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THE RELATIONSHIP BETWEEN COLLAGEN AND ULTRASONIC ATTENUATION AND VELOCITY IN TISSUE

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It is suggested that the biological macromolecule collagen, a structural protein, strongly affects the ultrasonic propagation properties in biological material. Collagen is the most abundant single protein in the animal kingdom, comprising approximately thirty percent of the total protein in the human body and, therefore, about six percent of the total body weight. A comparison from the literature of the ultrasonic propagation properties of attenuation and velocity to the tissue properties of water, total protein and, specifically, collagen has been accomplished.

INTRODUCTION

The complete specification of the ultrasonic wave properties of a medium require knowledge of the inertial, restoring and lost parameters as functions of the state, wave and material variables.. For an infinitesimal ultrasonic wave propagating in an isotropic, unbounded liquid-like medium, these become, respectively, the density, an elastic parameter such as the adiabatic compressibility, and the attenuation. The inertial and restoring parameters are embodied in the velocity and impedance parameters. The attenuation parameter includes the absorption of the ultrasonic energy into heat in addition to all other mechanisms by which energy is extracted from the wave process or redirected at material inhomogeneities. Knowledge of the ultrasonic velocity and attenuation as a function of acoustic and state variables, position, tissue and the state of tissue are all important for not only the elucidation of the mechanisms responsible for the interaction of ultrasound with tissue but also for a more quantitative interpretation of clinical diagnostic ultrasonic data.

The following comprises a brief review of the experimental data available for the ultrasonic propagation properties of tissue and represents a comparison of literature values of the ultrasonic attenuation and velocity properties of tissue to the properties of water, protein and collagen. Table I lists the ultrasonic attenuation at ultrasonic frequencies of 1, 3 and 5 MHz and velocity for the indicated biological materials. Table II lists the water, total protein and collagen content of the materials detailed in Table I. In those cases where blanks exist, the information was either not available or could not be found.

ROLE OF COLLAGEN

Collagen is closely associated in connective tissue of vertebrates. It turns out, in fact, that collagen is the most abundant single protein in the human body and the most common protein in the entire animal kingdom. Collagen comprises somewhere between one-quarter and one-third of the total protein in the human body and therefore about six percent of the total body weight [68]. It is more than the prevalence of collagen in the body, however, which fosters interest in its acoustical properties. There is some evidence to suggest that it is the elastic properties of most soft tissues, determined primarily by the content of collagen and other structural proteins, which define acoustic contrast during echographic visualization [74, 75]. This hypothesis is based on the fact that the static or low-frequency elastic modulus of collagenous fibers is at least 1000 times greater than those of soft tissues. Since the ultrasonic velocity is proportional to the square root of the elastic modulus, collagenous tissues are thought to introduce a greater impedance mismatch than would be the case for a soft tissue interface of similar elastic modulus, thereby increasing the acoustic reflectivity of soft-collagenous tissue boundaries.

In the mid 1950's the ultrasonic propagation properties of articular tissue were examined [2, 3] and it was concluded that tissues with higher collagen content exhibited higher values of ultrasonic attenuation and velocity, for the most part, as compared to soft tissue with lesser amounts of collagen. These authors also suggested that aging of dense fibrose tissue is accompanied by an increase in the ultrasonic attenuation.

Greenleaf and his colleagues [76, 77] have shown in excised, unfixed breast specimens at room temperature, that fat yields the lowest attenuation and lowest velocity compared to all other surrounding tissue. Additional relative comparisons of the ultrasonic propagation properties of breast showed the following: normal parenchymal breast tissue exhibited relatively high attenuation and medium high velocity, infiltrating medullary carcinoma exhibited an attenuation between fat and normal breast tissue and a high velocity, and connective tissue associated with muscle boundaries of a scirrhous carcinoma clearly exhibited the highest attenuation and velocity.

