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QUANTITATIVE ULTRASONOGRAPHY (DEVELOPMENT IN POLAND)

L. FILIPCZYŃSKI

Department of Ultrasonics. Institute of Fundamental Technological Research Polish Academy of Sciences
(00-049 Warszawa, Świętokrzyska 21)

Ultrasonography is based on the competent interpretation of ultrasonic images of the patients organs. Factors enabling a correct diagnosis are of qualitative character, mainly, because in the first place they depend on the experience of the specialist performing the examination.

However, a necessity of describing certain quantities with numbers appeared already in the early stages of development of ultrasonography. This need becomes more and more apparent and even essential in certain domains of ultrasonography where Doppler techniques are applied.

If 1958 would be accepted as the year of advent of clinical ultrasonography, then practically from that moment the following question was a live issue: if and when ultrasound can be harmful → especially to subtle fetal structures? This question gave origin to ultrasonic dosimetry, which was to answer how high intensities — how many W/cm² are introduced into examined structures and if it is permissible. This still remains a current and widely discussed problem.

Doppler techniques, strongly related at present with utrasonography, are the second domain requiring numerical parameters. The qualitative analysis of the morphology of the blood flow velocity curve was sufficient in the first stage of development of the Doppler technique. But before long quantitative indices were introduced and further developments were aimed at the determination of the blood's linear velocity in m/s, and then — volume velocity called also volume flow, measured in ml/min, most frequently.

The moment when microcomputer technique was introduced to ultrasonography, it became possible to determine linear dimensions of examined structures directly from ultrasonographic images, their surface, at certain additional assumptions concerning their volume, as well as the velocity of movable structures. It was also possible to introduce methods of spectral analysis in real time. This is of particular importance to cardiological ultrasonography. Quantitative determination of the blood pressure gradient from blood velocity measurement was also made possible.

And finally, the noninvasive determination of hemodynamic impendace (resistance) and vessel rigidity by means of associated ultrasonographic and Doppler techniques is the latest field developed at present.

This paper will discuss details of presented here methods and techniques, as well as prospects of their further development taking into account mainly the Polish achievements in this field.

Ultrasonography is based on the competent interpretation of ultrasonographic images of the patients internal organs. An old Chinese proverb says that one picture supplies more information than a thousand words. Factors which make a good diagnosis possible are mostly of qualitative character and are dependent on the experience of the specialist performing the examination.

Yet, the necessity of characterizing certain quantities with numbers appeared as early as the first period of development of ultrasonography. This necessity becomes more and more noticeable and even essential in certain ranges of ultrasonography, where Doppler techniques are applied.

The year 1958 can be accepted as the conventional date of birth of clinical ultrasonography, because it was then that the excellent British periodical "The Lancet" printed a paper by professor Donald from the University Clinic in Glasgow, doctor Vicar and enginner Brown from the Kelwin Hughes Company, containing for the first time images obtained with ultrasound of the uterus, cysts of the ovaries, ascites and neoplasmas in a pregnant woman [3]. In order to evaluate the progress made from that time, you only need to look at present obtained from computer-aided ultrasonographs ultrasonograms of the fetal head, which might be called portraits from profile or en face.

We owe this giant progress, happening during the life time of one generation, to the incredible development and pioneer research of acousticians, electronic engineers and computer scientists, supported by the research of clinicians applying the method of successive step by step development.

However, from the first moment the question arouse: may ultrasound be harmful – to subtle fetal structure especially and when can, this happen? Can effects of ultrasonic activity turn out to be as harmful as ionizing radiation? What is the permissible dose? These questions have accompanied all initial research within ultrasonography and they still remain the subject of international interest.

The first ultrasonograms in Poland were obtained in 1966 [14] with a UG-1 ultrasonograph (Figs. 1, 2) constructed by our team in the Institute of Fundamental Technological Research (IFTR) of the Polish Academy of Sciences. We obtained first ultrasonograms of pregnant women (Figs. 3, 4). As far back as then we developed two original methods of measuring the ultrasonic intensities radiated into the patients abdominal cavity (Fig. 5), achieving results of 2 mV/cm^2 SATA equivalent to about 5 mV/cm^2 SPTA [16]. Fig. 6 presents permissible doses of ultrasound intensity according to the American Institute of Ultrasound in Medicine AIUM [1]. Doses applied in our first and further research should be located near the lowest dashed line. Hence, they were about 10 times lower than permissible values.

The problem of permissible ultrasonic doses has acquired new dimensions at present, because of new additional safety criteria imposed on ultrasonic examinations including temperature effects. The last conference organized at the Illinois University in Urbana in June 1990 was dedicated to this issue. The AIUM-Institute recomends the criterion of maximal permissible increase of the fetus'es temperature equal to 1°C over the physiological temperature [1]. Examinations of seven species of mammals

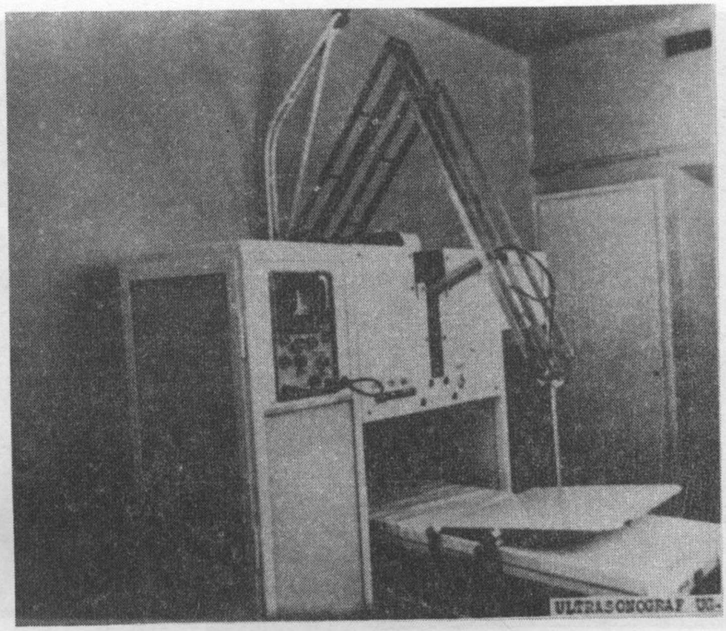

FIG. 1. The original ultrasonograph UG–1. The ultrasonic probe frequency 2 MHz was coupled mechanically by means of a pantograph with the movable cathode ray tube [14] (1966).

