ARCHIVES OF ACOUSTICS
8, 1, 83-94 (1983)

ULTRASONIC CHARACTERIZATION OF TISSUES IN CARDIOLOGY*

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In order to analyse the possibility of the determination of the properties of soft tissues using ultrasonic (noninvasive) methods, a review was made of the basic physical properties characterizing acoustic wave propagation in these tissues (propagation velocity, attenuation, scattering). In a discussion of the results of "in vitro" investigations, it was shown that investigations of backscattering can be very significant for cardiological applications; the heart muscle with scars caused by an infarct is characterized by an increased proportion of collagen-rich connective tissue which has the value of the backscattering coefficient greater by a factor of some dozens than that of normal muscle. This is related to the higher echographic visualizability of collagen than other soft tissues and suggests the practical possibility of noninvasive distinguishing of the regions of the muscle with scars caused by the infarct from normal muscle. This possibility was confirmed by "in vivo" investigations performed on dogs by the method of grey level histograms obtained from ultrasonograms of dog's hearts.

This paper has the character of a review.

1. Introduction

Information carried by ultrasonic waves penetrating the interior of the human body is encoded, in its time of passage, amplitude, frequency and phase. This information undergoes electronic processing and, when the pulse echo method is used, is displayed on the oscilloscope or kinescope screen in *A* (amplitude), — *B* (brightness) — or *M* (motion) — presentation. It is also possible to use information related to a frequency change caused by the Doppler effect

* Delivered at the International School of Ultrasonography at Erica (Sicilly) on 3 November, 1981.

[6] or ultrasonic holography. The latter method is now purely academic in significance; it has never been used practically. The recent times have seen attempts to use a method based on digital image reconstruction, as it is done in computerized *X*-ray tomography. This promising technique is now in its early development stage.

The visualization of the interior of the human body by means of ultrasound is made possible by the advantageous conditions of wave propagation in soft tissues. Wave attenuation increases in proportion to the first power of frequency. In the investigations of the organs of the pelvis, abdominal cavity and heart, ultrasonic waves of frequencies from 2 to 3 MHz cover distances of up to 25 cm, counting in one direction only. In ophthalmology, where the longest distances do not exceed 5 cm, higher frequencies, usually from 6 to 20 MHz, are used. Over this frequency range the wavelengths of ultrasound are contained within the limits 0.75-0.075 mm, which is then the resolution limit of ultrasonic diagnostic methods.

Another great advantage is the fact that the acoustic impedances of soft tissues only slightly differ from one another, mainly as a result of differences in the elastic properties of the tissues. E.g. at the interface of blood and muscle tissue only 0.1 % of the intensity of the wave incident perpendicularly on this interface is reflected. The other 99.9 % intensity penetrates deeper into the body, causing successive reflections from the increasingly deeper boundaries of tissues. Thus a large amount of information can be obtained about the successive, increasingly deeper, interior anatomical structures of the body.

The variety of the organs of the human body, the variety of their anatomical structure and physiological function causes ultrasonic diagnostic methods and ultrasonic equipment to be developed from the point of view of the specific properties of these organs. Accordingly, independent ultrasonic diagnostic equipment has been developed for the purposes of examining the organs of the pelvis and abdominal cavity, opthalmologic and cardiological problems, female breasts, peripheral circulation system etc.

2. Principle of obtaining ultrasonic images of tissue structure

There are a number of common, yet unsolved, problems which are essentially significant for further development of ultrasonic diagnostic methods. One of these is ultrasonic characterization of tissues, including a description of their properties without the necessity of using invasive investigation methods. Good results of investigations in this field can change essentially the previous significance and value of ultrasonic diagnostic methods for medicine, by permitting identification of pathological tissues discovered. However, this problem is very complex. Absorption, scattering, velocity of ultrasound, acoustic im-

pedance, its spatial distributions and frequency dependence, all affect in a variety of ways the propagation of ultrasound. As a result, the information obtained by means of ultrasonic waves "in vivo" is very complex and difficult for unambiguous interpretation.

The introduction of the grey scale into ultrasonic visualization methods was the basic condition for investigations to be initiated in the range of tissue characterization. The first ultrasonograms (ultrasonic images), obtained directly on the screens of standard oscilloscope tubes, gave highly contrasted images which showed in effect only the outline of tissue boundaries. However, soft tissues show a complex internal structure, with a large number of blood vessels with different size. Small structures, such as muscle fibres (with diameter 10-150 μm and length 1-20 mm) or small blood vessels (arterioles and capillaries with diameter 8-200 μm and length 0.1-0.2 mm) cause scattered images of ultrasonic waves [4], since their dimensions are comparable to or smaller than the wavelength.

