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STUDY OF SOFT TISSUES VISCOELASTIC PROPERTIES USING ACOUSTIC PALPATION METHOD

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The study of soft tissues shear elasticity modulus using the remotely induced shear waves is presented. Shear waves generation was carried out using transient acoustic radiation force with ultrasound intensity in the focal point equal to 145 W/cm^2. The transient acoustic radiation force duration was equal 2,18 ms. Measurements of the shear waves propagation velocity were made in the transducer focal plane by means of Doppler method using shear excitation propagation time. The following cow tissues were taken as the objects of study: liver, brain, udder, muscle tissues, spleen. The values of shear wave propagation velocity in tissues were obtained. The values of shear elasticity modulus were calculated using the known correlation between shear elasticity modulus, tissue density and velocity. It was shown that the studied soft tissues differ in shear modulus value and, moreover, muscle tissues have high anisotropy of properties directed lengthwise and across the muscle fibers. The tissues elasticity and viscosity modulus were evaluated on basis of the shear excitation relaxation analysis.

KEY WORDS: ultrasound, radiation force, soft tissue, shear strain, relaxation, shear modulus.

It is known that soft tissues can be described by means of several viscoelastic properties, such as shear elasticity modulus, viscosity, the Poisson coefficient etc. [1,2]. Intensive research during the past few years showed that changes of soft tissues mechanical properties and the shear elasticity modulus in particular are the sensitive indicator of different pathologies [3-5]. Changes of mechanical properties can also indicate a different physiological state of a tissue, for example for the muscle tissue its elasticity and viscosity are different at muscle quiescent mode and during contraction [6]. Specifically such a natural process as the ageing leads to a tissue elasticity and viscosity change [7]. Moreover, tissues viscoelastic properties can differ depending on an organ type, or they can reveal anisotropy of properties in different directions [8-10].

Tissue elasticity evaluation by means of palpation is one of the main approaches that are conventionally used by physicians to diagnose some diseases. Tissues changes became palpable only when their elasticity becomes higher or lower then that of a surrounding tissue. The subjective estimation of organ elasticity is an important part of diagnostics of such organs as liver, spleen, thyroid gland and even of an eyeball. Recently certain efforts were taken by some researchers to measure or to estimate some other mechanical properties of a tissue, such as nonlinearity of the elasticity modulus, viscosity, the Poisson coefficient and their time variation. It is supposed that these tissue parameters can provide us with some additive, diagnostically useful information, necessary to diagnose the disease more accurately [11, 12].

Ultrasound and nuclear magnetic resonance (NMR) are the main physical methods that are used for tissue elastic properties visualization and they promise to provide us with quantitative information on tissue elasticity [21,22]. Each of these methods has its own advantages and disadvantages. Though the ultrasound visualization as the elasticity visualization method appeared a bit earlier, still NMR method is being improved fast enough and can compete with ultrasound elasticity visualization method at least for some organs visualization.

The potential and promising fields of application of ultrasound and NMR elasticity visualization are the following:

1. Detection and characterization of superficial and deeply located soft tissue regions, including breast cancer, prostate gland cancer, nodules in glands, thyroid gland etc.
2. Quantitative estimations of organ and tissue elasticity changes in consequence of such diseases as cirrhosis, kidney diseases and thyroiditis.
3. Vascular studies: arterial wall elasticity and level of vein thrombosis estimation. The inflammation of arterial wall is characterized by elasticity changes. This phenomenon frequently leads to arising atherosclerosis plaques in a vessel. The continuous supervision of the wall mechanical properties can improve the opportune qualitative diagnostics. At present noninvasive achievement of this aim is quite a problem.
4. Estimation of effective tissue treatment volume during ultrasound, microwave and cryoablation therapy.
5. Supervision tissues fluid translocation in of patients having such diseases as lymphoedema, cyst formation etc.