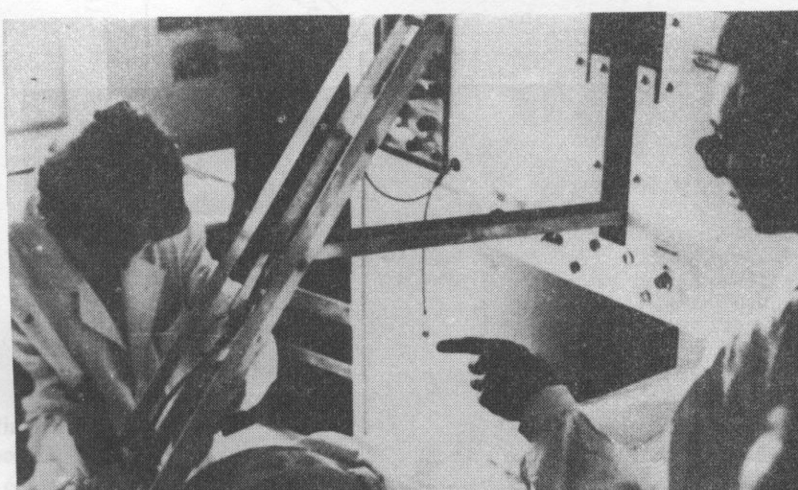

FIG. 2. Ultrasonograph UG–1 during examination of a pregnant woman. Left – dr G. Łypacewicz, right – dr J. Etienne [14] (1966).

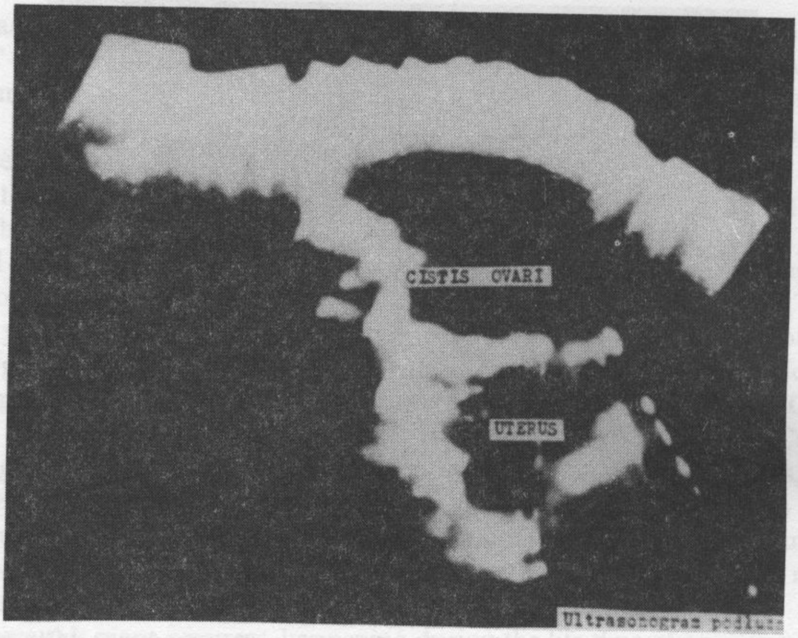

FIG. 3. Longitudinal ultrasonogram of the woman with visible cistis ovari and uterus [14] (1966).

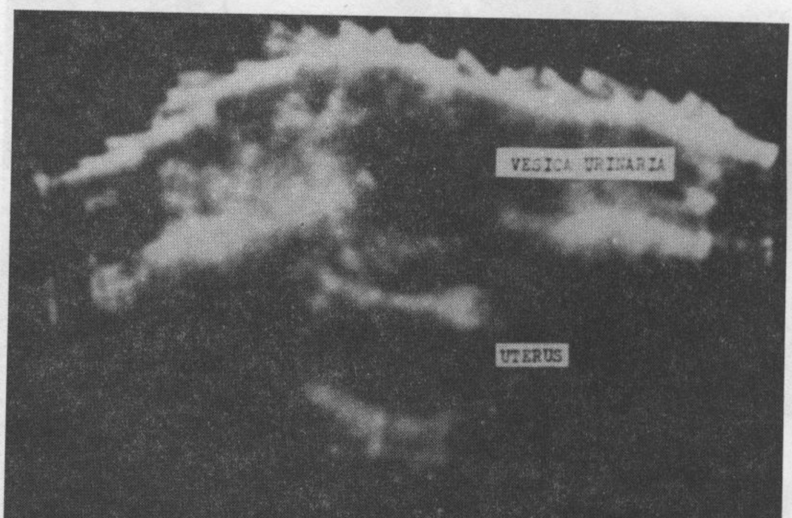

FIG. 4. Transverse ultrasonogram with visible vesica urinaria and uterus [14] (1966).

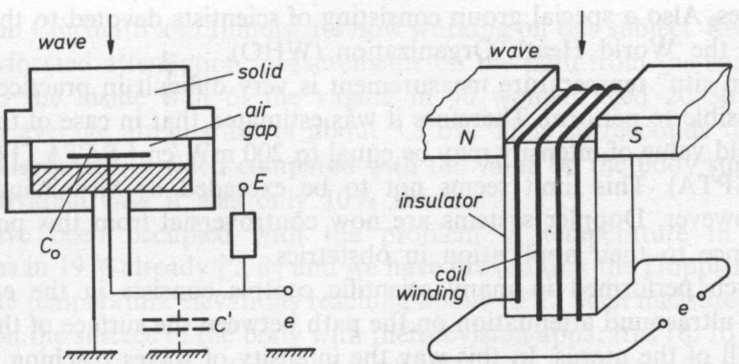

FIG. 5. Principle of the capacitance and electrodynamic absolute measurement methods of ultrasound intensity [14], [16], (1966).

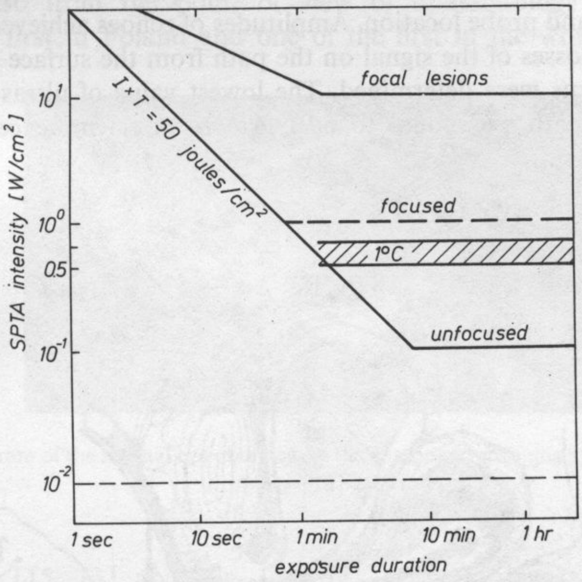

FIG. 6. Minimum SPTA (Space Peak Time Averaged) intensities required for ultrasonic bioeffects based on the specified AIUM (American Institute of Ultrasound in Medicine) recommendation. The hatched area corresponds to the lowest intensity levels which may cause a temperature rise of 1 C.

and anamnesis with mothers who had fever during their pregnancy indicate explicitly that a temperature elevation exceeding 2°C is very frequently the reason for teratism due to dysplasia of the embryo, since hyperthermia destructively influences the development of its nervous system.

