information relative to that obtained from sound speed or density mapping. Still, since the nonlinearity parameter was only available for eleven of the data points considered here, further study would be required to definitively assess correlations between B/A and other acoustic parameters of soft tissues.

The low correlation results between absorption and the other three parameters considered imply that multiple-parameter images including absorption maps [*e.g.*, Greenleaf and Bahn, 1981; Witten et al., 1988] may provide significant additional information beyond that obtained from maps of other parameters alone. However, because of the wide range of absorption values reported in the literature for most tissue types [Duck, 1990], the ultimate diagnostic value of quantitative absorption imaging cannot be assessed based on the data considered here. Still, the present results suggest that quantitative imaging techniques yielding maps of ultrasonic absorption as well as sound speed, density, or nonlinearity parameter are worthy of further study for medical diagnosis.

Acknowledgment

This research was funded by the Breast Cancer Research Program of the U.S. Army Medical Research and Materiel Command, under Grant No. DAMD17-98-1-8141.

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