

A pulsed Doppler ultrasonic system for making noninvasive measurements of the mechanical properties of soft tissue

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Abstract—In response to the need for a more precise means of predicting the interaction of a prosthetic socket with an amputee's residual limb, a gated Doppler ultrasonic motion sensing system was devised for making noninvasive measurements of the elastic modulus of soft tissue *in vivo*. Ultrasound was chosen for its ability to indicate the viscoelastic behavior of biological materials without damaging tissue. The system consists of a holding jig to support the limb being tested, a tissue vibrator, and an ultrasonic transducer to monitor the motion of the tissue. The ultrasonic transducer is controlled by an external computer to control the depth at which the sensor is measuring tissue displacement. This ultrasonic measuring technique provides as much information as more conventional techniques, but with more convenience and fewer restrictions.

INTRODUCTION

The mechanical properties of most engineering materials can be characterized quite precisely, but the mechanical properties of biologic materials have not yet been reduced to precise tables. Unlike traditional engineering materials, living matter is dynamic, its mechanical properties are functions of variables such as age, diet, disease, and heredity, and it tends to challenge our current ability to tabulate meaningful information. Consequently, while there is a vast quantity of data on the properties of various tissue systems (12), these average values do not provide the precise insight that is needed to predict the interaction of a prosthetic socket with an amputee's residual limb.

Although no characterization has predicted accurately the reactions of a material to all possible loading conditions, a number of models have been developed that are particularly useful in describing the behavior of materials under common conditions of stress; among these is linear viscoelasticity. Linear viscoelasticity theory has proven to be a useful basis for numerous studies of soft tissue behavior, particularly in the field of muscle mechanics. (1,4,6,9,12,13).

Of the numerous techniques that have been developed for interrogating the material under investigation, almost all are invasive and cannot be applied to the study of tissue properties *in vivo*, especially when the tissue of interest is deep under the skin's surface. However, because ultrasound waves are mechanical in nature, they can be used to study the viscoelastic behavior of biological materials without detectable tissue damage.

BACKGROUND

In order to explain how ultrasound can be used effectively to obtain useful information about the mechanical properties of living tissue, it is necessary to present the equations that govern the motions of theoretical particles within the tissue medium. Continuum mechanics provides two fundamental field equations that form the basis for inferring the properties of the tissue (10). The first equation is:

$$\nabla \cdot \rho \dot{\mathbf{u}} = - \dot{\rho} \quad [1]$$

where ρ is the tissue density, \bar{u} is the particle displacement vector, and the over-dot symbol indicates differentiation with respect to time. The second equation is:

$$\bar{f} = \rho\bar{g} + \rho \frac{D\bar{u}}{Dt} = \rho\bar{g} + \rho[\ddot{\bar{u}} + (\dot{\bar{u}} \cdot \nabla)\dot{\bar{u}}] \quad [2]$$

where \bar{f} is the force per unit volume, \bar{g} is the gravitational acceleration and $\frac{D}{Dt}$ is the total derivative.

For convenience in working with these nonlinear equations, the parameters in the equations can be separated into a linear portion, a series of higher order nonlinear terms, and a time and position portion. Then the first-order portion of the continuity equation can be rewritten as:

$$\rho_0 \nabla \cdot \dot{\bar{u}}_i = -\dot{\rho}_i \quad [3]$$

Similarly, Newton's Second Law can be expressed as:

$$\bar{f}_0 = \rho_0\bar{g} \quad [4]$$

$$\bar{f}_1 = \rho_0\ddot{\bar{u}}_1 \quad [5]$$

$$\bar{f}_2 = \rho_0\ddot{\bar{u}}_2 + \rho_0(\dot{\bar{u}}_1 \cdot \nabla)\dot{\bar{u}}_1 - \rho_0(\nabla \cdot \dot{\bar{u}}_1)\dot{\bar{u}}_1 \quad [6]$$