Improvements in ultrasonic technique, such as dynamic focusing with simultaneous control of the aperture of the piezoelectric transducer, permitted high resolution to be achieved over the entire length of the ultrasonic beam and, thus, images of the internal structure of tissues to be obtained. Microprocessor-controlled digital memory, permitting storing of hundreds of thousands of data obtained ultrasonically, brought the new possibilities of using a variety of electronic signal processing techniques for the purposes of reconstruction and improvement of ultrasonic images, for seeking and calculating essential quantitative data, for determination of grey level histograms in the images of structures being identified etc. All these techniques created completely new possibilities for ultrasonic tissue characterization.

The signals obtained from the interior of tissue structures have the nature of scattered reflections propagating in all directions; their intensity decreases rapidly as the distance increases, and it increases as frequency increases.

Much more energy is carried by the echoes caused by specular reflections from flat tissue boundaries. Maximum echoes can be stronger by as much as 100 dB than the weakest echoes scattered by the internal tissue structures. In order that all these echoes may be represented on the oscilloscope or kinescope tube screens (apart from their storing in digital memory), it is necessary to compress them over the range 20-40 dB, e.g. by using logarithmic amplifiers [5]. The electronic signal pre- and post-processing prior to and after storing in memory affects to a large extent the quality of images of tissue structures.

Ultrasonic images obtained in cardiology, even when using conventional equipment based on the echo principle, permit some conclusions to be drawn about the character of tissues [17]. E.g. blood is transparent for ultrasound, giving practically no reflection, when it is investigated using the echo method. When the Doppler method for investigation of the velocity of structures is

used, blood flows cause signals which sometimes superimpose on the Doppler signals from the moving heart tissues (e.g. valves). The character of these signals, however, is completely different and distinguishable.

It is easy to detect calcification of the heart tissues, since it involves changes in their elasticity and density, and therefore in their acoustic impedance, causing an increase in the amplitude of the echoes reflected. This can be seen distinctly in the case of calcified valves, for example.

3. Velocity, attenuation and absorption of ultrasound in soft tissues

In order to analyse systematically the possibilities of ultrasonic tissue characterization in cardiology, such basic acoustic quantities as the propagation velocity, absorption coefficient and scattering of ultrasonic waves will now be discussed.

Systematic data on the propagation velocity and attenuation of ultrasonic waves were recently collected from different literature sources [9, 10]. They contain more than 800 items on the propagation velocity and more than 1000 on the attenuation of ultrasonic waves in different mammalian tissues. However, only 16 concern the velocity in the animal heart. There are no data on the human heart. The data on attenuation are more ample: 51 on the animal heart and 2 on the human heart.

Analysis of propagation velocity in different mammalian tissues indicates that it increases as the protein content increases [2]. The lowest velocity is characteristic of fat tissue, on average 1460 m/s; the highest, of tendons with 1740 m/s. The velocity in the myocardial tissue is almost equal to the mean velocity of all soft tissues, i.e. about 1580 m/s.

Apart from velocity, most information concerns attenuation measurements in mammalian tissues, while absorption measurements were not paid much attention. It is necessary to distinguish clearly between those two phenomena. Attenuation is a decrease in the amplitude of the acoustic signal as a function of the distance covered by the wave. This quantity includes all losses. In turn absorption is a phenomenon in which the energy of the acoustic wave is locally transfered to the medium where it propagates, followed subsequently by conversion of acoustic energy into heat. Attenuation is therefore a broader notion, including the phenomena of absorption, and also those of scattering, reflection, refraction and diffraction.

Attenuation in muscle tissue, collected from 65 literature items and represented as a function of frequency, shows a very large scatter of measured values. DUNN showed [2] that attenuation values arrange themselves along a straight line given by the equation

$$A = 0.140 f^{0.926}, \tag{1}$$

where A is attenuation [cm^{-1}] and f frequency [MHz]. The correlation coefficient is $R = 0.748$.