MATERIALS AND METHODS OF THE RESEARCH

The aim of this study was to quantitative assessment the shear elasticity modulus of some cow soft tissues *in vitro*. Research was carried out on soft cow tissue, in particular: liver, brain, breast, cardiac muscle, kidney, spleen and also muscle tissues that were studied for two cases of share wave propagation direction: lengthwise and across muscle fibrils. The studied tissues have passed veterinary survey and had no pathological changes. The tissues after extraction and before studying were kept during 12-14 hours under the room temperature. Measurements were made under the temperature equal to 22°C. The probing ultrasound focused transducer with the operating frequency equal to 3.5MHz was used during the studies. The subsidiary high power ultrasound transducer with the operating frequency equal to 1MHz was used for local straining as well as for shear wave excitation in biological tissues. Studies carried out were implemented by means of the experimental ultrasound Doppler equipment described in detail in [13-15].

The acoustic radiation force is a phenomenon connected with wave propagation through the dissipative mediums. It is occurred by the acoustic energy density gradient presence observed in the medium that appears as a result of acoustic waves absorption or reflection. The acoustic energy density gradient leads to the unidirectional force occurrence in the direction of wave propagation. In the absorbing medium and under a plane wave approach this force can be represented as follows: $F = 2\alpha I/c$, where F denote the acoustic radiation force, α - the absorption factor of the medium, I – the time averaging wave intensity in the given space point, c - longitudinal sound-wave velocity. The displacement of tissue induced by radiation force in the measurement volume is the most informative parameter using which one can define the shear modulus and velocity of induced shear waves.

The algorithm of signals phase calculation using the elements of input data set was used in the presented experimental research. On the output of a digital receiver there was observed a sequence sampling of the complex Doppler signal $U(j) = U(jT_{prf}) = \exp(-i\varphi_j)$, where j – is the probe number. The Doppler signal phase φ_j at jT_{prf} is directly connected to the reflector location and its velocity V within the measurement volume:

$$\varphi_j = 2kx_j = 2kVjT_{prf}, \tag{1}$$

Our equipment allowed us to calculate directly the Doppler signal phase φ_j and using its estimated value to calculate the reflectors displacement, including the full displacement after the termination of acoustic radiation force action. The displacement between two probe pulses is equal to:

$$x_j - x_k = (j-k)VT_{prf} = (\varphi_j - \varphi_k)/2k. \tag{2}$$

The calculations presented above were performed by a signal processor in the real time.