These are exact equations derived from the laws of physics, independent of material properties except for density. To employ these equations to allow acoustic interrogation to measure tissue properties, it is necessary to relate force to displacement using a mathematical model for the material characterization. In the case of linear elastic solid, Hooke's Law is the model and can be expressed as:

$$T_{ij} = E_{ijkl}\varepsilon_{kl} \quad [7]$$

where the element T_{ij} of the stress tensor is defined as the force per unit area acting along the X_i axis on a plane perpendicular to the X_j axis, and the strain tensor ε_{km} is given for linear terms as:

$$\varepsilon_{km} = \frac{1}{2}(u_{k,m} + u_{m,k}) \quad [8]$$

where the “,” subscript is used to represent partial differentiation with respect to the i direction, and summation over repeated “dummy” indices is implied. A similar relationship exists for Newtonian fluids:

$$T_{ij} = V_{ijkl}\dot{\varepsilon}_{kl} \quad [9]$$

where E and V are both fourth-order symmetric tensors relating stress and strain.

From Equations [7], [8], and [9], it can be inferred that:

$$T_{0ij} = E_{ijkl}u_{0k,m} \quad [10]$$

and

$$T_{1ij} = E_{ijkl}u_{k,m} + V_{ijkl}\dot{u}_{k,m} \quad [11]$$

A material that can be represented by Equation [11] is frequently referred to as a Voigt medium [7]. A similar relationship might be postulated for higher order terms, but for the purpose of this discussion it will be assumed that, by keeping the magnitude of the displacements small, the nonlinear terms will be rendered negligible and the acoustic properties will thus be embodied entirely in the first-order linear equations.

So far, it has been assumed that the tensors are constant tensors. While, in the conventional sense, they are treated as such, biological soft tissues are far from conventional, and it is evident that these tensors may well be functions of frequency. In fact, there is no reason not to treat the linear viscoelastic properties of tissues as transfer functions. If λ is defined as the impulse response tensor of a tissue, Equation [11] can be written as:

$$T_{ij} = \lambda_{ijkl} * u_{k,m} \quad [12]$$

where the * is used to denote linear time convolution.

By summing all forces acting on a particle, it is possible to write

$$\rho_i = T_{ij,j} \quad [13]$$

from which the linear wave equation

$$\rho_i\ddot{u}_i = \lambda_{ijkl} * u_{k,mj} \quad [14]$$

can be obtained. Taking the Fourier transform of this equation results in

$$-\rho_0\omega^2 M_i = \Lambda_{ijkl} M_{k,mj} \quad [15]$$

where Λ and M are the transforms of λ and \bar{u} respectively. If one could measure M and $M_{k,mj}$, one

could then (in theory) solve for Λ_{ijkm} ; however, this is a complex task with no clear direct method.

It may also be desirable to use multiple measurements of M and $M_{k,mj}$ under a variety of applied acoustic perturbations to increase the signal-to-noise ratio and therefore the overall accuracy of the measurements. By minimizing the total of the squared errors from all equations over all frequencies, the probability that Equation [15] represents the material under investigation will be maximized [8].

Unless the form of the tensor function Λ is known, it is difficult to solve the system of equations. However, a simple means of providing a solvable form is to assume that Λ can be written as a sum of constant tensors multiplied by basic functions. Then, by separating the variables into real and imaginary parts which are set equal to zero, it is possible to take the partial derivatives. Then, by combining the real and imaginary parts, a set of simultaneous equations can be obtained.

Hence, given a series of measurements u_p and $u_{pk,mj}$ for a variety of acoustic perturbations, and assuming that the material under investigation is well-behaved, the values of the 81N tensor elements can be obtained. Fortunately, Λ is symmetric, so that only 21N unknowns must be found. This number can be further reduced by making additional assumptions about the material. First, though, it is helpful to make specific assumptions about the forms of the basic functions and the forcing functions used.

Any number of basic functions could be used, but one that is particularly useful is that of the power series. Although such basic functions are not necessarily orthogonal and their inverse Fourier transform does not lead directly to a recognizable impulse function, they are simple, they lead to real values of Λ_{ijkm} , and they are compatible with the conventional definitions of elasticity and viscosity.