Johnston and Dunn [78] developed a model to describe the transmission of ultrasonic energy into the brain, through the meninges from physiological saline. The meninges consists of the three membranes which envelop the brain, viz., the outer dura mater, the intermediate arachnoid and the pia mater. The model assumed was a three layer transmission model with the brain and the physiological saline assumed to possess the same impedance. In order for the model then to fit the transmission data as a function of frequency, the intermediate layer was assigned a thickness of 250 μm and a speed of sound of 1800 m/s, 300 m/s greater than the other two media. An examination of Table I indicates that such a high velocity would correspond to a very high collagen content material which, in fact, the meninges is.

Articular capsule, skin, cartilage and tendon typically have collagen contents in the range from 10 to 35 percent wet weight. This is at least a factor of five greater than the other materials listed in the two tables, with the exception of bone and lung. It is unmistakable that the high collagen content materials exhibit a greater attenuation than the low collagen content materials. Further examination of the data of Tables I and II suggests a quantitative relationship between the ultrasonic propagation properties of attenuation and velocity and the tissue constituent collagen can be developed. Figure 1 represents a summary from the literature of the ultrasonic attenuation at a frequency of 1 MHz as a function of the wet weight percentage of collagen for thirteen biological materials. The range of data for a particular tissue represents the maximum values reported for attenuation and for collagen content.

The data can be grouped into three relative categories, viz., low collagen content and low attenuation, medium collagen content and medium attenuation, and high collagen content and high attenuation. Further, a mathematical relationship between the ultrasonic attenuation and the percentage of tissue collagen has been derived using linear regression by the method of least squares. Assuming the relationship can be described by a power function, to a first approximation (omitting bone and lung)

TABLE I

Ultrasonic Attenuation and Velocity for Various Biological Materials

BIOLOGICAL MATERIAL	ATTENUATION (cm^{-1}) @ 1 MHz	@ 3 MHz	@ 5 MHz	VELOCITY (m/s)
Amniotic Fluid[1]	0.0008	0.0036	0.0078	1510[1]
Articular Capsule[2,3]	0.38	0.81	1.29	
Aqueous Humor[4-6]	0.01-0.017(E)	0.033-0.044(E)	0.06-0.07(E)	1481-1530[4,6]
Blood[7,8]	0.023	0.087	0.16	1550-1571[8-10]
Bone - Skull[11-14]	1.5-2.2	8-20		2920-3360[11,14,15]
- Long[3,15,16]	1.4	1.5-6		3160-4360[16-18]
				1390-1970(S)[17]
Brain - Human[19-22]	0.074-0.23	0.29-0.69	0.58-1.38	
- Animal[19,23-27]	0.032-0.11	0.12-0.43	0.28-0.54	1506-1580[27-29]
Cartilage[2,3]	0.58	1.44	2.19	1665[2,3]
CSF[13]	0.0012			1499-1515[9]
Fat[2,3,19,30-35]	0.044-0.090	0.076-0.46	0.14-1.0	1410-1479[2,3,29,31]
				1438-1602(OF)[34]
Heart[24,37-39]	0.09-0.24	0.16-0.64	0.36-0.87	1570-1585[29,40]
Kidney[24,37,41,42]	0.09-0.12	0.28-0.35	0.5-0.6(E)	1558-1568[28,29,40]
Lens[4,5,43]	0.1-0.2(E)	0.6-0.7	0.7-1.1	1500-1680[4,6]
Liver[2,19,24,33,37,42,44-47]	0.074-0.15	0.19-0.50	0.35-0.79	1553-1607[28,29,40]
Lung[3,48-50]	3.5-5.0	3.6-8.8	6.0-11.6	300-1118[48,49,51]
Milk - Whole (10 °C)[45,52]	0.04-0.042	0.12-0.14	0.20-0.26	1480-1485[45,52]

TABLE I (cont.)