This problem is of lively interest to scientists investigating the effect of ultrasound on living tissues, clinicians applying ultrasonic devices and producers of these devices. Also a special group consisting of scientists devoted to this issue was created by the World Heath Organization (WHO).

The "in situ" temperature measurement is very difficult in practice or may be even impossible to perform. Therefore it was estimated that in case of this criterion, the threshold value of intensity may be equal to 200 mW/cm² SATA [1] (about 500 mW/cm² SPTA). This limit seems not to be exceeded by visualizing ultrasonic systems, however, Doppler systems are now controversial from this point of view with reference to their application in obstetrics.

Research performed in many scientific centres consists in the experimental research of ultrasound attenuation on the path between the surface of the body and internal wall of the uterus. In this way the intensity of waves reaching the embryo can be determined and the temperature increase may be estimated [25].

We have taken up this subject concerning early pregnancy [4] as the first already in 1976. Our method consisted in the insertion of reflectors in the form of stainless steel balls mounted on a rod into the uterus of a patient immediately before legal abortion (Fig. 7). Then the measurement was repeated in water for the same geometry of the ball and probe location. Amplitudes of echoes achieved in both cases were compared and losses of the signal on the path from the surface of the body to the inside of the uterus were determined. The lowest value of ultrasound intensity attenuation on this path was equal to 6dB. American scientific centers, such as

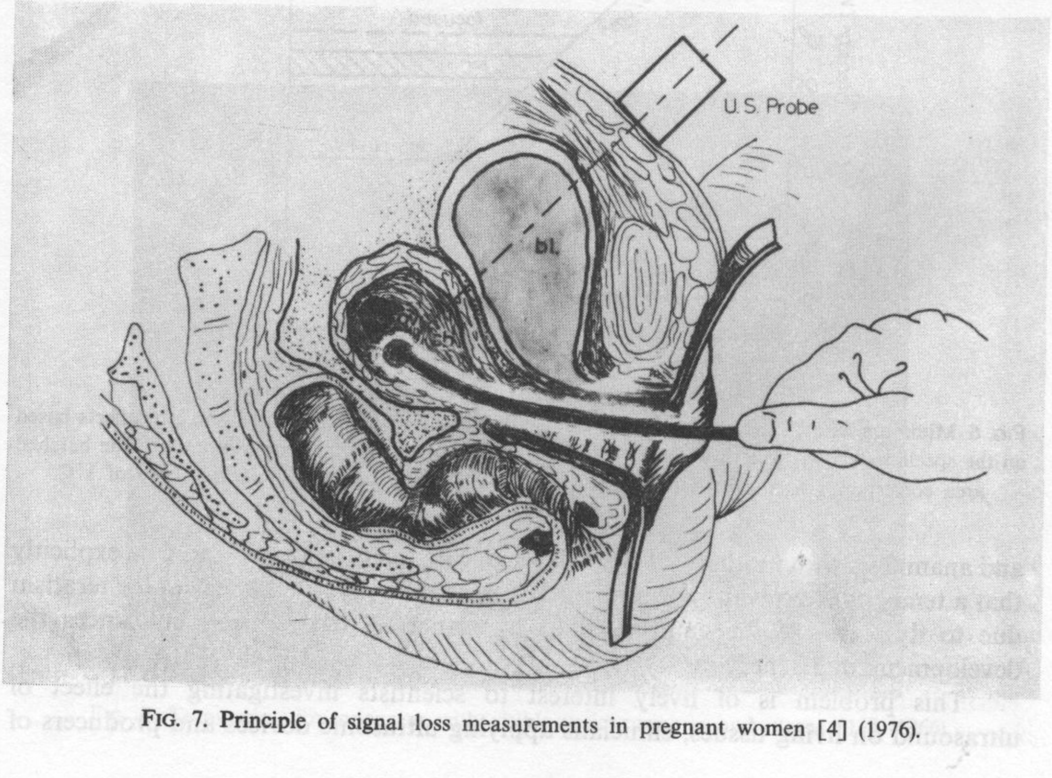

FIG. 7. Principle of signal loss measurements in pregnant women [4] (1976).

universities in Cincinatti and Illinois, are now working on this subject. Recently prof. O'Brien performed attenuation measurements on the path from the surface of the abdomen to the inside wall of the vagina in 40 women aged 20–30 years and obtained an average attenuation of about 3.5 dB. Thus corresponds to an about 2 times smaller intensity when compared with the value on the body surface. In an extreme individual case it was only 10% smaller.

We have been occupied with the problem of temperature in diagnostic examinations in 1976 already [7, 8] and we have proved that the Doppler apparatus may generate temperature elevations reaching about 10°C. Such measurements were performed on the surface of the body with thermovision apparatus [6, 10]. It was an extreme case concerning one of the first foreign Doppler apparatus for examination of the peripheral circulatory system.

We have dedicated several papers concerning diagnostic devices, as well as lithotripsy lately, [9, 11, 23, 25] to the problem of heat generation.

We have continued work on the visualization and permissible doses of ultrasounds also from the point of view of ophtalmology since 1967. Figure 8 presents the first in Poland and one of the first in the world ultrasonogram of

FIG. 8. Ultrasonogram of the normal eye obtained by the compound scanning system with frequency of 10 MHz [15] (1967).

a normal eye [15, 13] and Fig. 9 shows a special ophtalmic ultrasonograph constructed by us at that time. Performed by us quantitative investigations of the influence of ultrasound intensity on eye tissues of a rabbit proved that first signs of lesions in the eyes retina were observed at intensities of approximately 200 W/cm^2 (SATP) [21]. On the basis of these results the intensity of ultrasonographs produced in Poland according to our conception was limited [18].