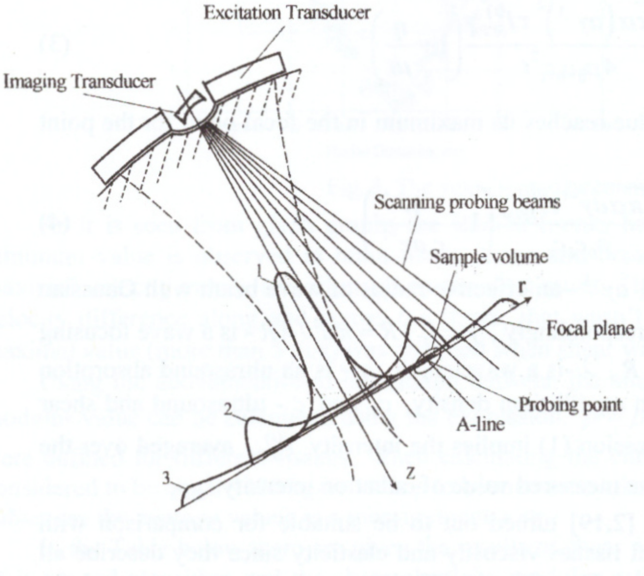

Fig.1 Schematic drawing of the approach used for elastic properties measurement

On Fig.1 there is a schematic drawing of the approach used for biological tissues elastic properties measurement that is based on analysis of shear displacements induced by acoustic radiation force and on usage of the Doppler method. As it is seen from the Figure a high-power ultrasound pulses were radiated along the given direction Z, inducing the maximal radiation pressure force in a focal area of the subsidiary transducer. On completion of a radiation force action the shear disturbance induced in the focal area starts the radial propagation from the subsidiary transducer axis. Therefore the displacement for the points outside the focal area is going to be maximal in certain point of time τ, this value is inversely proportional to shear wave propagation velocity: $\tau = r/c_S$, where r denote a radial coordinate of the probe point, and c_S a shear wave velocity. Measurements of tissues displacement amplitudes and propagation times τ of shear waves were made sequentially in different points located in the focal plane.

The results of measurement of shear wave propagation time to the probe point were used for the shear modulus value estimation. The average value of shear wave velocity in the measurement zone was calculated using the obtained values of propagation time. Velocity value c_S is directly connected to the shear elasticity modulus according to the known correlation: $c_S = \sqrt{\mu/\rho}$, where μ - denote a displacement modulus, and ρ denote a tissue density.

Scheme of organs or their fragments location during the measurements is given on Fig. 2. A narrow zone round the focal that is perpendicular to the transducer acoustic axis is of total length about 40 mm and about 5-6 mm wide. In this zone the measurement of shear wave propagation time values was carried out from the focal point to the point of measurement. The number of points was varied in a random way and came to the value from 100 to 300. Tissues that did not have an expressed direction of structure were placed arbitrarily relatively to the scanning plane, the only condition was an equidistant location of the measurement zone relative to a tissue boundaries.

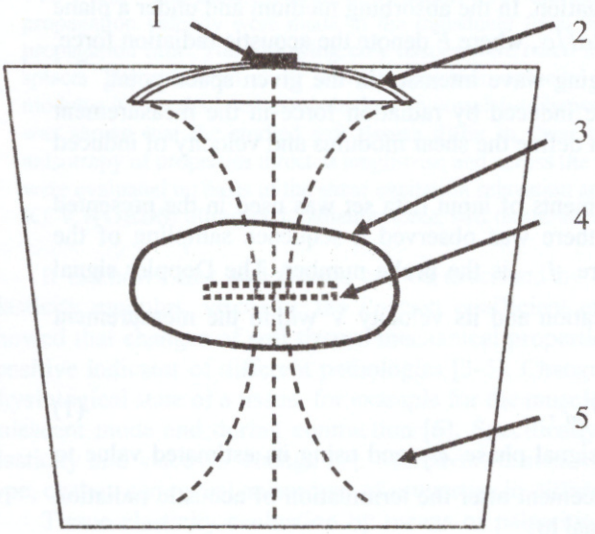

Fig 2. Scheme of organs location during the measurements. 1 –probing transducer, 2 – subsidiary transducer, 3 – organ fragment, 4 – measurement zone, 5 – volume filled with gelatine.

A skeletal muscle is the most mechanically complex biological tissue. It is anisotropic, dynamic, elastic and viscous tissue. The preliminary data obtained in [16-17] basing on NMR elastography approach show that elasticity and viscosity are anisotropic and besides they are not passive parameters but they change essentially when contracting. Therefore in this work when a muscle tissue studying there was also registered the muscle fibres direction relative to the shear wave propagation direction. Tissue was placed in two ways: fibers lengthways and across the shear wave propagation direction.

