Ultrasound in Medicine—A Review

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Abstract—**Ultrasonic techniques are becoming increasingly important in medicine, both as a diagnostic tool and as a therapeutic modality. Although ultrasound has been used in medicine since the 1930's, it is only recently that these techniques have been widely used and their potential fully recognized. Medical ultrasonics is now in a period of rapid growth and is on the verge of making a significant impact on clinical medicine. The field provides challenging and important engineering problems, which are unique to medicine and biology. It is an open proving ground to many techniques developed for other applications and gives inspiration to the development of new technological advances. This review outlines some of the basic principles of ultrasonics, discusses the acoustical properties of biological tissues, provides a historical perspective of the use of ultrasound in medicine, describes ultrasonic techniques presently used in the clinic as well as those now under development, and reports on the standardization of medical ultrasonic procedures and measurements.**

INTRODUCTION

Ultrasound is becoming increasingly important in medicine and is now taking its place along with X-ray and nuclear medicine as an important diagnostic tool. Every day in thousands of hospitals and medical centers around the world, ultrasound is in routine clinical use in such diverse body regions as the brain, heart, liver, kidney, fetal and reproductive systems. In many ways ultrasound is an ideal diagnostic tool—it is noninvasive, externally applied, nontraumatic, and as all available data indicate, apparently safe at the acoustical intensities and duty cycles encountered in existing diagnostic equipment.

The goal of this paper is to present a tutorial review of the principles of medical ultrasonics and an introduction to a variety of its applications. An effort has been made, wherever possible, to present the discussion in terms familiar to both engineers and physicians. This review provides a historical perspective of ultrasound in medicine, discusses the acoustical properties of biological tissues, outlines some of the basic principles of ultrasonics, describes techniques presently used in the clinic as well as those now under development, and reports on the standardization of medical ultrasonic procedures and measurements. Diagnostic techniques are emphasized since they are the most common and, at present, are the most successful. The reader interested in pursuing the subject of medical ultrasonics in greater depth may wish to consult any of the several books listed at the end of this article.

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I. HISTORICAL PERSPECTIVE

The use of ultrasound in medicine was initiated by a relatively small number of investigators, most of them still alive and active, who span the time from the inception of fundamental ideas and the beginning of medical applications to the present clinical systems. These investigators came from a variety of disciplines and generated the interaction between technology and medicine which led to the first generation of ultrasonic devices that now provide the basis for present medical practice.

The interaction between ultrasound and living systems has been studied since the 1920's. It was the discovery of the piezoelectric effect and its utilization in the construction of high frequency mechanical vibrating sources coupled to high frequency electronic drives that provided the basis for this work. Without attempting to be exhaustive, Table I shows the chronology of some pertinent developments. During the 1940's and 1950's, ultrasound was in a rather slow evolutionary period. The techniques and technology developed during this period and now in common use are indicated in Table I and discussed further in Section IV. During the 1960's an ever-increasing number of physicians began to accept ultrasound and to use this modality in the clinic. In the 1970's we are now witnessing the widespread use of ultrasound, as well as the development of new and innovative techniques, as detailed in Table I and Section VI.

Some early research workers identified irreversible interactions between ultrasound and living systems [4], [5], [116]–[121]. The mechanism of this interaction was often only qualitatively investigated. It was apparent that absorption coefficients for tissue and biological systems were such that thermal damage could be produced [26], [27], [122]–[124]. Cavitation, which was a grossly observed phenomena associated with high frequency sound fields in liquid media, was presumed to be responsible for irreversible changes [121]. Other possible mechanical effects were suggested, but no definitive experiments were performed.

With evidence of interactive effects on biological systems and with equipment that could produce low intensity ultrasound (maximum intensity of a few watts/cm^2) readily available, there arose medical application groups interested in this modality for human therapeutics [124].