Plasma[7,19]	0.01-0.02	0.03-0.06	0.067-0.10	1571[10]
Skin[2,3]	0.14-0.66	0.3-1.2(I)	0.43-1.7	1498[2,3]
Spinal Cord - Neonate[53,54]	0.09-0.13			
Spleen[33]	0.06	0.23	0.46	1515-1591[28,29,40]
Striated Muscle[30,42]	0.12(I)			1568-1595[29]
- Against Grain[3,19,34]	0.064-0.15	0.22-0.30	0.40-0.70	1545-1631[28,34,36,40]
- With Grain[3,19,34]	0.16-0.20	0.44-0.56	0.70-1.4	1585-1603[28,40]
Tendon				
- Against Grain[2,3]	0.54-0.73	1.25-1.88	1.95-2.86	1750[2]
- With Grain[2,3]	0.41-0.58	1.37	2.35	
Testis[55]	0.019	0.040	0.040	
Tongue				
- Against Grain[37]	0.29	0.87	1.5	
- With Grain[37]	0.14	0.42	0.70	
Vitreous Humor[4,5]	0.010-0.017(E)	0.033-0.044(E)	0.06-0.07(E)	1490-1544[4,6]
Water (20-40 ^{o}C)[56]	0.0001-0.0003	0.0013-0.0023	0.0037-0.0063	1483-1529[57]

References in left column refer to attenuation parameters

E - Extrapolated, I - Interpolated, S - Shear, OF - Orbital fat

TABLE II

Water, Total Protein and Collagen Content for Various Tissues

BIOLOGICAL MATERIAL	WATER (Percentage)	TOTAL PROTEIN (Percentage) Wet	TOTAL PROTEIN (Percentage) Dry	COLLAGEN (Percentage) Wet	COLLAGEN (Percentage) Dry
Amniotic Fluid	96.5-98.5[1,58]	0.26-0.27[1,58]			
Articular Capsule	70-73[59,60]	(20-25)	75-83[60]	10-20[61] (12-21)	46-70[60]
Aqueous Humor	99.0-99.9[58,62]	0.01-1[58,62]			
Blood	74-83[58,63]	12-18[64,65]			
Bone	22-34[60,63,66]	(13-20)	20-26[60]	(13-20)	20-26[60]
Brain	72-85[58,63,67]	10.4[67] (6-11)	40[68]	(0.03-0.34)	0.22-1.22[60]
Cartilage	70-73[59,60]	(20-25)	75-83[60]	10-20[61] (12-21)	46-70[60]
CSF	99[58]	0.015-0.040[58,68]			
Fat	10-35[63,66,67]	3.2-17[67,69]			
Heart	63-79.2[63,67]	15-19[67]		(0.40-2.6)	1.9-7.0[60]
Kidney	75.9-82.7[63,67]	15.4-16.8[67]		0.39-1.47[60] (0.31-1.28)	1.8-5.3[60]
Lens	63-69[62,70]	25-36[62,68,70]			
Liver	66.9-72.2[63,67]	16.5-21.2[67]		0.2[60] (0.18-1.1)	0.64-3.9[60]
Lung	76.7-79.0[63,67]	16.8-19.3[67]		(1.8-2.4)	8.6-10.3[60]
Milk - Whole	87-88[67,68]	3-4[67,68]			
Plasma	90-95[57,58,66,68]	5.4-8.0[7,57,64,66,68]			

TABLE II (Cont.)

Skin	72[63]	(17-28)		18.6-27.5[60] (17-22)	63-80[60,61,72]
Spinal Cord - Neonate	82[58]				
Spleen	74.4-77.4[63,67]	17.1-18.8[67]		(0.5-1.2)	2.4-4.8[60]
Striated Muscle	63-75.7[63,67]	17.3-21.8[67]		2[60] (0.4-3.1)	1.7-12.7[60]
Tendon	62.9[60]	34.7[60] (22-35)		30-31.6[60,71] (22-35)	60-95[60]
Testis	84-85[72,73]	(9-11)	65-70[73]		
Tongue	61-74.3[67]	13.7-18.5[67]			
Vitreous Humor	99.0-99.7[58,60-62]	0.021-0.25[58,62,70]		0.01-0.067[58,60,61;70]	
Water	100				

Parentheses indicate calculated values

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$$A = 0.11\, C^{0.51} \qquad (1)$$

where A is the ultrasonic attenuation in cm^{-1} and C is the wet weight percentage of collagen. The best fit parameter, the coefficient of determination, r^2 yielded a value of 0.93 (unity represents a perfect fit). Equation (1) is represented on Figure 1 by the solid straight line. Logarithmic, exponential and linear functions were also analyzed but yielded worse fits than Equation (1).