It was shown recently [8] that values of the attenuation coefficient in tissue depend to a large extent on the measurement technique used. As a result of heterogeneity of tissues the ultrasonic wave undergoes phase shifts on its path. These cause partial cancelling of the signal in the piezoelectric receiver transducer. Because of this, attenuation measurements taken by means of piezoelectric transducers give apparently higher values than those transducers which are insensitive to cancellation, such as acoustoelectric transducers [1]. It is possible to obtain a threefold difference in attenuation values, depending on the measurement method used [8]. In addition, the measured results are also affected by other factors, such as temperature, sample preparation etc. This is confirmed by the example in Fig. 1 which shows the coefficients of

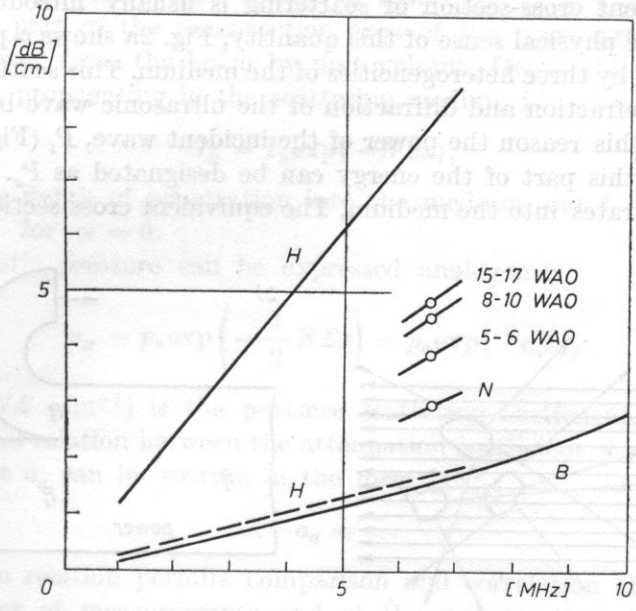

Fig. 1. The coefficients of attenuation (solid line) and absorption (dashed line) of the heart *H*, according to Goss *et al.* [8], and of blood *B*. Points mark attenuation in normal *N* and ischemic *WAO* regions of dog's hearts. In the latter case the period (from 5 to 17 weeks) following the closure of coronary circulation, acc. to O'Donnoll *et al.* [13], is given

attenuation and absorption of the heart *H* and attenuation of blood *B* as a function of frequency. These data were collected from literature and based on measurements taken mostly by means of piezoelectric receiving transducers [8-10]. Absorption was determined using the transient thermoelectric method at a temperature of 37°C [8]. In turn, the point *N* represents the attenuation coefficient obtained in the myocardium of normal dogs by means of an acoustoelectric receiving transducer [13] which eliminates the cancellation of signals with different phases on the surface of the transducer.

It can be concluded therefore that the piezoelectric technique used in conventional ultrasonic diagnostic devices cannot provide sufficiently accurate information about attenuation in soft tissues under investigation.

4. Scattering of ultrasonic waves

In contrast to the measurements of propagation velocity and attenuation, the investigations related to backscattering of ultrasound in the myocardium seem interesting and promising. These investigations were recently published by O'DONNOLL *et al.* [13].

In order to describe quantitatively the phenomenon of scattering, the notion of the equivalent cross-section of scattering is usually introduced. In order to illustrate the physical sense of this quantity, Fig. 2a shows a plane ultrasonic wave scattered by three heterogeneities of the medium. This scattering is a result of reflection, refraction and diffraction of the ultrasonic wave by these heterogeneities. For this reason the power of the incident wave, P_i (Fig. 2b), is partly scattered and this part of the energy can be designated as P_s. The remaining power P_t penetrates into the medium. The equivalent cross-section of scattering