TABLE I
CHRONOLOGY OF PERTINENT DEVELOPMENTS RELATING TO ULTRASOUND IN MEDICINE

Piezoelectric effect[1]	J. Curie, P. Curie	1880
Electronic vacuum tube[2]	L. Deforest	1907
Sonar[3]	P. Langevin	1918
Effects on biological systems[4,5]	A. L. Loomis, R. W. Wood, E. N. Harvey	1927-28
Early real time ultrasonic imaging[6,7]	S. Sokolov, R. Pohlman	1929-49
Low intensity medical therapeutics[8-12]	R. Pohlman, H. Gohr, T. Wedekind, A. Denier, J. Lehmann, J. Aldes	1939-54
Pulse echo in NDT[13]	F. A. Firestone	1942
Ultrasonic Transmission imaging in tissue[14,15]	K. Dussik, T. F. Hueter	1942-50
Pulse echo in medicine[16-18]	J. Wild, J. Reid, D. Howry	1950-52
Ultrasonically generated lesions in Central Nervous System (CNS)[19-25]	J. Lynn, T. Putnam, W. Fry, F. Fry, T. Hueter, H. T. Ballantine, M. Oka, P. P. Lele, T. Takeuchi	1944-63
Thermal effects[26-28]	J. Herrick, F. Krusen, J. F. Lehmann, J. Gersten	1950-53
Other basic mechanism studies in tissue[20,29-44,49]	F. Fry, W. Fry, F. Dunn, P. Schwan, W. Nyborg, E. Bell, Y. Kikuchi, P. P. Lele, E. L. Carstensen, C. R. Hill, K. Taylor, J. Pond, M. Dyson	1950-69
Absorption (blood)[43,44]	H. P. Schwan, E. L. Carstensen	1952-59
Medical scanning[16,18,45-50]	D. H. Howry, J. Holmes, J. Wild, L. Leksell, Y. Kikuchi, T. Wagai, W. McKinney	1950-69
Heart[51,52]	C. H. Hertz, T. Edler, S. Satomura	1954-57
Obstetrics and gynecology[53-55]	I. Donald, G. Kossoff, T. Wagai	1958-65
Eye[56,62]	G. Baum, A. Oksala, I. Greenwood, W. Bushmann, E. Purnell, A. Sokollu, N. Bronson, K. Ossoinig	1956-65
Brain - Prefrontal lobotomy[63]	P. A. Lindstrom	1954
Brain - Stereotaxic neurosurgery and brain scanning (human)[64,65]	F. J. Fry, W. J. Fry, R. Meyers, R. F. Heimburger	1958-70
Blood flow - transit time[66-67] Pulsed[68] Doppler[69] Pulsed Doppler[70,71]	H. Kalmus, J. Herrick D. Franklin, D. Baker D. Franklin D. Baker, P. Peronneau	1954-55 1959 1961 1969
Optical holography[72]	D. Gabor	1948
Meniere's disease[73-75]	F. Altmann, M. Arslan, G. Kossoff	1959-64
Proof that normal liver is non transonic; characterization of liver and breast tissue; identification of acoustic attenuation of breast tumors[76-80]	E. Kelly Fry	1966-71
Application of computer to ultrasonic visualization and tissue modification[81-83]	W. J. Fry	1965-68
Laser, maser[84-87]	C. Townes, A. L. Schawlow, T. H. Maiman, N. G. Basnov, A. M. Prokhorov	1954-60
Acoustic holography[88-91]	P. Greguss, R. Mueller, A. Metherell, B. Brenden	1965-68
Acoustic parameter determination[30,36,92-97]	R. Pohlman, E. Carstensen, H. Schwann, D. Goldman, T. Hueter, W. J. Fry, F. Dunn, J. Jones	1939-73
Synergistic effects[98,99]	K. Woeber, C. Hill	1954-70
Bragg imaging in acoustics[100]	A. Korpel	1966
Time delay spectrometry[101]	R. Heyser	1967
Sokolov Tube[102]	S. Sokolov	1937
Medical imaging with Sokolov Tube[103]	J. Jacobs	1964
Acoustic microscope[104-109]	S. Sokolov, F. Dunn, W. Fry, E. Suckling, C. Quate, A. Korpel, L. Kessler, B. Auld	1949-72
Random signal radar[110]	G. Cooper	1966
Random signal Doppler[111-112]	V. Newhouse, C. Jethwa	1973-74

Physical medicine and chiropractic practice have continued to employ similar devices. Although there are a number of contraindicated body regions for ultrasound irradiation delineated by this experience, results of more recent experiments indicate the possibilities of new areas of therapy in some of these very regions. These possibilities will be discussed in Section VII.

Somewhat later, the possibilities of using ultrasound of much higher intensities (up to several thousand watts/cm^2) [19]–[21] to create lesions in biological tissues and of using ultrasound of much lower average intensities (several hundred milliwatts/cm^2) [16]–[18] for diagnostic purposes were investigated. The high intensities were shown to produce quantitatively reproducible lesions in central nervous system (CNS) [19]–[25], [31], [35], [125]–[127] tissue and subsequently other tissue (liver [33], [34], [42], muscle [129], blood vessels [130]) with the potential as a precise lesioning technology for a variety of activities including surgery [64], [65], [125], [127], [131], [132].

The low intensities operating in a pulse-echo (sonar) mode were shown to be capable of discrimination between a wide variety of nonbone tissue types leading to soft tissue acoustic visualization systems [16]–[18], [133]–[135].

II. PRESENT STATUS OF ULTRASOUND IN MEDICINE

The noninvasive character of ultrasound and its ability to distinguish interfaces between tissues of different acoustical impedances has been its main attraction as a diagnostic procedure. In contrast, X-rays only respond to atomic weight differences and may require the injection of a more dense contrast medium for visualization of nonbony tissue. Nuclear medicine techniques, which measure the selective uptake of radioactive isotopes in particular organs and thus produce information concerning organ function, provide a third form of medical diagnostic practice involving imaging that is of great clinical significance. Radioactive isotopes and X-rays are both clearly invasive [113]–[115].

Although ultrasound has been used in diagnostic medicine for over twenty years, it is only within the last few years that its use has become wide spread. This slow growth may be due to the fact that ultrasound (or at least pulse-echo procedures) generally presents diagnostic information in a form somewhat foreign to the radiologist or nuclear medicine specialist. Moreover, ultrasonic equipment presently available requires considerable training and practice on the part of the physician or technologist using the instrument. We should be careful to note that, despite these limitations, medically useful information is routinely obtained. Even more important, much of the information obtained by ultrasound could not be obtained with any other modality or without procedures that may be inherently more dangerous to the patient.

In diagnostic ultrasound there are more than 7500 devices, including Doppler systems, now operated in the United States. Several thousand physicians and ultrasonic technologists routinely use this modality. Today the most widely represented medical areas for ultrasound are cardiology, obstetrics, and gynecology, with somewhat lesser activity in abdominal organ scanning, brain midline detection, thyroid evaluation, eye scanning, and blood flow determination.

Unfortunately, ultrasound in the frequency range presently used for diagnosis and therapy cannot penetrate any substantial gas layer because of the high tissue-to-gas impedance mismatch. Diagnosis of lung conditions that are overlayed with normal gas-containing lung tissue cannot be performed with ultrasonic devices presently available. Other body areas difficult to reach with present equipment are those obscured by mature adult bone (such as the brain).