The acoustic palpation method gives a principal ability of experimental study of shear displacements excitation and relaxation processes and their comparison with theoretically calculated values. Previously to define the role of shear viscosity in relaxation process and to obtain the analytical expressions the following model was analyzed in which not only the lengthwise distribution in ultrasound waves beam is Gaussian but also the envelope of ultrasound pulses that generate the radiate pressure force. As a result to define the value of shear strains in the shear excitation relaxation process the following expression was obtained [18,19]:

$$S_x(r,t) = \frac{\sqrt{\pi}\alpha\left(a\gamma^{-1}\right)^2 \tau I_{SPPA}^{(t)}}{4\rho_0 c_0 c_t^2 t}\left(1+\frac{\eta}{\mu t}\right) \tag{3}$$

Besides it was shown that a tissue displacement value reaches its maximum in the focal point for the point of time $t = a\gamma^{-1}/c_t$:

$$S_{MAX}(0) = \frac{\sqrt{\pi}\alpha a\gamma^{-1}\tau I_{SPPA}^{(t)}}{\rho_0 c_0 c_t}\left(1-\frac{4\nu}{c_t a\gamma^{-1}}\right) \tag{4}$$

where r - is a radial coordinate in the focal plane, a and $a\gamma^{-1}$ - an effective radius of wave beam with Gaussian profile on the radiation surface and in the focal plane correspondingly , $\gamma = l_F / R = \pi a^2 / \lambda R$ - is a wave focusing level by the emitting surface with a radius of curvature R, λ -is a wavelength, α - is an ultrasound absorption coefficient, ν - is a tissue kinematic viscosity, ρ_0 - is an equilibrium density, c_0 and c_t - ultrasound and shear waves velocity in tissue. The radiation intensity in expression (1) implies the intensity $I_{SPPA}^{(t)}$ averaged over the pulse duration in the focal point F which is defined by the measured value of radiation intensity I_{SPPA}.

The expressions (3) and (4), as it was shown in [2,19] turned out to be suitable for comparison with experimental data and for simultaneous definition of soft tissues viscosity and elasticity since they describe all the peculiarities of viscosity influence on shear strains. Therefore in [2] these expressions were used for numerical evaluation of viscoelastic properties of soft tissues phantoms and tissues *in vitro* by means of procedure of relaxation curve adjustment to the given functional dependence. To eliminate the drawbacks of this procedure that turned out to be susceptible to noises at high relaxation times it was decided to use later on another interpolation formula that gives the correct values for the extreme cases of relaxation time $t \to \infty$ and $t = 0$ [20]:

$$S(t) = P_0 \frac{P_1(c_s)}{D(c_s, \eta) + t} \tag{5}$$

The nondimensional parameter P_0 was introduced to account the task parameters that depend on features of ultrasound system generating beam waves of high capacity. This parameter is defined as it is described in [2] during a calibration process of the method using a suit of soft tissues phantoms for which the shear modulus and dynamic viscosity are known. To determine the shear modulus and dynamic viscosity one has by means of experimental curve fitting to calculate the value of $\hat{P}_1$ and $\hat{D}$ parameters and to solve the system of equations [20] to obtain the value of tissue viscosity and elasticity modulus.

RESULTS AND DISCUSSION

The results of measurements of shear wave propagation average velocity in different organs tissues are presented on Fig. 3-5. On this Figures X axis corresponds to the radial distance to measurements point in the focal plane and Y axis corresponds to the measured value of shear wave propagation time up to the certain point. The obtained results present the joint measurements made using three tissue samples of each type, basing on them the shear wave velocity and tissue shear elasticity modulus were calculated.

Obviously some tissue zones can provide the velocity value that differs from the average value measured at general zone. Therefore to measure the velocity in tissue the appropriate zones were selected using ultrasound scanner «B»-image, those that had visible homogeneous echo signal structure.

It is clear that selection of zones with homogeneous echo signal structure does not guarantee us that the shear wave velocity will be equal in all chosen zones. But this approach for measurement zone selection minimized the measurement errors related with shear wave propagation velocity strain when it passes through the tissue structures that have obviously different velocity, through blood vessel wall, for example. The experimental points were approximated to the linear dependence $y = a + kx$, and shown as V – lines. At that the parameter $1/k$ corresponds to the shear wave velocity c_S. Data processing were made using the «Origin» software.