After 20 years we still perform intensity measurements of various types of foreign and Polish ultrasonographs in our laboratory using for this purpose membrane PVDF hydrophones. As for ophtalmology, we should mention the quantitative determination of the distance between various structures in the eye the so-called eye biometry with special ultrasonographs with presentation A. This method is nowa-

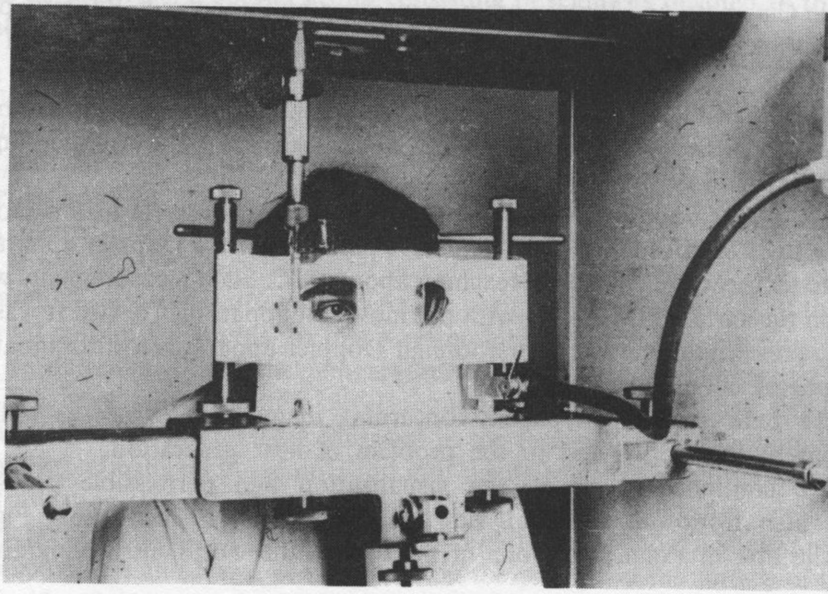

FIG. 9. The original compound scanning ultrasonograph for visualization of the eye [15] (1967).

days also applied to determine the parameters of plastic lenses implanted in the eye during cataract operations.

Noninvasive Doppler technique, strongly associated with ultrasonography at present, is the next domain which requires numerical parameters. In the first stage of development of this technique, the qualitative morphological analysis of the blood velocity curve was sufficient. Before long quantitative indices were introduced and further development was aimed at the determination of the linear velocity of blood in m/s, and then volume velocity, called volume flow, measured most frequently in ml/min. It is impossible to localize an examined vessel with the simplest continuous wave technique, whereas by means of the pulse method not only vessels can be localized, but also blood velocity and its distribution inside a vessel can be measured.

We have made first quantitative measurements of volume flow of blood in the carotid arteries in humans in 1975 [2], using several various ultrasonic methods at the same time [34, 46, 17] and obtaining the average value of 0.53 l/min (Fig. 10). Several techniques based on designed by us instruments have been applied in this research; visualization (Fig. 11) continuous wave Doppler technique, spectral analysis, pulse Doppler with double switchable beams. This last technique made it possible to eliminate the generally unknown inclination of the ultrasonic beam with respect to the direction of the blood flow. It was used by us to measure profiles of blood velocity distribution in the artery during the full cycle of the heart action. The information on the inclination angle and the geometry of the vessel can be nowadays read directly off the screen when the Doppler method is incorporated into the ultrasonographic equipment.

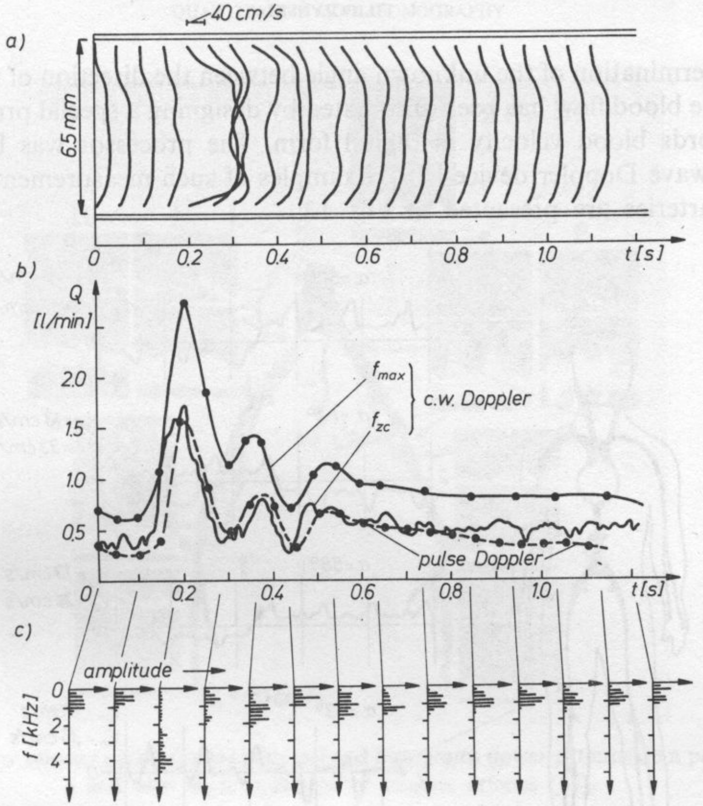

FIG. 10. Results of blood flow measurements in the carotid artery during one cycle of the heart action carried out by means of the pulse method (a), continuous wave method (b), and spectral analysis (c) [2] (1976).

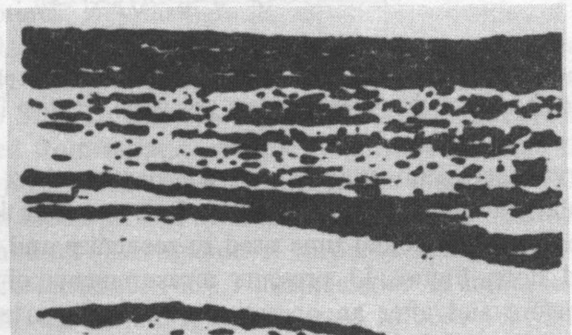

FIG. 11. The image of the carotid artery where measurements of the blood flow velocity and its distribution were carried out [2] (1976).

The determination of the unknown angle between the direction of the ultrasonic beam and the blood flow has been automated by designing a special processor which directly records blood velocity in digital form. The processor was built into the continuous wave Doppler device [45]. Examples of such measurements carried out in various arteries are presented in Fig. 12.

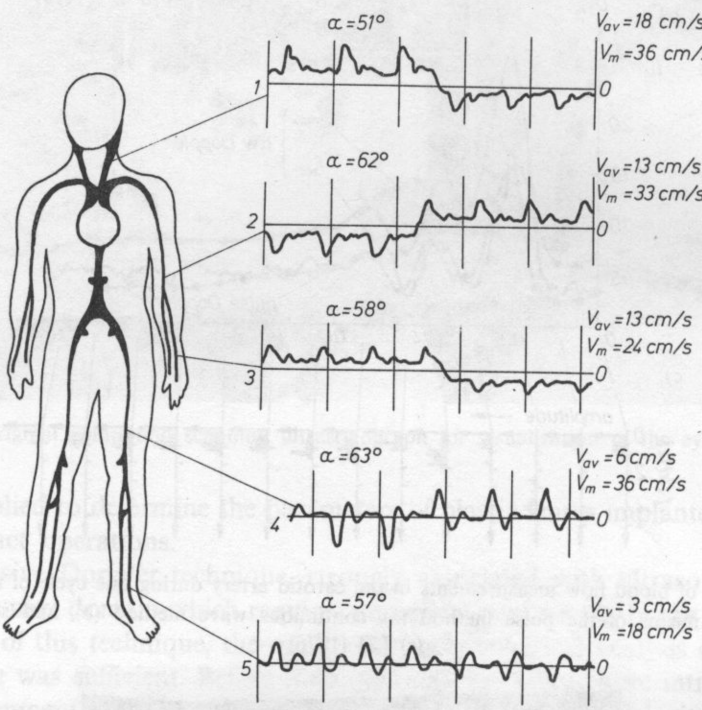

FIG. 12. Quantitative blood velocity examinations by means of an automatic Doppler system eliminating the angle dependence between the ultrasonic beam and blond direction [17, 45] (1978).