In the past, clinical users of ultrasonic techniques were largely self-taught since formal training programs were nonexistent. Formal ultrasonic instruction programs are just now beginning at a few medical centers. Such programs are quite encouraging since in medicine, as in any other discipline, a new status is reached when the educational process recognizes the need to instruct its newest members in the latest achievements. Moreover, with the advent of computer technology, integrated circuits, sophisticated signal processing procedures, acoustic holography and imaging, and a variety of other technologies and methods being promulgated by a number of young investigators seeking ways to display their talents in a more societally relevant way, there has surfaced in the last decade a much broader interest in ultrasound in medicine. Private companies and foundations, research institutes, and governmental agencies are supporting interdisciplinary groups that are developing the next generation of ultrasonic devices. These devices are of a variety of types and, for the most part, have yet to be given clinical trials. Recently, U. S. Federal agencies have funded various task groups [136]–[138] to help define problem areas and aid in the establishment of priorities to assist these agencies in relating to this activity. Current research is following the explosive growth of technology and represents one of the most exciting and rewarding areas of applied science and engineering. Many fundamental problems are unsolved, and there is a real need to improve currently available instrumentation.

Closely related to the growing stature of ultrasound in medicine is the parallel emergence of a new group of bioengineering professionals just now appearing in reasonable numbers. Until now most people in the physical sciences who attempted to apply ultrasound to medicine were required to acquire their medical skills on their own. Similarly, physicians who attempted to improve state-of-the-art ultrasonic techniques were largely self-taught in the physical sciences and engineering. The groundwork is now being laid for a much closer and a more formal collaboration between medicine and the physical sciences and en-

gineering. This interaction should significantly advance ultrasound in medicine as well as medical technology in general.

III. ACOUSTICAL PROPERTIES OF BIOLOGICAL TISSUE

The human body and even relatively homogeneous tissue, such as the normal liver, exhibit tremendous complexities in their interaction with sound. Accurate physical measurements are often very difficult to make in the low Megahertz frequency range since the finite size of the measuring transducer often distorts the value of the very quantities being measured. In addition, measurements on living tissue are generally difficult to obtain, particularly in the case of human patients where medical standards and protocols must be maintained. If measurements are made *in vitro* or with fixed tissue, the measurements must be compared with *in vivo* results to be biologically meaningful. These practical problems account for the present paucity of reliable, well-documented information in this area, which only now is receiving the much needed attention it deserves.

In biological tissues, there is only a minor dependence of the sound velocity on frequency, at least in the 1–20 MHz frequency range that covers most medical applications at present. For example, a small dispersion amounting to approximately 0.15% velocity change for a 1–10 MHz frequency change has been recorded for beef hemoglobin [37]. At present, it is unclear how even a small velocity dispersion effects or limits the resolution of various acoustic imaging systems.

Since live human tissue is generally at a constant normal body temperature of 37°C, there is little need in present diagnostic regimes to consider effects of temperature on the acoustic properties of tissue. This is not to imply that such temperature effects should be ignored, since interesting possibilities utilizing temperature changes have been suggested for experimental studies with the aim of possible future medical applications [139]–[141].

Acoustic absorption plays a major role in all tissues of medical interest. The sound intensity I decreases with the distance of propagation x according to

$$I = I_0 e^{-2\alpha x} \tag{1}$$

where I_0 is the intensity at $x = 0$, and α is the acoustic pressure absorption coefficient. The factor of 2 in the exponential results from transforming pressure into intensity, since under plane wave conditions the intensity is proportional to the square of the pressure. For tissue, absorption is approximately proportional to frequency [143], ($\alpha \propto f$), whereas classical absorption mechanisms result in a quadratic frequency dependence ($\alpha \propto f^2$), [142]. Individual tissues may vary somewhat from this relation. For instance, hemoglobin in solution has an absorption $\alpha \propto f^{1.3}$ in the frequency range from 35 Hz to 10 MHz [44].

Absorption in tissues is primarily related to the protein content, although there is a component of absorption that is apparently related to other constituents [143]. In general, it appears that acoustic absorption in tissue can be described by a relaxation process in which acoustic energy is highly attenuated at certain particular frequencies, which are determined by the material's molecular properties [142]–[145].

Since most ultrasonic diagnostic equipment operates in a pulse-echo mode, it is important to consider the interaction of various acoustic pulse waveforms with tissue. A highly damped oscillatory waveform is typically generated. Thus short bursts of sound having significant amplitude for only a few cycles are transmitted through the tissue and undergo absorption loss described by (1). These short acoustic pulses are refracted, reflected, and scattered by structural details within the tissue. Because of relatively small velocity changes in various soft tissue media, refraction is generally not a serious problem. It is, of course, much more pronounced if bone is involved in the sound pathway. Velocities and directions of both longitudinal and shear waves are related in terms of Snell's law. Soft tissues are perhaps also isotropic, although piezoelectric action in cholesterol plaque and bone has been reported, which demands anisotropy.