If the form of the forcing function used to deform the material, and hence \bar{u} , is chosen carefully, the governing equations can be simplified greatly. If one limits the acoustic perturbations to sinusoids of pure frequency, the displacement will be of the form:

$$\bar{u}_p = \bar{X}_p \cos \omega_p t + \bar{Y}_p \sin \omega_p t \quad [16]$$

or

$$\bar{Z}_p = \bar{X}_p + j\bar{Y}_p$$

Solving for Λ then results in the system of equations:

$$\begin{aligned} \Lambda_{iqrst} (-1)^{t-1} \operatorname{Re} [(-j\omega_p)^{n+t-2} Z_{pk,mj} Z_{pr,st}] \\ = \rho_0 \operatorname{Re} [(-j\omega_p)^{n+1} Z_{pk,mj} Z_{pi}] \end{aligned} \quad [17]$$

When the tissue under investigation poses certain properties of symmetry, these equations can be further simplified. For example, in a tissue that possesses three mutually perpendicular planes of symmetry (an orthotropic material), only those terms of Λ_{ijkm} for which $i = j$ and $k = m$, or $i = k$ and $j = m$, and their symmetric equivalents will be non-zero. Thus for orthotropic materials, Equation [17] reduces to 9N equations in 9N unknowns. For isotropic materials, Equation [17] reduces to 2N equations in 2N unknowns and from measurements of \bar{u} , $\nabla \cdot \bar{u}$, and $\nabla^2 \bar{u}$ under conditions of applied sinusoidal acoustic perturbations, the linear viscoelastic constants of a material can be found by solving four linear equations in four unknowns.

The question, then, is how to measure \bar{u} and its gradients. One method is to measure the speed of sound's propagation and its attenuation. This approach is facilitated by assuming that the acoustic wave propagates as an attenuated plane wave.

While it is possible to obtain the values of the viscoelastic constants simply by measuring the speed of sound and the viscous absorption coefficient for both compressional and shear-wave propagation, several difficulties arise when applying this approach. The measurement of shear acoustic velocity and attenuation requires the use of specialized equipment and techniques which require direct contact with the tissue of interest (3). Even if shear effects can be neglected, the distinction between the absorption and scattering components of acoustic attenuation is difficult, and multiple mechanisms are known to contribute to acoustic absorption (2).

Although accurate measurement of compressional wave propagation requires extreme precision, such measurements are practical, and the overall technique could be a useful one. But there could be some question as to the validity of using ultrasonic interrogation to quantify the overall viscoelastic properties of tissues, since measurements made at high frequencies may not accurately reflect the viscoelastic properties of tissues under ordinary dynamic loads. On the other hand, when low frequency acoustic perturbations are used, it becomes impractical to measure the speed of compressional sound, since the wavelength becomes exceedingly

long. At 1 KHz, for example, if one assumes that the speed of sound is similar to that for ultrasound, the wavelength would be on the order of one and one-half meters. Though shear-wave wavelengths would be smaller, it is still obvious that it would be difficult to use bulk properties to describe propagation in most biological specimens at such frequencies. So, other means of measuring values of \bar{u} and its positional derivatives must be investigated.

Ironically, the best answer to this problem involves the use of ultrasound, using it not to directly measure the mechanical properties of tissues but to measure internal displacements which result from the application of an external acoustic perturbation. Although pulse echo ultrasound provides an excellent means of measuring the positions of internal scatterers within a tissue, some pattern recognition is required to measure displacements of these scatterers, and difficulties arise when a scatterer moves outside the path of the interrogation beam. A better technique involves the use of ultrasonic Doppler methodologies to measure actual tissue flow in the

presence of the acoustic perturbation. This has the advantage of not requiring any pattern recognition, and direction components can be obtained through triangulation. Further, by using pulsed Doppler techniques, tissue scatterer velocities can be determined within a small volume, so that the positional derivatives can be obtained.