The time interval histogram analysis was the next method which made the evaluation of vascular flow disturbances possible. It is a certain kind of simplified spectral analysis performed in actual time used to recognize and evaluate disturbances of the blood flow. Figure 13 presents measurements of blood flow and histograms made before and after an operation of stenotic arteries [54].

The possibility of determining the size of collateral circulation in the thigh as the difference between the total flow, determined by means of the rheographic method in a thigh segment, and the amount of blood flowing through the femoral artery, determined by means of the ultrasonic Doppler technique is an interesting example of quantitative ultrasonography. On this basis the collateral circulation index can be determined; this quantity may be of great diagnostic significance [55, 37].

From the moment when microcomputer techniques were introduced to ultrasonography it became possible to determine linear dimensions of examined struc-

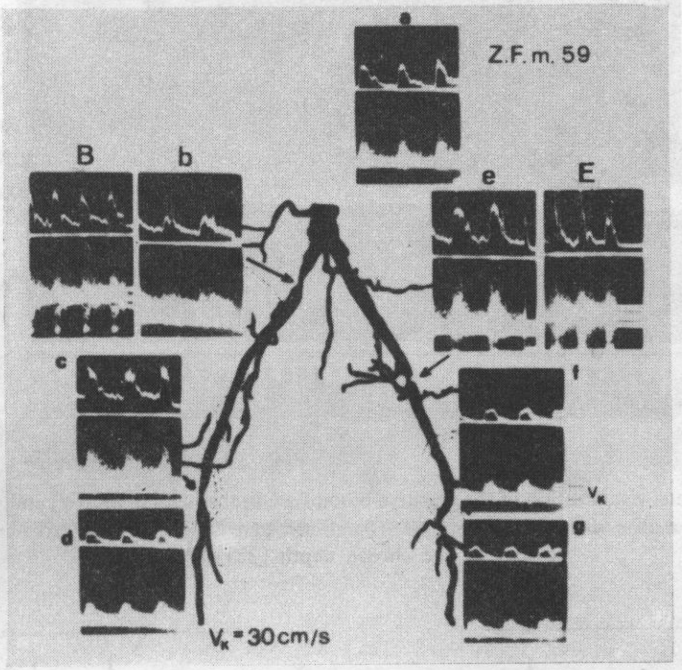

FIG. 13. Blood flow velocity curves (upper patterns) and histograms (lower patterns) in a patient before b, e and after B, E operation of stenotic arteries [53].

tures directly from ultrasonographic images, their surface, their volume at certain additional assumptions, grey histograms, as well as velocities of moving structures. This is of particular importance in cardiology. The visualization of flowing blood became possible by connecting the ultrasonograph with the Doppler technique and by developing the SEC Doppler technique (Stationary Echoes Cancellation) [39], which was adapted from radar technique. Figure 14 presents the visualization of blood flow in the jugular vein and the aorta at the same time [22], while in Fig. 15 we have records of blood flow in several heart structures obtained by means of this method. The method for investigation of coronary graft patency was developed on the basis of the SEC technique [40]. The application of colour is the further stage of development of this technique. It can be used to code the direction or even the velocity of blood flowing in big vessels, the heart above all.

At the present moment foreign centres are working on the idea of denoting the direction of blood flow with vectors in the form of small arrows additionally printed on the colour. Also a method for the determination of the stroke volume in liters of blood was worked out for cardiologic application. It is done by measuring the blood velocity in the aorta and by measuring the diameter of the aorta. An original method for detecting innocent vibratory heart murmurs in children was elaborated on the basis of the cepstrum analysis [38].

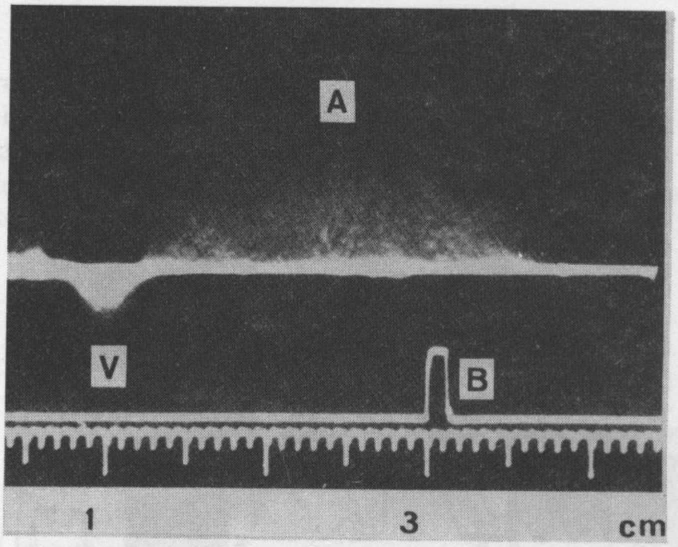

FIG. 14. Simultaneous visualization of the negative blood flow in the jugular vein (V) and the positive one in the aorta (A) by means of the SEC technique. The electric gate (B) enables measurements of the blood velocity at the chosen depth [22] (1982).

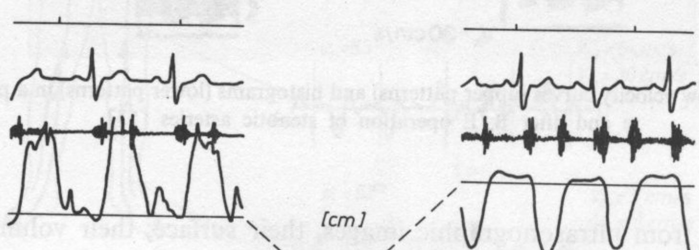

FIG. 15. The succeding records of time markers, ECG (a) FONO (B) and of Doppler blood velocities (c) carried out at 6 points at different depth in a childs heart by the UDP-30-SEC apparatus [22] (1982).

The Doppler transcranial technique for measurements of blood flows in cerebral arteries is an interesting method. Qualitative data achieved from the analysis of the blood veocity curve in terms of time are supplemented with spectral analysis in real time. However, this method does not result in quantitative data, yet it makes it possible to estimate disturbances of blood flowing in examined arteries. An example of such an examination is shown in Fig. 16.