At the boundary between two media having different densities and/or acoustic velocities, a reflection will occur. For normal incidence of unbounded longitudinal waves on an infinite plane surface, the pressure amplitude reflection coefficient R is given by [159]

$$R = \frac{Z_1 - Z_2}{Z_1 + Z_2} = \frac{\rho_1 c_1 - \rho_2 c_2}{\rho_1 c_1 + \rho_2 c_2} \tag{2}$$

where ρ is the density, c is the sound velocity, and $Z = \rho c$ is the specific acoustic impedance of the medium. The pressure amplitude transmission coefficient is simply $(1 + R)$. These equations represent only the ideal case since angular variations of the incident beam with respect to the boundary will be the general situation met in tissues; however, they serve as guidelines for order of magnitude determinations in approaching the more complex situations. It should be noted also that if the sound passes from a lower to a higher impedence, the reflected wave is in phase with the incident wave, but it suffers a 180° phase reversal if the sound passes from a higher to a lower impedance medium.

A chart showing the velocity of sound, the density, and the characteristic acoustical impedance of selected materials is shown in Fig. 1. Table II list absorption coefficients for similar materials. Table III gives the reflection coefficients for some interfaces of importance in medical diagnosis. Acoustic parameter determination for normal and pathological tissues has yet to be extensively developed, which accounts in part for the paucity of information in Tables II and III. However, this area is extremely important since, as will be discussed further in Section VI, it appears that many types of normal and abnormal tissues can be uniquely classified in terms of their acoustical

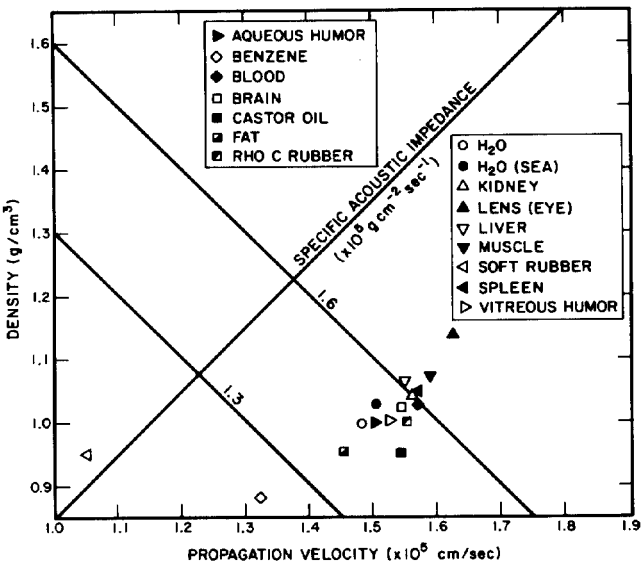

Fig. 1. Velocity of sound, densities and characteristic acoustical impedances of biological tissues and other selected materials.

TABLE II
ACOUSTIC PRESSURE ABSORPTION COEFFICIENTS

Material	Frequency MHz	α (cm^{-1})
Brain	1.0	.10
Brain tumors (formalin fixed)	5.0	
Meningioma	5.0	.73
Glioblastoma	5.0	.38
Metastatic tumor	5.0	.50
Normal brain	5.0	.44
Fat	1.0	.08
Muscle	1.0	.13
Liver	2.0	.19
Kidney	2.0	.27
Blood	2.0	.04
Bone (human skull)	1.2	1.7
	2.25	5.3
	3.5	7.8

properties and that such a classification scheme could be incorporated into a diagnostic system. For example, recent studies [147] have indicated that specific brain tumors can be uniquely classified according to their acoustic reflection patterns. Other studies have shown that normal liver is nonsonoluscent and that it can be characterized according to internal structural reflections [76]–[78], [148]–[150]. *In vivo* and *in vitro* studies of female breast tissue have demonstrated that normal tissue can be characterized according to its structural elements and, more importantly, that certain malignant breast tumors may be classified by their acoustical attenuation properties [79], [148], [151]–[156]. The possible macromolecular level of this attenuation as correlated with the structural components of the tumor (determined by whole breast pathology) is a significant aspect of this work [80], [156], [157]. Another study has suggested that the elastic properties of soft tissues are largely responsible for their echographic visualizability and that these properties are determined in some cases by structural collagen-containing compounds [158].

Scattering of ultrasound by biological materials is an extremely important, yet largely neglected, field of study. It is particularly important in the study of blood flow [69], [161]–[163]. Doppler methods can be used to determine blood flow by measuring the frequency shift in the reflected ultrasonic wave due to the flowing blood. The blood cells in the flowing stream backscatter energy to a pickup transducer. Obviously, some knowledge of the scattering process is required for optimum system design. Although the scattering of ultrasound by biological materials is not well understood, several workers have been able to classify specific tissue types and disease states on the basis of their scattering properties [164]–[168]. For example, the frequency spectra of scattered signals from the surface of an exposed amphibian muscle is changed after vascular occlusion [146]. Further knowledge of the scattering process and better *in vivo* measurement techniques may eventually provide an additional basis for tissue differentiation. The study of scattering is still in its infancy and offers an important area for both fundamental and applied research.

The ultimate resolution capability of a wave interrogating a structurally inhomogeneous medium is a volume element about one wavelength in diameter. Since the sound velocity in soft tissue is about 1500 meters per second, the ultimate resolution in millimeters (R_{mm}) can be expressed as a function of frequency (f in MHz) by

$$R_{mm} = \frac{1.5}{f}. \tag{3}$$

Ultimate resolution is approximately 1 mm at 1.5 MHz and 0.1 mm at 15 MHz. The 1-mm resolution would be adequate for many large body structures such as a tumor or cyst in the abdomen, whereas the 0.1-mm resolution might be needed for visualization of structures in the eye. Practical limitations such as aperture size, target parameters (including patient organ movement), attenuation, scattering, acoustical nonlinearities, velocity dispersion, and electronic and detector signal-to-noise ratios combine to decrease the maximum resolution. System performance is primarily limited by tissue absorption characteristics and detector noise levels. Shorter wavelengths lead to excessive attenuation in thick structures, which cannot be overcome by increasing the input power levels at will, since nonlinear propagation effects alter the nature of the wave [160] and because an upper dosage limit is presumed to exist. As discussed in Section IX, biological effects can be demonstrated in longer pulse regimes, but for pulse lengths less than one millisecond the information is not extensive.