One can then conceptualize the construction of a device which could simultaneously apply an acoustic perturbation while measuring the induced tissue flow. This device would make use of a vibrating head that had several ultrasonic transducers embedded in it. Transducers could be used to triangulate tissue particle velocities at various locations. A minimum of 12 transducers making 27 measurements would be required to fully characterize the viscoelastic motion at any given depth, but by restricting the motion of the head to combinations of pure compression and pure longitudinal shear, and by assuming that the tissues can be idealized as isotropic, this can be reduced to 3 transducers making 8 measurements, as illustrated in Figures 1a and 1b.

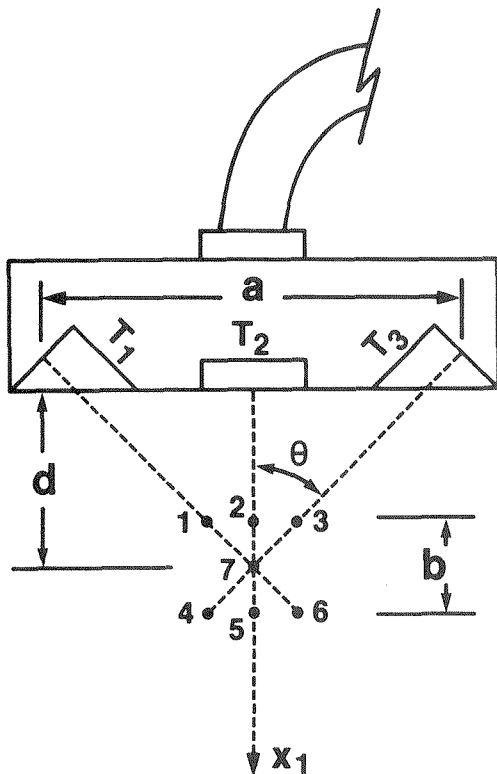


Figure 1a
Schematic of an Ultrasonic Transducer to Measure the Properties of Soft Tissue.

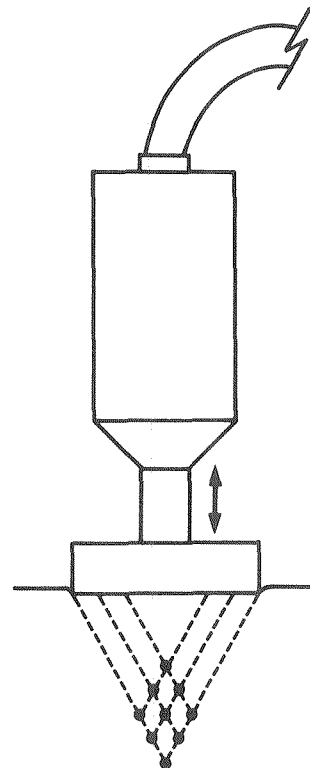


Figure 1b
A Simplified Ultrasonic Transducer.

For an individual measurement, one need only obtain the components of the displacement phasor and three of its positional second derivatives. When this is done, the governing equations become:

$$\begin{aligned}\nabla_1 \nabla \cdot \bar{Z}_p &= (1 - 2\nu)Z_{p1,11} \\ &= (1 - 2\nu)(X_{p1,11} + jY_{p1,11})\end{aligned}\quad [18]$$

$$\begin{aligned}\nabla_2 \nabla \cdot \bar{Z}_p &= \nabla_3 \nabla \cdot \bar{Z}_p \\ &= \nabla^2 \bar{Z}_{p2} = \nabla^2 \bar{Z}_{p3} = 0\end{aligned}\quad [19]$$

$$\nabla^2 \bar{Z}_{p1} = Z_{p1,11} = X_{p1,11} + jY_{p1,11}\quad [20]$$

where ν is Poisson's ratio relating lateral to longitudinal strain under the conditions of pure compressional stress. From this, the expressions for the material properties are found to be approximately:

$$E = -3\rho_0\omega_p^2(X_{p1,11}X_{p1})/2(X_{p1,11}^2 + Y_{p1,11}^2)\quad [21]$$

and

$$\eta = \frac{-\rho_0\omega_p(X_{p1}Y_{p1,11} - Y_{p1}X_{p1,11})}{(X_{p1,11}^2 + Y_{p1,11}^2)}\quad [22]$$

where E is the elastic modulus and η is the shear viscous coefficient.