Similarly, to a first approximation, the ultrasonic velocity was examined as a function of collagen content for nine materials (excluding bone, lung and skin) and yielded the expression

$$v = 1588 + 32 \ln C \qquad (2)$$

where v is the ultrasonic velocity in m/s and $r^2 = 0.84$.

Thus, to a first approximation, there appears to be a correlation between the ultrasonic propagation properties and the collagen content of tissue. There are, of course, other tissue properties which similarly need to be analyzed before conclusions can be drawn but this quantitative approach appears to suggest that specific tissue properties may be, at least, partially responsible for affecting the ultrasonic propagation properties of tissue.

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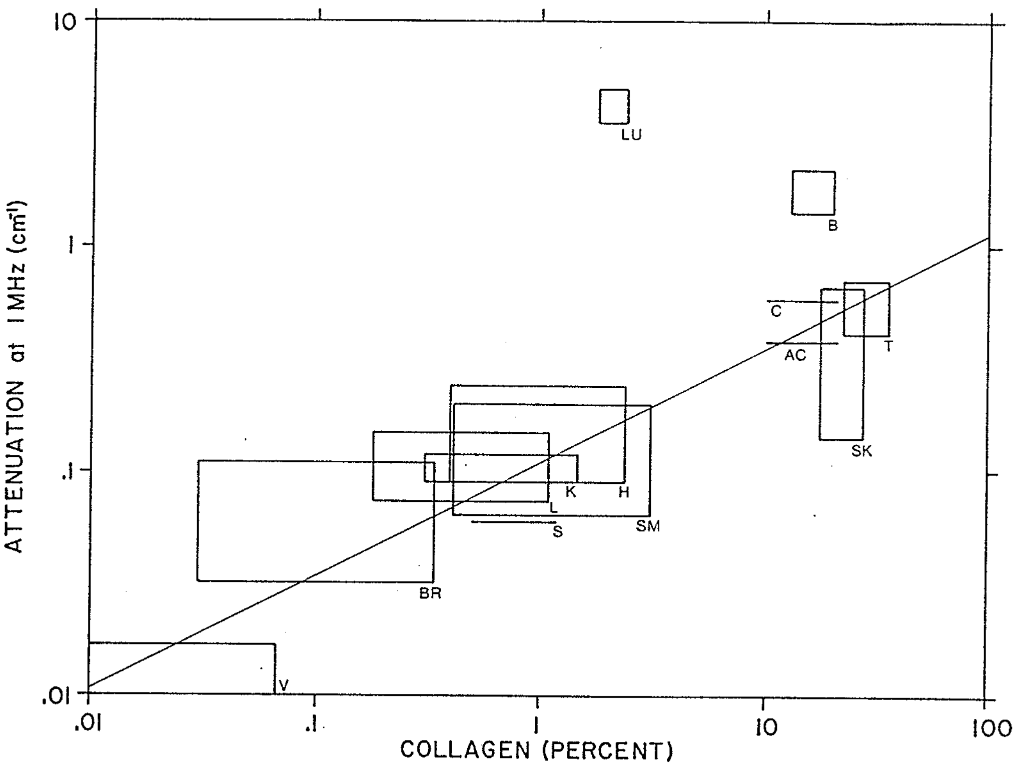

Figure 1 Graphical summary of ultrasonic attenuation at 1 MHz versus wet weight percentage of collagen for thirteen biological materials. The solid line represents equation (1). AC-Articular Capsule, B-Bone, BR-Brain, C-Cartilage, H-Heart, K-Kidney, L-Liver, LU-Lung, SK-Skin, S-Spleen, SM-Striated Muscle, T-Tendon, V-Vitreous humor.