IV. PRESENT STATE OF THE CLINICAL ART

A-Mode Ultrasound Instrumentation

The oldest and simplest type of diagnostic ultrasound instrument uses *A*-mode or a time base oscilloscope dis-

TABLE III
ACOUSTIC REFLECTION COEFFICIENTS—ABSOLUTE VALUES

	Water	Fat	Muscle	Skin	Brain	Liver	Blood	Skull Bone	Lucite
Water	0.0	.047	.02	.029	.007	.035	.007	.57	.35
Fat			.067	.076	.054	.049	.047	.61	.39
Muscle				.009	.013	.015	.02	.56	.33
Skin					.022	.0061	.029	.56	.32
Brain						.028	.00*	.57	.34
Liver							.028	.55	.32
Blood								.57	.35
Skull bone									.29

* Clotted and freshly injected blood can be detected ultrasonically in the live and formalin fixed brain.

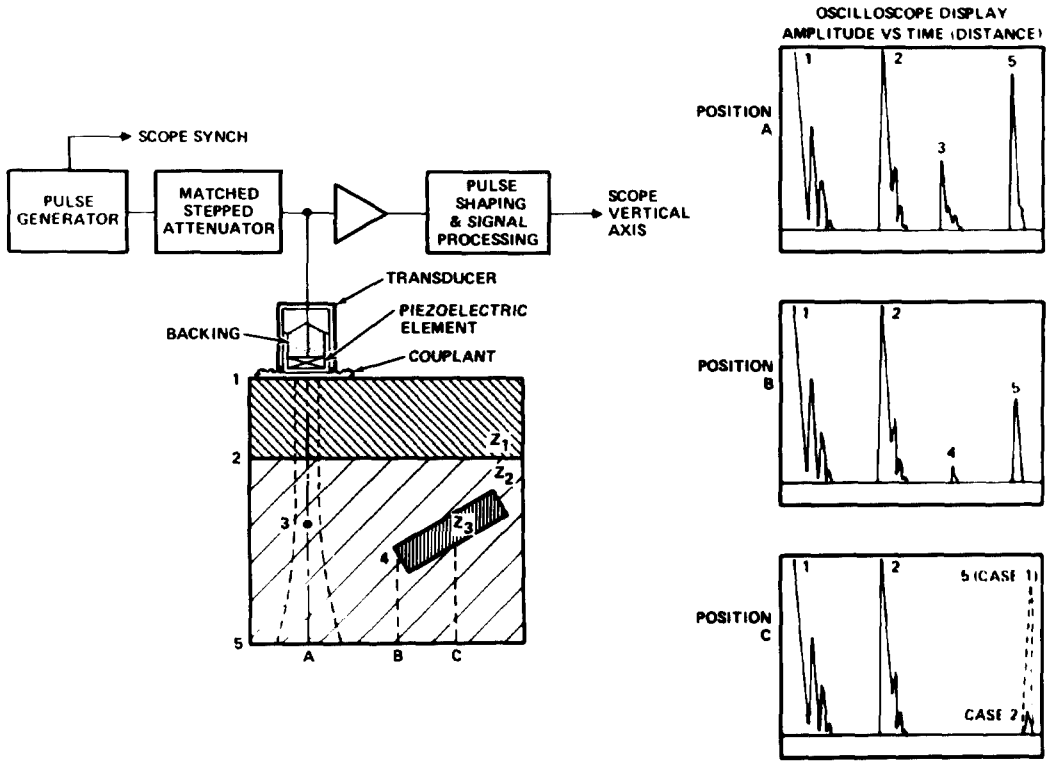

Fig. 2. Elements of an *A*-mode pulse-echo system and information presentation format.

play of received echo amplitudes. Figure 2 shows the basic elements in such a system, which was first introduced by Firestone [13] for industrial nondestructive testing.

The pulse generator typically produces a 100 volt to 1 kV spike waveform with a very fast rise time. This wideband waveform is sent through a matched stepped attenuator, and it is applied to a piezoelectric element such as Lead Metaniobate or Lead Zirconate Titanate (PZT), typically 1 to 2 cm in diameter, of which the resonance frequency is usually in the 0.5–25 MHz range. The piezoelectric element usually has a backing structure that provides damping to the resonant element producing wider bandwidth (bandwidths of 50% for 3 dB loss are typical) and absorbs the acoustical wave radiated from the back side. Pulse repetition rates vary from 500 Hz to 2500 Hz with 1000 Hz being a typical value. Peak acoustic intensities vary from 10 to 100 watts/cm^2 [342].

Acoustical pulse shape and width determine the axial resolution capability of the system. The spectrum of frequencies in the wave is determined by the electrical input spectrum multiplied by the transducer frequency response.

The ultrasound pulse is coupled to the subject through an aqueous gel or oil for a contact scanner. Deep tissue structures to be interrogated lead to transit times for the double path length from transceiver to target of up to 250 μsecs.