METHODOLOGY

This theoretical base has been used to develop a gated ultrasonic Doppler motion-sensing system to measure the elastic modulus of soft tissue *in vivo*.

Figure 2 illustrates the ultrasonic sensor that was employed to characterize the modulus of the soft tissue in the forearm or leg of a series of six volunteer subjects. The system consists of three major components. The first is a holding jig to support the limb that is being tested. The jig is capable of being adjusted while holding the tissue firmly during the data acquisition. The second component of the system is the tissue vibrator. The vibrator consists of a high-torque, low-speed DC motor that is attached to a linkage so that the amplitude of the vibrator can be adjusted for maximum effect. The motor includes a tachometer to measure the frequency of vibration to an accuracy of ± 0.002 Hz.

The final part of the system is the ultrasonic transducer used to monitor the motion of the tissue. This transducer produces tone bursts with a duration of 0.4 microseconds, which emanate from a disk that is 4 mm in diameter. Using this technique, the ultrasonic signal is not used to excite the tissue but it is used as a means of determining the motion gradient that results when the tissue is vibrated at

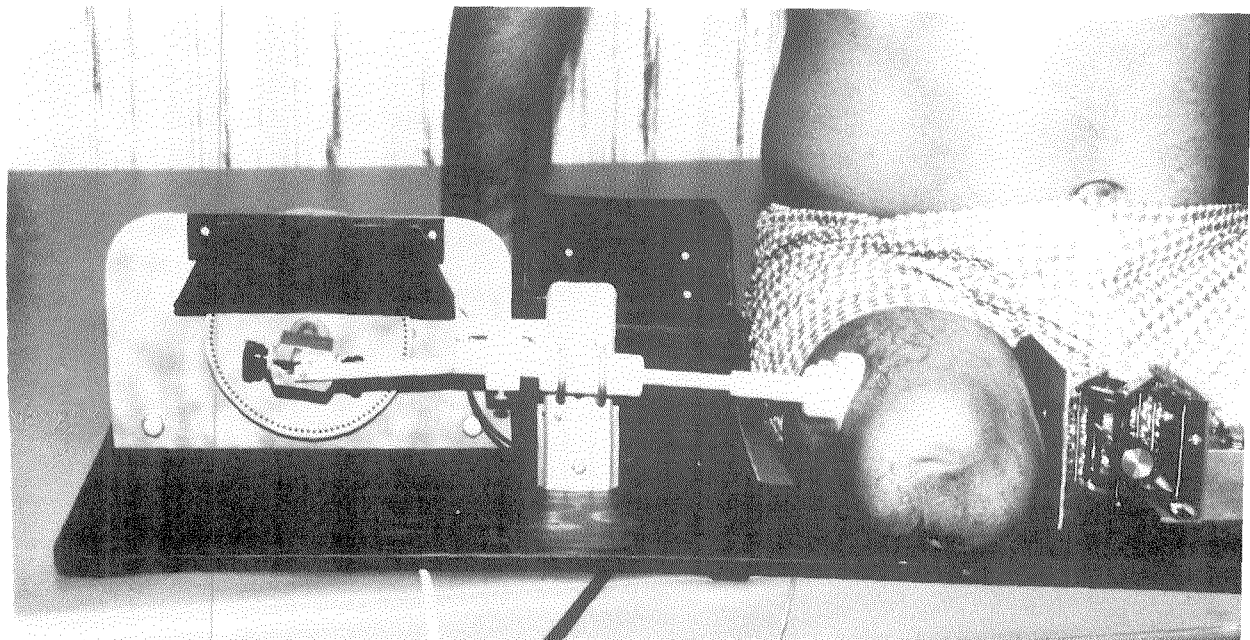


Figure 2
Ultrasonic sensor used to characterize modulus of soft tissue.

much lower frequencies, e.g., subsonic frequencies. The ultrasonic transducer is controlled by an external computer, an Apple IIe, to control the depth at which the ultrasonic sensor is measuring the tissue displacement.