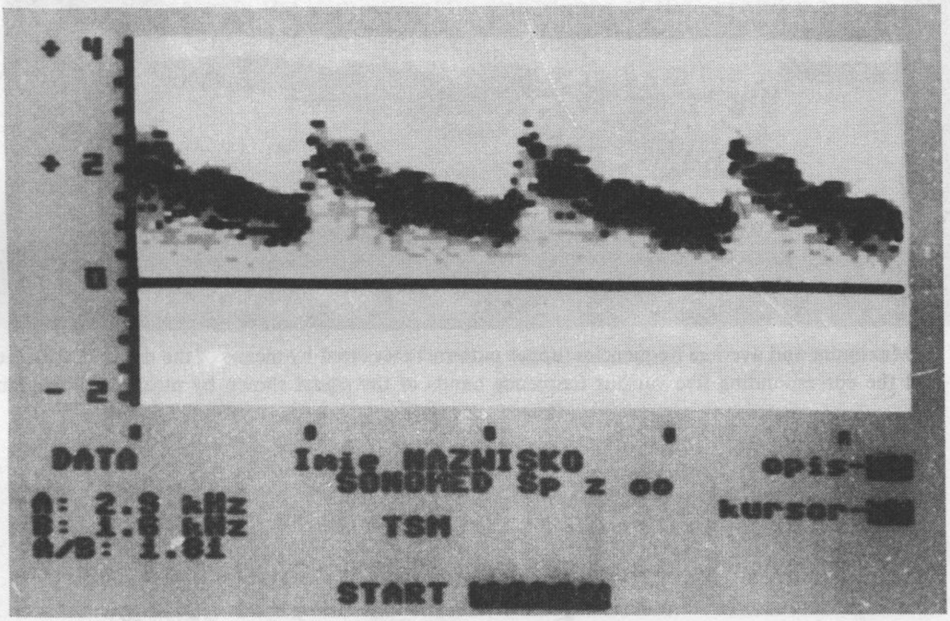

FIG. 16. Blood velocity measurements in the middle brain artery in terms of time carried out by means of the transcranial Doppler device IPPT PAN-Sonomed, Warsaw

The analysis of blood flow disturbances due to vascular pathologies is the subject of many papers, including Polish ones [41]. First of all, a system and device for bidirectional measurements of blood flow was developed to make correct interpretations of flows in disturbed areas possible [44]. Further research concentrated on methods for evaluation of the degree of disturbance by means of the analysis of Doppler signals in the domain of time [42] (Fig. 17). They were found helpful in determining methods of maximum blood flow velocity measurements using time interval histograms.

The determination of pressure gradients by means of blood velocity measurements is an interesting example of quantitative application of ultrasonography. This technique is based on the simplified Bernoulli's theorem [29, 37].

Another method of determining pressure in vessels was elaborated in our Department in 1985. This method consists in tracing movements of both vessel walls and measuring their displacement by means of the echo method in presentation A

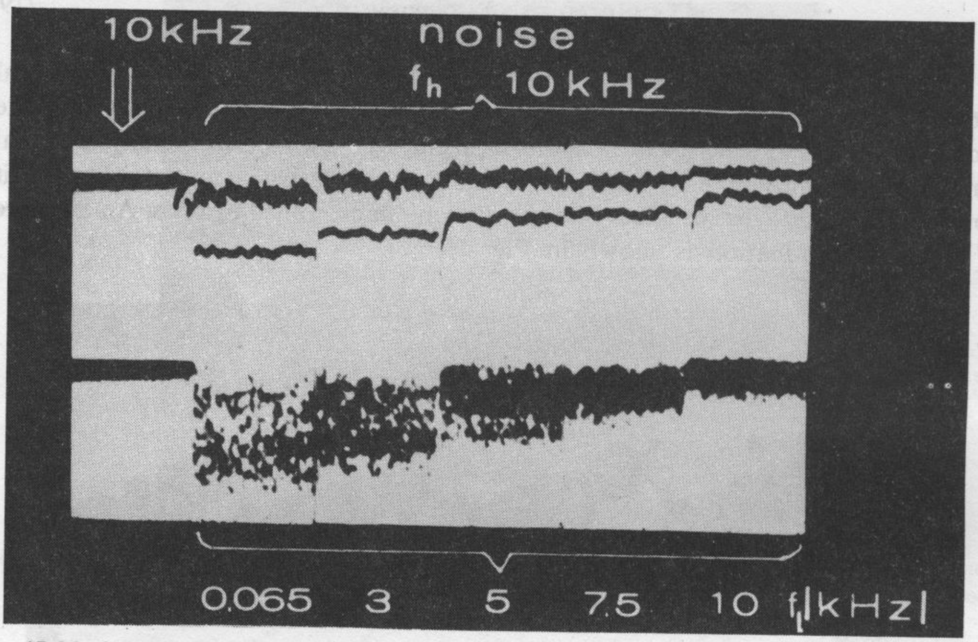

FIG. 17. Maximum and average frequencies (upper patterns) measured by means of the developed method [42] and the corresponding five various frequency bands of the signal shown by means of histograms (lower patterns).

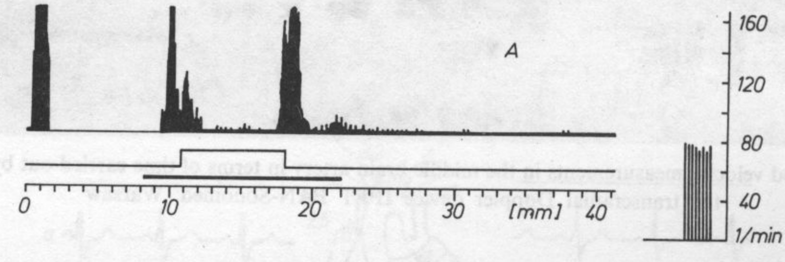

FIG. 18. Simultaneous recordings of the measured carotid artery walls movements and the heart beat frequency (A), changes of the carotid artery diameter (B) and the blood velocity (C) [46, 47] (1981, 1988).

[49, 51]. On the basis of a wide experimental material a relationship between the change in the vessels cross-section and internal pressure can be found [50]. The volume flow in ml/min is determined by measuring blood flow velocity with the Doppler method and by measuring the vessels cross-section (Fig. 18) On the basis of blood pressure and volume flow changes determined at the same time, the microprocessor calculated the hemodynamic impedance of the vascular system [48, 47].