The amplifier used must have very good overload capabilities and a short recovery time since the electrical impulse to the transducer is often directly coupled as in Figure 2. Amplifiers must have a wide dynamic range (up

to 60 dB for certain cases) and often have a logarithmic stage. Usually some form of time-varying gain is included to compensate for signal attenuation with distance in tissue (approximately 1 dB/cm at 1 MHz). The amplifier must have a low noise level to receive deep targets and is often bandpass tuned, although broadband units are very common. Historically, the frequencies used in medical diagnosis are nominally 1 and 2.25 MHz for abdominal, cardiac, and brain measurements, and 10–25 MHz for eye work. These frequencies are chosen in a trade off between resolution, power levels, and the attenuation of the intervening tissue.

Pulse shaping and signal processing usually include full wave rectification and envelope detection (carrier frequency removal) and baseline display clipping. More sophisticated processing is often used.

Using a time base oscilloscope display with the transducer in Position A (Figure 2), we see at 1) the complex of echoes resulting from the transducer excitation and subsequent mechanical "ringing." Echo 2) is the first interface reflection. Echo 3) is the back-scattered reflection from a small spherical target centered on the transducer axis and, 5) is the reflection from the large impedance discontinuity at the bottom of the structure.

The radiation pattern of the transducer is shown in dotted lines. The acoustical "beam" has a finite width. As the transducer is moved horizontally, the sphere echo appears as the sphere enters the beam, generally peaks on axis, and then decreases.

If the tranducer is moved to Position C, the beam encounters the tilted pillbox structure of impedance Z_3 encompassing the entire beam. There are a number of cases of interest here.

Case 1: $Z_3 \simeq Z_2$. In this case, the beam will be refracted at the interfaces and emerge with its axis displaced just as a light beam would propagate. The small amount of reflection energy at each interface is directed away from the transducer and never received. A large return from surface 5 is received, but it is displaced in time because of the change in pathlength and sound velocity in Z_3.

Case 2: $Z_2 \simeq Z_3$, with Z_3 highly attenuating. This case is similar to Case 1 except that the received back-surface reflection is greatly reduced. This "shadow" effect is often used to differentiate solid cysts from fluid-filled cysts in a diagnosis, since solid cysts are often highly attenuating and fluid cysts are always acoustically transparent or "sonoluscent."

Case 3: $Z_2 < Z_3$. This would be the case, for example, of a metal fragment imbedded in tissue. One would ordinarily expect to see a very large reflection from the metal, but its inclination directs the energy away from the transducer and it is not seen. The back-surface reflection is also missing.

A-scan ultrasound has been very successful in the detection of foreign objects such as metal shards in a hemorrhaging eye [169]. This success is due to the rough shape of such objects and to the fact that they do not usually encompass the entire beam. Indeed, in Figure 2, if the transducer is moved to Position B, a small signal (4) arising from back-scattered edge diffraction at the corner of the pillbox would be received.

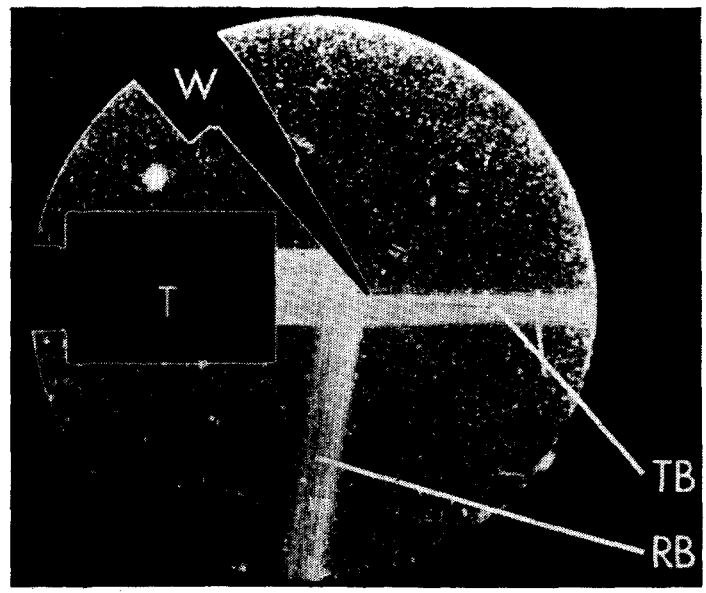

Fig. 3. Schlieren presentation of acoustic continuous wave beam partially blocked by a reflecting wedge. T—transducer; W—wedge; TB—transmitted beam; RB—reflected beam.

The finite width of the acoustic beam is one of the major limitations of present ultrasound systems and is the subject of considerable research. Figure 3 shows an ultrasound beam visualized in a water tank using a Schlieren optical system. It can be seen that the ultrasound does indeed form a beam (because the diameter of the piezoelectric element is about 100 sound wavelengths) and that it propagates much like a light beam. The ultrasound beam shown in Fig. 3 is a continuous wave, but pulsed ultrasound behaves similarly. Reflection from an interposed plastic wedge is almost 100%, and some diffraction can be seen at the edge. Unlike most optical systems, ultrasound systems are strongly dominated by diffraction effects because the ultrasound wavelength is not small with respect to the radial dimensions of the transducer (1 to 2 cm). A typical 2.25 MHz unfocused transducer operating in water has the following properties (see Section VI for a more complete discussion): azimuthal resolution (spot diameter or beam size)—6 mm, depth of field—60 mm (from 50 to 100 mm on axis), axial (time) resolution—1.3 μsec. = 2mm. Although ultrasound beams can be focused with an acoustic lens, diffraction is still very important. Focusing also leads to the classical dilemma of trading depth of field for focal spot diameter (azimuthal resolution).