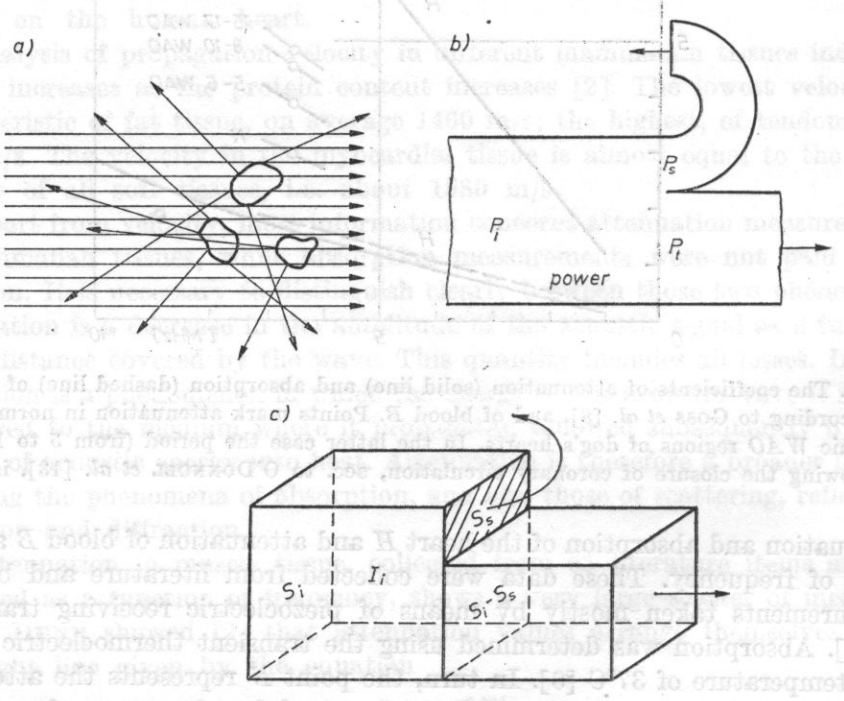

Fig. 2. Scattering of ultrasonic waves by heterogeneities in the medium (a). The division of the power P_i of the incident ultrasonic wave into the power P_s of the scattered wave and the power P_t of the wave penetrating into the medium (b). Geometrical interpretation (c)

is defined as the ratio

$$\Sigma = P_s/I_i, \tag{2}$$

where I_i is the intensity of the plane wave incident on the scattering object.

Since the scattered power $P_s = I_s S_s$,

$$\Sigma = P_s/I_i = I_i S_s/I_i = S_s \quad [\mathrm{m}^2]. \tag{3}$$

Formula (3) permits a simple, direct interpretation of the equivalent cross-section of scattering ($\Sigma = S_s$) as part of the area (S_i) of the cross-section of the plane incident wave which is removed from the beam by the scattering object (Fig. 2c).

When in a unit volume of the medium there are N (m^{-3}) scattering objects, each with the equivalent cross-section of scattering Σ (m^2), the product $N\Sigma$ (m^{-1}) is then part of the cross-section area of the plane propagating wave, which is removed from the beam by unit volume. Hence the intensity of the plane wave I_x propagating in the scattering medium is

$$I_x = I_0 \exp(-N\Sigma x), \tag{4}$$

where x is the depth of penetration into the medium and I_0 is the intensity of the wave for $x = 0$.

The acoustic pressure can be expressed analogously

$$p_x = p_0 \exp\left(-\frac{1}{2} N\Sigma x\right) = p_0 \exp(-\alpha_s x), \tag{5}$$

where $\alpha_s = \frac{1}{2} N\Sigma$ [cm^{-1}] is the pressure scattering coefficient.

The general relation between the attenuation coefficient A and the absorption coefficient α_a can be written in the form [14]

$$A - \alpha_a = \alpha_s. \tag{6}$$

The above relation permits comparison and correlation of the results of a large number of measurements and of the investigations of attenuation, absorption and scattering, which were usually obtained by different techniques. This may permit some general conclusions to be drawn about the structure and acoustic properties of soft tissues [8, 14]. In general case the phenomenon of scattering is not isotropic but depends on the direction. Therefore the differential form of the scattering coefficient per unit volume, referred to the spatial angle, is introduced. It has the shape

$$\eta = \frac{dN\Sigma}{d\Omega} = 2\frac{d\alpha_s}{d\Omega}. \tag{7}$$

The quantity η is called the differential scattering coefficient. In view of the measurement technique used, the backscattering coefficient $\eta_{180°}$ is significant. It involves the measurement of the magnitude of the wave scattered,

using the same transducer which transmits and receives at the same time [15] (see Fig. 3). However, in this case the scattering coefficient a_s cannot be determined, since the angular relation $\eta = \eta(\theta, \Phi)$ is not known. In general case, according to expression (7),

$$a_s = \frac{1}{2}\int_{\Omega} \eta(\theta, \Phi) d\Omega = \frac{1}{2}\int_0^{\Pi} \sin\theta d\theta \int_0^{2\Pi} \eta(\theta, \Phi) d\Phi, \tag{8}$$

where θ and Φ are plane angles (Fig. 3).