The computer also provides a convenient way for the investigator to select the regions of tissue that are to be characterized and it provides for real-time data analysis so that spurious data points can be ignored and replaced with new data. To accomplish this task, two A/D channels and one D/A channel are used. The D/A channel provides the mechanism to increment the depth at which the tissue motion is being monitored. The first A/D channel is connected to the depth output of the ultrasonic sensor and is used to quantify the sampling depth. The second A/D channel provides data about instantaneous tissue displacements.

The algorithm for collecting the data consists of two programs that run concurrently. The first program is an interrupt-driven machine language routine that can provide an interrupt every 100 milliseconds. This program is used to detect the endpoints of the tissue motion. At time intervals defined by one-half the period of the subsonic perturbation and the elapsed time since the last maximum or minimum peak in the displacement, the program searches for a new peak in the tissue motion. The second program is written in Basic; it averages several displacements for each depth setting. When a peak value has been identified, it is compared to the running average. If the difference between these two numbers is less than a preset value, typically 1 percent, the peak-to-peak displacement value at that depth is recorded. If the difference is greater than the allowable difference, the fourth value is averaged into the previous set and a new value is identified and compared to the average. If this procedure is repeated five times without success, the depth is incremented and new data are processed. The program keeps in memory the locations of missing data so that when the modulus is calculated, a proper weighting can be done with the available data.

In each testing session, the subject was positioned so that the soft tissue of interest was preloaded with a known strain level that assured that the sensor head would remain in contact with the tissue. After a series of tests to determine the vibration frequency that would give good resolution and motion amplitude in the tissue, the data were collected and recorded on a data form.

The data included the initial strain imposed on the tissue, the amplitude of the mechanical vibration, the frequency of the vibration, the depth of the scatterer being interrogated, and the magnitude of the motion of the scatterer.

It was found that the soft tissue contains an ample number of randomly spaced points that serve as scatterers. One must be careful, however, not to use edges of blood vessels larger than arterioles, because their motion is not representative of the soft-tissue mass and data from them produce extraneous results, results that do not make sense physically—e.g., that produce a negative number for the modulus. Moreover, for the 10-MHz ultrasonic signal that was employed in this study to monitor tissue motion, it was found that the mechanical excitation of the tissue needed to be $10 \text{ Hz} \pm 0.5 \text{ Hz}$ for optimal results. Data were collected at 0.5-mm intervals through the depth of the tissue, so that the modulus that was calculated represents a weighted average of all the tissue in the region.

From these data, the modulus of the tissue was calculated using the following equation that is derived from Equation [21]:

$$E = \frac{3}{2} \rho \omega^2 \frac{u_2(x_3 - x_1)}{\frac{u_1 - u_2}{x_2 - x_1} - \frac{u_2 - u_3}{x_3 - x_2}} \quad [23]$$

where u_i corresponds to the motion amplitude at the point corresponding to the depth x_i , ω is the frequency of the cyclic displacement, and ρ is the density of the soft tissue.

To study the effect of the tissue density assumption on the modulus calculation, a sensitivity analysis was performed with Equation [23]. The density of the tissue comprising a stump ranges from 0.92 g/cm^3 for fat to 1.1 g/cm^3 for skin [11]. The skin value is a weighted average for the epidermis and dermis. If the value of the tissue density used in the modulus calculation is 1.00 g/cm^3 , the maximum error in the modulus due to this assumption is ± 9 percent when the perturbation frequency is 10.0 Hz . If the density of the tissue is adjusted to reflect muscle and fat content, 1.02 g/cm^3 for muscle regions and 0.96 g/cm^3 for atrophied regions composed primarily of fat, the maximum error in the calculation is reduced to ± 4 percent.