Applications of A-Mode Ultrasound

One of the most useful and widespread applications of *A*-mode ultrasound has been echo-encephalography [47], [170], [171]. Using a simple time-base display allows position measurement of prominent brain structures such as the septum pellucidum, third ventricle, and lateral

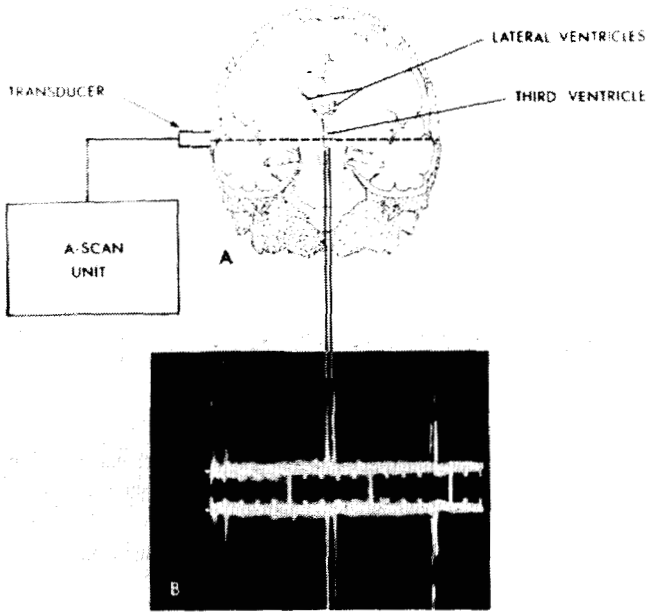

Fig. 4. An *A*-scan of human brain. A, human brain atlas cross section details; B, echo pattern showing third ventricle wall reflections. Observations of reflections from lateral ventricles requires a different transducer orientation.

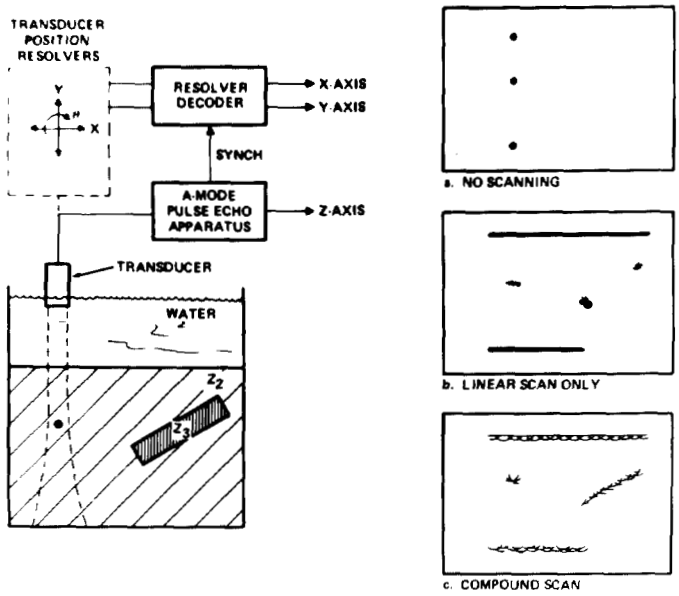

Fig. 5. Elements of a *B*-scan system and information presentation format.

ventricles, as shown in Figure 4. This test is used in emergency rooms and ambulances for rapid assessment of possible brain trauma, which displaces these structures. Echoencephalography is also used to detect space occupying lesions such as a tumor (which also displaces these structures) as well as for detection in the extraction of foreign objects from the hemorrhaging or clouded eye [169].

B-Scan Instrumentation

B-scanners use an *A*-mode unit together with transducer position sensors and an intensity or *Z*-axis modulated display to map out the reflectors in a two-dimensional

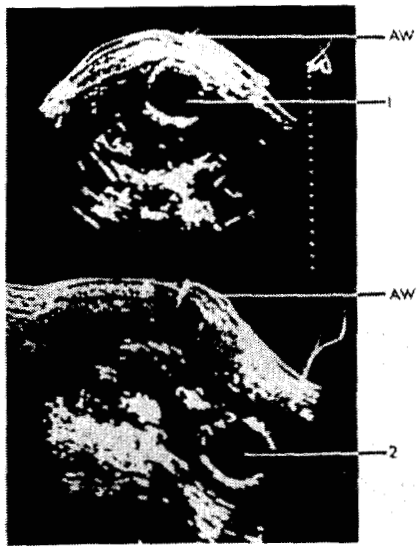

Fig. 6. *B*-scan of twins *in utero*. Two different scan planes are shown to best visualize the head of each twin. AW, anterior abdominal wall; 1, head of twin number one; 2, head of twin number two. (Courtesy of Dr. William Ragan, Assoc. Prof., Dept. of Obstetrics and Gynecology, Indiana University School of Medicine).

cross section. Figure 5 shows typical displays of the structure used for the Figure 2 display. With the transducer stationary (5a), dots are written on the screen at the position corresponding to the interfaces. If the transducer is scanned linearly in the X direction (5b) without rotation, the interfaces will be mapped on the display. Note that the small spherical target is displayed as a short horizontal line because of the transducer beamwidth. The ends of the Z_3 material are displayed, but the center portion at an angle is not. The back surface of the structure is also obscured by Z_3.

Most *B*-scanners in use today have provisions for compound scanning (restricted angular rotation of the transducer along with rectilinear motion in this example). This produces a much better mapping (5c) since the Z_3 interface is normal to the transducer axis for a fraction of the scan. It also produces a better indication that the sphere is a point target.