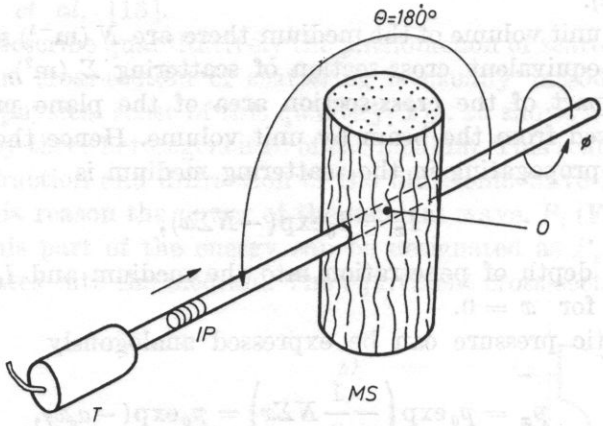

Fig. 3. The measurement of the backscattering coefficient

T – the piezoelectric transmit-receive transducer, *IP* – the pulse of the incident ultrasonic wave, *MS* – the biological sample measured; θ, Φ – plane angles

In the case of scattering objects which are very small compared to the wavelength isotropic scattering can be assumed in approximation; thus formula (8) gives directly the relation

$$a_s = 2\pi\eta_{180°} \quad [\mathrm{cm}^{-1}]. \tag{9}$$

O'DONNOLL *et al.* determined the relation between the backscattering coefficient $\eta_{180°}$ and collagen concentration in the hearts of normal dogs and those with ischemia of the myocardium caused by occulsion of the coronary vessels [13]. The aim of these investigations was to explain the mechanism of scattering of ultrasonic waves by the myocardium. The authors took "in vitro" measurements in the myocardium tissues obtained from 17 dogs subject to three different periods of ischemia of this muscle. Ischemia was caused by occlusion of the left anterior descending coronary artery. After 5, 8 or 16 weeks following the coronary occlusion the animals were killed.

The total number of ischemic regions was 18; the same number of normal regions in six hearts were examined after 5-6 weeks after the coronary occlusion. A related number of myocardial regions were examined after 8-10 and

15-17 weeks from the coronary occlusion. Fig. 4 shows the results of ten averaged measurements of each sample as a function of frequency. The change in the value of the backscattering coefficient is striking. For a frequency of 3 MHz this coefficient is greater by a factor of about 50 than in the normal myocardium.

In turn, attenuation measurements on the same samples, taken using an acoustoelectric receiving transducer, in the case of ischemia, only slightly differed from one another; it is shown in Fig. 1 by means of three points designated by the abbreviation *WAO*.

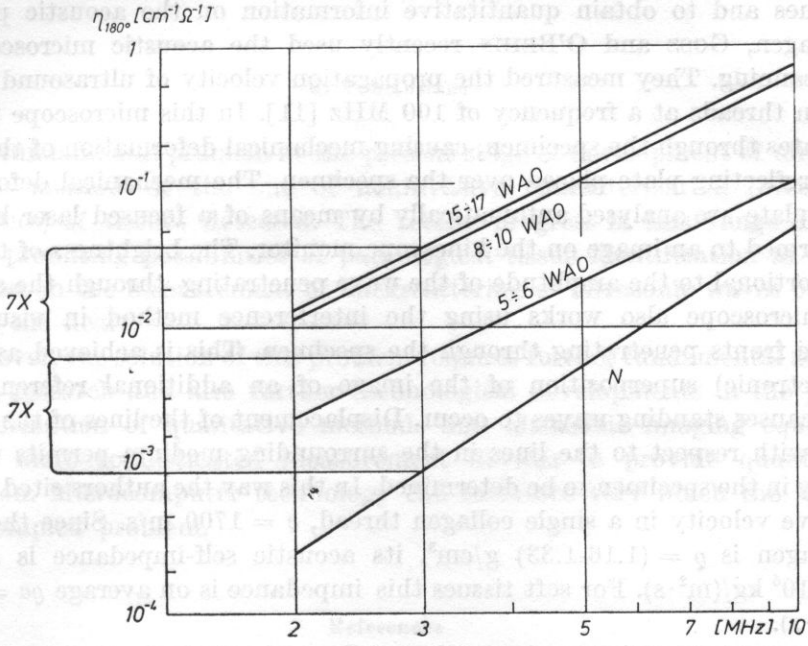

Fig. 4. The backscattering coefficient measured by O'Donnoll *et al.* as a function of frequency [13]: *N* — normal dog's myocardium, *WAO* — ischemic areas of dog's myocardium 5-17 weeks after closure of the coronary artery

In addition to changes in the backscattering coefficient, collagen concentration was estimated by a quantitative biochemical assay for hydroxyproline. The mean concentration of hydroxyproline, which is a quantitative index of the molecular content of collagen, increased ten times as much in the ischemic regions [13].