To evaluate the validity of the constants calculated from the data collected from the ultrasonic system, the subjects were also tested using an Instron Testing

Machine to load the tissue at the same point used in the ultrasonic experiment. Force-displacement data were collected and the modulus of the tissue was calculated at the point where the displacement was equal to the displacement used to drive the tissue during the data collection done with ultrasound. In these tests, care was taken to position the limb in the Instron so that the load was applied in a manner identical to that of the mechanical vibration used to excite the tissue, and so that the strain rate was of the same order of magnitude as the loading rate used in the ultrasound experiments. The Instron data were reduced to modulus information using the technique described by Krokosky [5]. In the tests using the ultrasonic monitoring system, the strain rate for the tissue at the surface of the limb was 0.4 (inches/inches) per second. Thus, for the Instron testing, the head movement was set in the range of 18–24 inches/minute, which gave a strain rate of from 0.37 to 0.42 (inches/inches) per second at the surface of the extremity. The exact strain rate depended on the original thickness of the tissue being tested.

RESULTS

A comparison of the results from the Instron testing and the ultrasonic testing is given in Figure 3. It can be seen that the modulus, as calculated by using either technique, is very close (within 7 percent) to that obtained using the other. This difference

is well within the estimated error associated with mechanical testing, ± 10 percent. Table 1 summarizes the modulus changes that occurred as the muscle mass was contracted.

Table 1

Contraction State	Modulus (psi) at 10% strain level
relaxed	0.9 ± 0.07
mild (supporting 5 lb. weight)	5.2 ± 0.2
maximum	15.8 ± 0.3

DISCUSSION

The ultrasonic measuring technique appears to provide information that is consistent with information that can be collected using more conventional, but much less convenient, techniques to characterize the mechanical properties of soft tissue. The utility of the technique is not restricted by a lack of suitable scattering points in the tissue mass. However, care must be taken to assure that the apparent scatterers are not the walls of large blood vessels; these could be distinguished from the scatterers by their characteristic motion that does not mirror the forcing function. Also, it was found that care must be taken to locate the skeletal member