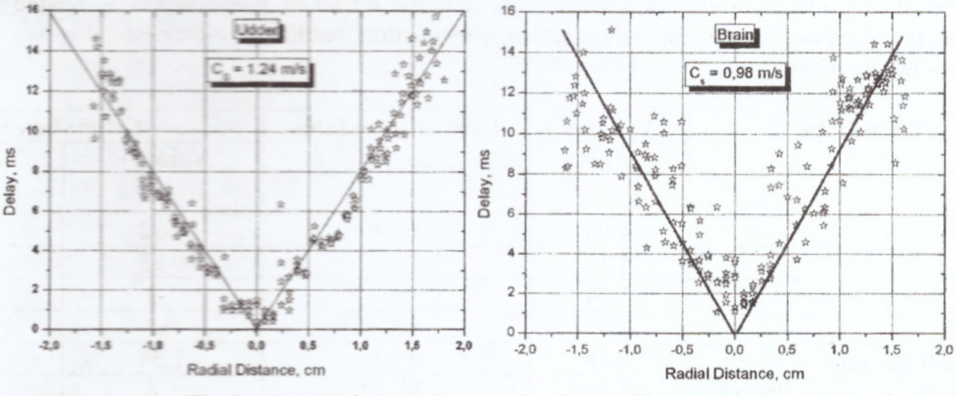

Fig. 3. The velocity measurement in udder and brain tissues.

As it is seen from given graphs the studied tissues have different value of shear velocity. The velocity minimum value is observed in brain tissue. Liver and breast tissues have higher values of the velocity. The maximal velocity values are observed in muscle tissues. The muscle tissue feature is an essential shear wave velocity difference along and across the fibers, that wasn't observed for tissues of other types. The velocity maximal value (more than 5 m/s) was obtained when shear wave propagation along the muscle fibers.

Using the abovementioned correlation between the shear wave velocity and shear elasticity modulus the modulus value can be calculated using the expression: $\mu = \rho \cdot c_s^2$. Thus the average values of elasticity modulus were defined for different tissues. When calculating the elasticity modulus value the tissue density value was considered to be equal 1100 kg/m^3. It has to be mentioned that the obtained velocity and shear elasticity modulus values are the average values in a measurement zone.

In the Table below there are given the results of shear wave velocity measurement, its evaluation by means of improved algorithm and the shear elasticity modulus estimated values. As one can see from this data, the values of shear wave average velocity measured using SWEI method well correspond with its estimation values obtained as a result of a new interpolation algorithm implementation.

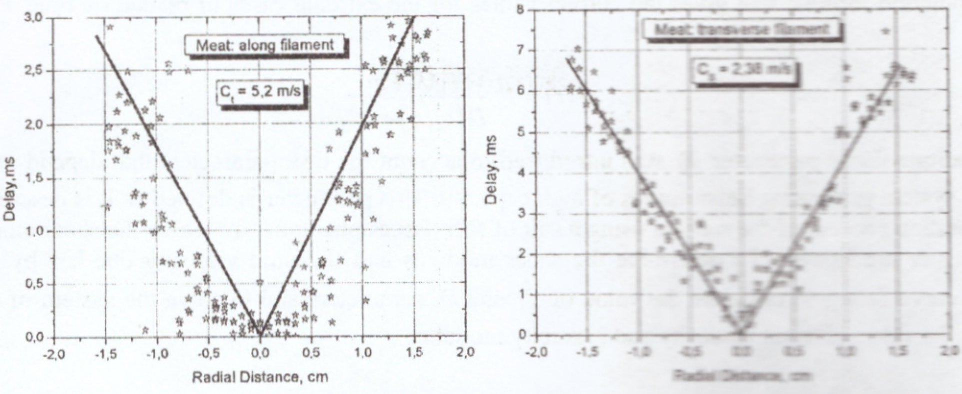

Fig. 4. The velocity measurement in muscle tissue along and across the fibers.