5. Discussion

The fibres of the normal myocardium are the essential object scattering ultrasonic waves over the range of a few MHz. The myocardial infarct is a dynamic process in the course of which the necrotic muscle fibres are replaced by connective tissue. It was suggested previously by Fields and Dunn [3]

that the elastic properties of connective tissue cause this tissue to be predominantly visualized in ultrasonograms. The greatest collagen concentration occurs in connective tissue. Collagen constitutes about 30 % of the total albumin amount in the system. Its composition included glycine (over 24 %), hydroxyproline (about 13 %) and a dozen or so of other amino acids in smaller proportion.

The normal myocardium show little collagen content, while the scarred myocardium contains much of it.

In order to verify the role of collagen in ultrasonographic visualization of tissues and to obtain quantitative information on the acoustic properties of collagen, Goss and O'Brien recently used the acoustic microscope with laser scanning. They measured the propagation velocity of ultrasound in single collagen threads at a frequency of 100 MHz [11]. In this microscope the wave penetrates through the specimen, causing mechanical deformation of the surface of the reflecting plate placed over the specimen. The mechanical deformations of the plate are analysed automatically by means of a focused laser beam and transformed to an image on the kinescope monitor. The brightness of the image is proportional to the amplitude of the wave penetrating through the specimen. This microscope also works using the interference method in visualization of wave fronts penetrating through the specimen. This is achieved as a result of (electronic) superposition of the image of an additional reference wave, which causes standing waves to occur. Displacement of the lines of the standing waves with respect to the lines in the surrounding medium permits the wave velocity in the specimen to be determined. In this way the authors cited obtained the wave velocity in a single collagen thread, $c = 1700$ m/s. Since the density of collagen is $\varrho = (1.16\text{-}1.33)$ g/cm^3, its accustic self-impedance is about $\varrho c = 2.1 \cdot 10^6$ kg/(m$^2 \cdot$s). For soft tissues this impedance is on average $\varrho c = 1.6 \cdot 10^6$ kg/(m$^2 \cdot$s).

These results indicate clearly that collagen is particularly strongly distinguishable in ultrasonographic images in contrast to other tissues. In view of these results it becomes clear why collagen concentration occurring in the myocardium with post-infarctional scars causes such a large increase in the backscattering coefficient.

It is interesting to note here the large potential possibilities of ultrasonic microscopy, creating a new field of biophysical investigations — sonohistology.

In cardiological terms again, it can be stated that it seems possible to distinguish between the regions of normal tissue and those pathological, on the basis of measurement of backscattering of ultrasound.

The first attempts at such a solution were published at the Sixth International Symposium on Ultrasonic Imaging and Tissue Characterization at Gaithersburg (USA) in June 1981 by Skorton *et al.* [16]. These authors investigated backscattering of ultrasound, making two dimensional ultrasonograms of hearts in awake dogs with operated (closed) chests, following circumflex coro-

nary occlusion. For the imaging of the heart they used a phase-array real-time equipment working at a frequency of 2.25 MHz. By means of an automatic digital system they determined the grey level distribution on the negatives of pictures taken of two heart regions; the interventricular septum (control region) and the posterior wall of the left ventricle (infarcted area). Grey level histograms were taken before and two days after the coronary occlusion.

The results of these preliminary investigations suggest that an acute infarct of the heart can be diagnosed from analysis of grey level distributions, comparing the regions examined with the control region separated by the ventrical cavity.

6. Conclusions

The fundamental problem at the present stage of development of ultrasonic diagnostic methods is the one of noninvasive characterization (description of properties) of tissues detected. The recent progress in this range provides the very promising possibilities of pathological tissue identification in cardiology, based on the measurement of backscattering of ultrasonic waves penetrating into the heart.

However, the solution of this problem requires further fundamental acousto-biological research and also further technological developments in the process of transformation of qualitative methods and ultrasonic imaging equipment into still more sophisticated measurement devices to provide quantitative information. Microcomputer technology can facilitate very much the solution of this complex problem.

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Received on November 27, 1981; revised version on May 21, 1982.