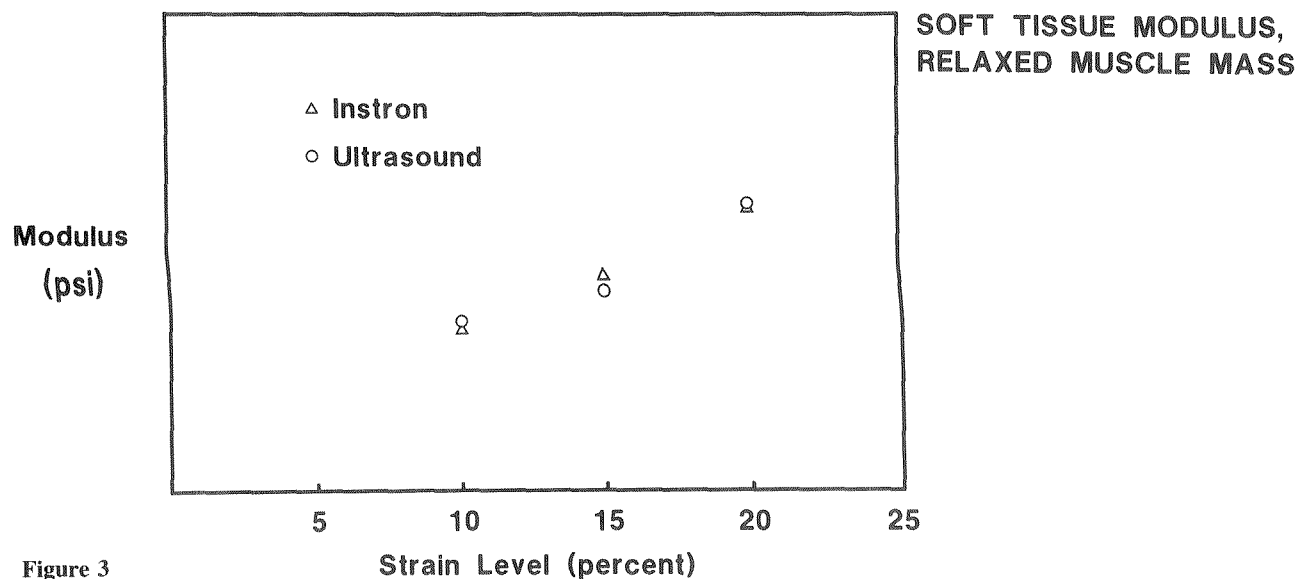


Figure 3

within the soft tissue mass, since the motion of the soft tissue can be significantly influenced by compression against a bone, and that restriction will cause the technique to yield useless data.

The technique was found to provide reproducible data and if the corresponding data parts were repeated and averaged, the composite data points produced results that were quite reproducible.

It was also noted during the study that, by using the ultrasonic technique, it is possible to calculate the modulus of soft tissue in a very small region, i.e., 0.5 mm × 0.5 mm; or the readings could be taken over a region corresponding to one-half the distance between the skin surface and the underlying

skeleton. The technique then produces a modulus characteristic of the weighted average for all the tissues comprising the region.

Based on the results of the experiments conducted in this study, it appears that:

1. The pulsed-Doppler ultrasonic sensor system can be used effectively to characterize the mechanical properties of soft tissue while *in vivo*;
2. The characterization is sensitive enough to detect changes in the contraction of underlying muscle; and
3. The system can be used to evaluate the effect of strain rate and strain level on the elastic modulus.

REFERENCES

1. COX RH. Anisotropic properties of the canine carotid artery *in vivo*. *J Biomech* 8:293-300, 1975.
2. DUNN F AND O'BRIEN WD. Absorption and Dispersion. In: Fry FJ (ed), *Ultrasound: Its Applications in Medicine and Biology, Part One*. pp 393-439. New York: Elsevier, 1978.
3. FRIZZELL LA AND CARSTENSEN EL. Ultrasonic Heating of Tissues (Ph.D. thesis). Electrical Engineering Technical Report #GMO9933-20. University of Rochester College of Engineering and Applied Science, Rochester, New York, 1975.
4. HUTCHINSON KJ, KARPINSKI E, CAPIACK CE. The effect of variation of longitudinal stretch on the dynamic elastic properties of isolated segments of canine carotid arteries. *IEEE Trans Biomed Engineering*, 25(1):55-63, 1978.
5. KROKOSKY EM AND KROUSKOP TA: Synthetic aortas for systemic simulators. *J Biomed Mater Res*, 2:357-375, 1968.
6. LOEFFLER L AND SAGAWA K. A one-dimensional viscoelastic model of cat heart muscle by small length perturbations during isometric contraction. *Circulatory Res*, 36:498-512, 1975.
7. NYBORG WL. Physical Properties of Ultrasound. In: Fry EJ (ed), *Ultrasound: Its Applications in Medicine and Biology, Part One*. New York: Elsevier, 1978.
8. PAPOULIS A.: *Probability, Random Variables, and Stochastic Processes*. New York: McGraw-Hill, 1965.
9. PATEL DJ, JANICKI JS, VAISHNAV RN, YOUNG JT. Dynamic anisotropic viscoelastic properties of the aorta in living dogs. *Circulatory Res*, 32:93-107, 1973.
10. SEGEL LA AND HANDELMAN GH. *Mathematics Applied to Continuum Mechanics*. New York: Macmillan, 1977.
11. SNYDER WS (ed). *Report of the Task Group on Reference Man*. ICRP Publication 23. Oxford, England: Pergamon Press, 1975.
12. TROUNG XT. Viscoelastic wave propagation and rheologic properties of skeletal muscle. *Amer J Physiol*, 226(2):256-264. 1974.
13. TROUNG XT, JARRET SR, NGUYEN MC. A method for deriving viscoelastic modulus for skeletal muscle from transient pulse propagation. *IEEE Transact Biomed Engineering*, 25(4):382-384, 1978.