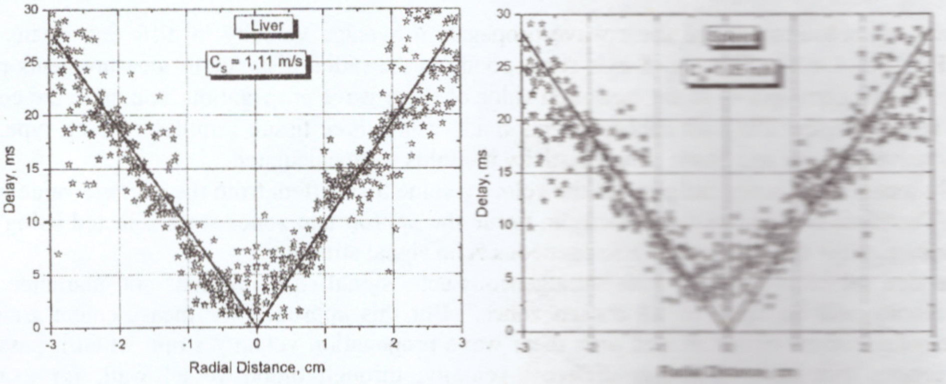

Fig.5. The velocity measurement in liver and spleen tissues.

Unfortunaly absence of opportunity to measure the tissue viscosity directly does not allow us to compare the obtained estimated value of viscosity with its real value. However the qualitative analysis of relaxation curves obtained for liver and brain tissues for points located in the transducer focus and having a small delay of relaxation curve maximum occurrence lets us assume that the observed phenomenon is related with high viscosity of this tissue types. The corresponding viscosity evaluation that has an increased value (see the Table) justifies the assumption made.

	Tissue type	Velocity c_S, m/s	Elasticity modulus μ, Pa	Estimation value	
				Velocity $\tilde{c}_{S}$, m/s	Viscosity $\tilde{\eta}$, $Pa \cdot s$
1	Brain	0.98	1056	0.92	0.28
2	Liver	1.11	1355	0.98	0.26
3	Udder	1.24	1691	1.1	0.22
4	Spleen	1.05	1220	0.9	0.24
5	Muscle tissue (across fibers)	2.38	6230	2.54	0.67
6	Muscle tissue (along fibers)	5.20	29744	5.8	1.27

CONCLUSIONS

As a result of the research the value of shear wave velocity in tissues was measured and shear elasticity modulus was estimated. The results obtained show the considerable difference of shear elasticity modulus values for different tissues. It was shown that the parenchyma tissue of different organs in a normal state differs in about 20% in elasticity modulus value. The muscle tissue differs from other tissues in shear modulus value μ in about 5 up to 20 times. It was showed that the muscle tissue feature is the difference of its elastic properties along and across the muscle fibers. Namely the shear elasticity modulus of muscle tissue has pronounced properties anisotropy relative to muscle fiber direction, along which the velocity is almost two times higher than the one across the fibers.

Knowledge of soft tissue mechanical properties is also necessary for elasticity imaging methods optimization and for comparison of its visualization methods precision. The results obtained are of interest for medical diagnostics namely for creation of data base of different tissues elastic properties. The study showed that the Doppler methods measuring of displacements caused by ultrasonic radiation force in tissues allows to define distinction of elastic modulus of various tissues with a satisfactory precision. In compare with sonoelastography [3,11,12], the usefulness of which is clearing by clinicians now, the proposed method has its own advantages and can be a good complementary method for study of tissue viscosity and elasticity.

In spite of relatively high error of shear wave propagation velocity measurement this approach can turn out to be useful when quantitative estimation of liver diseases (for example, fibrosis or adiposis) since it is known that a liver elasticity modulus changes at that more than in two times, and viscosity is a parameter clinically connected with an adipose tissue presence. The approbation of the new algorithm for simultaneous definition of tissue parameters carried out using parenchyma tissues showed that the measured values match well with the obtained estimated values of shear wave velocity.

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