Figure 19 presents the hemodynamic impedance of the carotid artery, obtained with this method. The whole calculation procedure is automatic and it is carried out by a special computer while the measurement is made with a duplex type special

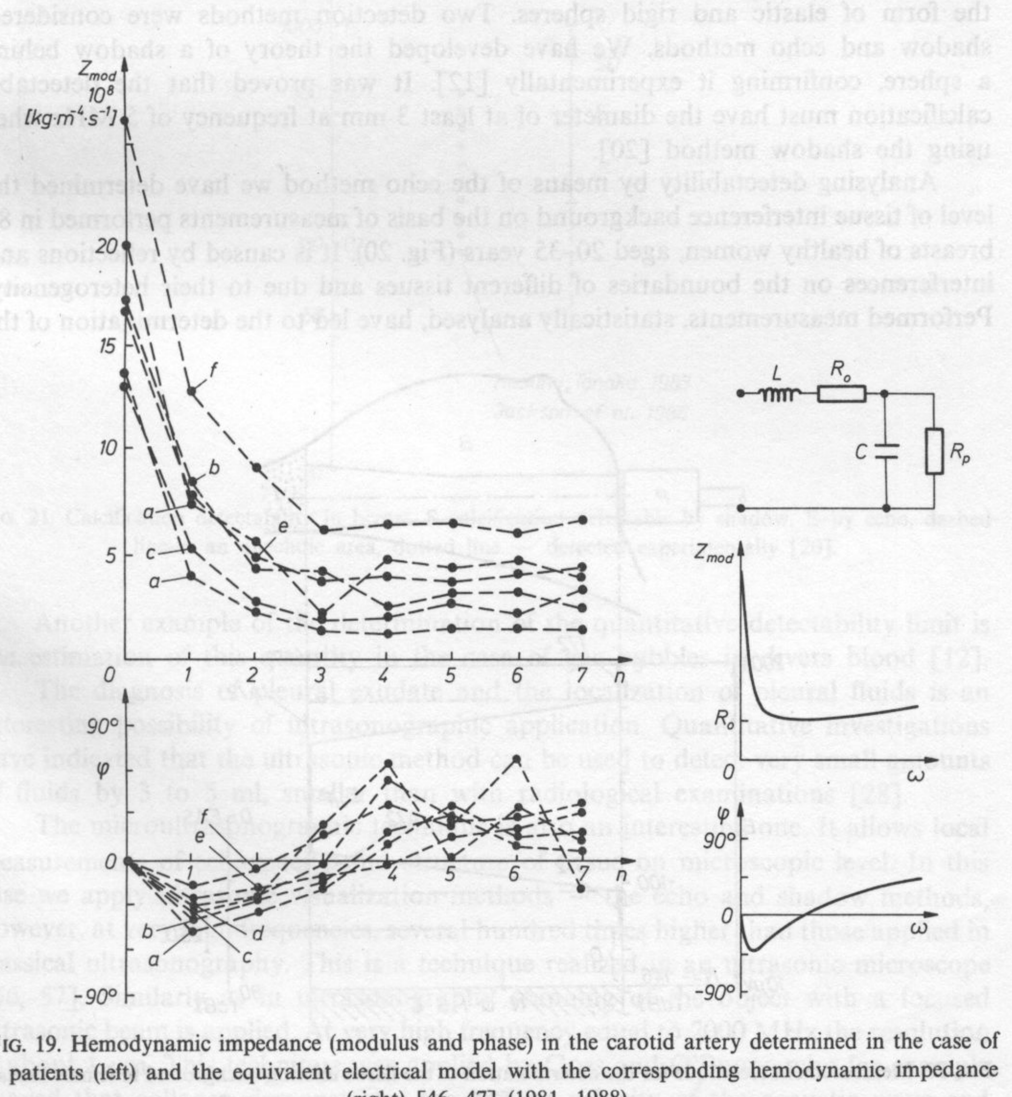

FIG. 19. Hemodynamic impedance (modulus and phase) in the carotid artery determined in the case of 6 patients (left) and the equivalent electrical model with the corresponding hemodynamic impedance (right) [46, 47] (1981, 1988).

head. This method can be used not only for the noninvasive determination of the hemodynamic impedance, but also for the determination of the vessels rigidity by means of joined ultrasonographic and Doppler technique.

The determination of a quantitative limit of pathologic structure detectability with ultrasonography is a very significant problem. The general case of this problem is very complicated because of various shapes, acoustic properties and structures of detected tissular systems. However, it is worth to make an atempt of answering this question for particular cases.

We have chosen calcifications occurring in the early stage of the neoplastic disease in breasts. This issue was analysed on two models, namely calcifications in the form of elastic and rigid spheres. Two detection methods were considered, shadow and echo methods. We have developed the theory of a shadow behind a sphere, confirming it experimentally [12]. It was proved that the detectable calcification must have the diameter of at least 3 mm at frequency of 5 MHz when using the shadow method [20].

Analysing detectability by means of the echo method we have determined the level of tissue interference background on the basis of measurements performed in 82 breasts of healthy women, aged 20–35 years (Fig. 20). It is caused by reflections and interferences on the boundaries of different tissues and due to their heterogeneity. Performed measurements, statistically analysed, have led to the determination of the

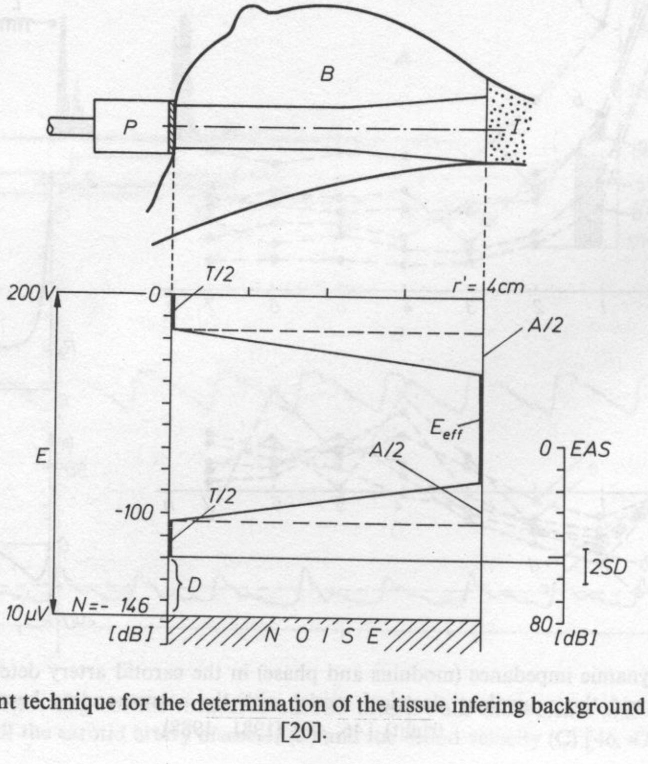

FIG. 20. Measurement technique for the determination of the tissue infering background in female breasts [20].

minimum diameter of detected calcifications, equal to 0.4 mm [20, 52]. The possibility of distinguishing echoes of calcifications increases during the detection of calcifications on the background of the neoplasms shadow.

If the tissue interference background is neglected, then detectability increases by one order of magnitude, as marked with a dashed line in Fig. 21.

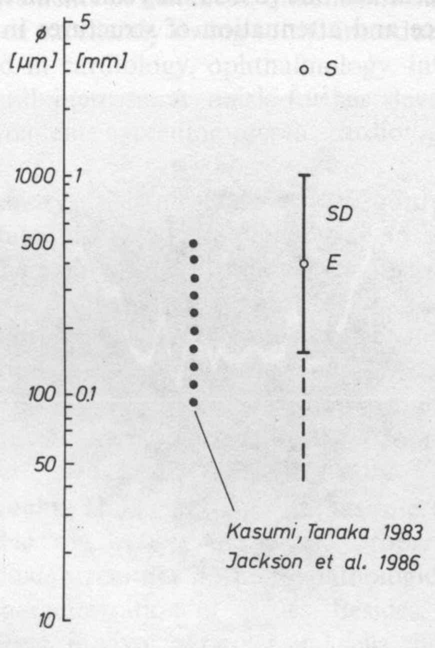

FIG. 21. Calcification detectability in breast. S–calcification detectable by shadow, E–by echo, dashed line-in an anechoic area, dotted line – detected experimentally [20].

Another example of the determination of the quantitative detectability limit is the estimation of this quantity in the case of gas bubbles in divers blood [12].

The diagnosis of pleural exudate and the localization of pleural fluids is an interesting possibility of ultrasonographic application. Quantitative investigations have indicated that the ultrasonic method can be used to detect very small amounts of fluids by 3 to 5 ml, smaller than with radiological examinations [28].

The microultrasonographic technique is also an interesting one. It allows local measurements of echogeneity and structure of tissue on microscopic level. In this case we apply ultrasonic visualization methods – the echo and shadow methods, however, at very high frequencies, several hundred times higher than those applied in classical ultrasonography. This is a technique realized in an ultrasonic microscope [56, 57]. Similarly as in ultrasonography scanning of the object with a focused ultrasonic beam is applied. At very high frequency equal to 2000 MHz the resolution is about 1 μm. This technique was applied by GOSS and O'BRIEN, who for example proved that collagen demonstrates the highest velocity of the acoustic wave and therefore highest impedance and, what follows, the highest echogeneity among soft tissular structures [27].

The possibility of investigations of cells in vivo, e.g. neoplastic cells, of determining acoustic parameters of these objects and of observing their dynamics are the important advantages of an acoustic microscope. An in vivo image with a signal distribution along a determined line [33, 31, 32] can be an example. It can be used to determine the impedance and attenuation of structures in observed cells (Fig. 22).

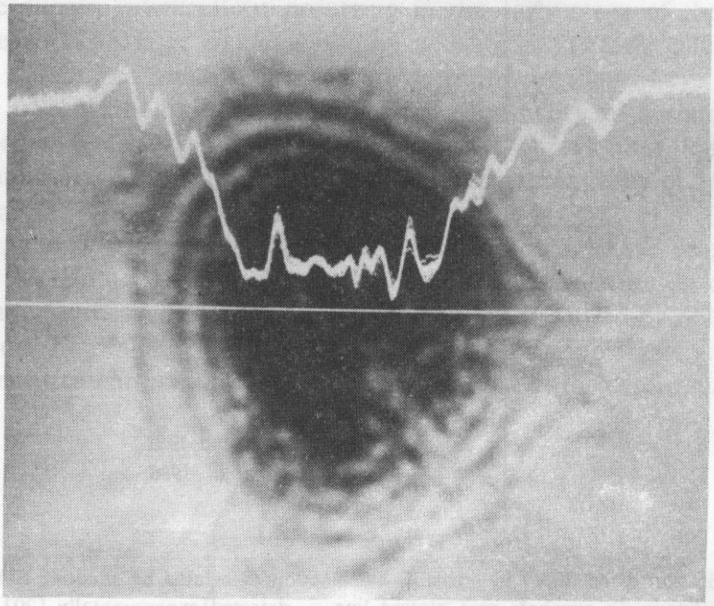

FIG. 22. Distribution of the acoustic signal along the living cell obtained by means of the acoustical microscope with the frequency of 2GHz enabling the determination of the local impedance, attenuation and thickness [33, 32]

Conclusions

To finish this review it seems useful to consider the following five trends of quantitative ultrasonography development:

1. Tissue characterization. Research is aimed at the determination of types of pathologies of detected structures. It is a very complicated problem. Information about these structures which should be obtained in vivo depends on many parameters, such as: frequency, attenuation, scattering, geometry, spectral parameters of tissues, parameters of ultrasonic beams penetrating the tissues etc. Thus, the work performed within this topic during the last 20 years has not given satisfactory results. Several leading centres have developed certain conceptions, but they are put to clinical use only within those centres for their own use [53]. Clinical investigations on a large scale, which would allow the acceptation or rejection of these conceptions, can not be carried out due to a lack of highly advanced and availabe apparatus. Producers of ultrasonographs have yet not decided to take the risk of investing in this type of equipment.

2. Biometry. Measurements of distances, dimensions and velocities of examined structures have developed excellently owing to the introduction of microcomputers. They are widely applied in cardiology, ophthalmology, internal medicine etc. and their application will still increase. A quick further development of blood flow visualization and measurements exceeding present cardiological applications should be expected.

3. Ultrasonic dosimetry. This problem is constantly current' especially in obstetrics, since it was stated that ultrasound may have an harmfull thermal effect on the nervous system of the embryo. Several groups of scientists abroad are working on this problem right now. The creation of a special committee for the investigation of this problem in the World Health Organization indicates its importance. It seems an optimal solution to design a special dosimetric device which would measure the dose accepted by every patient during an ultrasonic examination. On the basis of such an information it would be possible to carry out credible epidemiologic research in this field.

4. Microultrasonography. This new technique has interesting perspectives. First of all it makes possible to determine acoustic properties and, consequently, echogeneity of various tissue structures including pathological ones. This could be of great importance for characterization of tissues. Besides, this new field can find application in examinations "in vivo" of tissues and cells, their dynamics etc., what is impossible with such techniques as optic or electron microscopy.

5. Vascular ultrasonography. It seems that this specialization will develop quickly and will be quickly introduced to clinical ultrasonography. There are already possibilities of measurements of movements of vascular walls of blood flow determination, measurements of blood pressure dynamics as well as determination of hemodynamic impendance and even the rigidity of vessels. This absolutely new information can be achieved with fully noninvasive ultrasonic method "in vivo".

Moreover, further progress in microelectronics and in ultrasonic technology undoubtedly will result in the development and price decrease of the existing ultrasonic instrumentation and in the construction of new models, which will enable the introduction of new ideas of quantitative ultrasonography to clinical practice.

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