Generally, the transducer is scanned manually with an articulated (pantagraph) arm to transmit the transducer motions to the position resolvers. The system is arranged so that any motion of the transducer in the plane is reproduced on the display allowing scanning through a curved surface such as a maternal abdomen. The transducer is once again coupled to the skin with an aqueous gel or mineral oil. The display is usually a two-level storage CRT (a binary display). Echoes are required to exceed a threshold to write on the display. This threshold, together with the transducer beamwidth, causes the spherical target to be displayed as the intersection of several uniform lines, as in Figure 5 (c). Figure 6 shows a scan of twins *in utero* made with such a hand-operated compound *B*-scanner. Compared to a photograph or the layman's idea of an X-ray, this picture appears quite crude; however, useful diagnostic information can be extracted, which is not easily obtainable with alternate modalities.

A disadvantage of the hand-driven *B*-scanner is the subjective human element manual operation introduces into the mapping. In a very real sense, the technologist, like an artist, "paints" the image on the display. An experienced technologist can make excellent meaningful scans by knowing which features to emphasize and which controls to adjust on the echoscope. Unfortunately, well-trained technologists or ultrasonographers have been in short supply.

An additional problem with present *B*-scan systems is that many separate scans must be made to obtain a volume mapping. Typically, the physician then places Polaroid pictures of these slices side by side and then attempts to mentally synthesize a volume image. This is an example of a system not well matched to human perceptual capabilities.

Mechanized scanners are used in many research clinics throughout the world. These systems produce more consistent echograms, are more expensive than the contact scanners, but also allow the use of a gray scale display with integration of the mapping on film [82], [134], [172]–[179]. With these systems, the display of the sphere echoes begins to look more like a dot than the rosette pattern in Figure 5 (c). Recently, manufacturers have been selling similar gray scale displays with film integration for use with hand-operated scanners. This would appear to place a heavy burden on the technologist.

Another limitation of current *B*-scanners is the time involved in making a scan. Patient motion and target motion, including respiration, can cause registration errors in the scanning process. Often, as in fetal mapping, the technologist ends up chasing the baby around the uterus. In some cases this causes the effective system resolution to be reduced by a factor of ten. Moreover, the requirement for separate scans to image a volume increases the time required for *B*-scanning and leads to a decreased patient load. A patient load of two to three patients per hour is typical.

Applications of B-Scanners

The areas of the body accessible to contact *B*-scanning are limited to those with targets lying under a smooth large area of the skin without a large amount of intervening obstructions, such as bones or bowel gas. With a long water path between the transducer and the patient, the requirement for a smooth area is somewhat relaxed.

1) Obstetrics. *B*-scan can be used to determine the presence of one or more fetuses from the third to ninth month. Fetal abnormalities may be determined and the placenta localized. With a chronological sequence of images, growth rates can be established. Immediately before delivery, the position and condition of the fetus can be determined [53], [180]–[193].

2) Gynecology. Intrauterine tumors, hydatiform moles, and cysts may be detected early enough for surgery with a high rate of complete recovery [54], [180], [191], [193]–[195].

3) Abdominal organs. The kidney, liver, and spleen can be mapped for detection of tumors, cysts and calcifications, and determination of organ size [54], [195]–[200]. *B*-scan systems are also useful for positioning needles and other instruments.

4) Ophthalmology. Intraocular and orbital tumors as well as retinal detachments can be mapped in a clouded eye [58], [201], [202].

M-Mode Ultrasound

M-mode uses a standard *A*-mode instrument with a modified display. The *M*-mode display resembles the *B*-mode or intensity-modulated display with the exception that the horizontal axis is a slow time sweep with the vertical axis a fast time sweep corresponding to the distance from the transducer (pulse propagation time). The *M*-mode is useful for mapping moving objects such as heart structures or arterial walls. Figure 7 illustrates an *M*-mode display of a moving pendulum. Gray scale displays are fairly common in *M*-mode instruments.

Application of M-Mode to Echocardiography

One of the most interesting and rapidly growing ultrasound diagnostic arts is echocardiography [203]–[208]. Here, ultrasound can present motion versus time information about important heart structures that can be correlated with the electrocardiogram.

Figure 8 (a) illustrates a cross section of the heart showing regions accessible to the transducer beam as it is tilted. Figure 8 (b) shows an idealized *M*-mode display of those structures. Figure 8 (c) is an actual echocardiogram corresponding to the idealized display. The echocardiogram is currently the best method for diagnosis of the mitral valve condition, and it is often used for the aortic valve, although the latter is difficult to detect because of intervening rib bone. The tricuspid and pulmonary valves are even more difficult to detect. Another very important use is in detection of pericardial effusion, which is the abnormal collection of fluid between the heart and the pericardial sac. Once again it should be stressed that these examinations can be performed quickly and easily, at the bedside if necessary, without apparent risk to the patient.

Although echocardiograms have a picture quality similar to that of *B*-scan, cardiologists can extract medically useful quantitative information from the data presentation format. Acceptance of this technique may be because the recording is clearly a time series rather than an attempt to be an image, the nature of the technique is less demanding, and gray scale strip chart recorders were introduced early. In any case, echocardiography is now an accepted part of the cardiologists' repertoire.

Doppler Ultrasound Instrumentation

The continuous wave Doppler ultrasound instrument is the most common ultrasound diagnostic tool [209], [210]. This is primarily because of its simplicity and low cost, but is also due to the audible sounds it produces, which are somewhat similar to a stethoscope. Moving targets (such as blood cells or a heart valve) with a velocity v

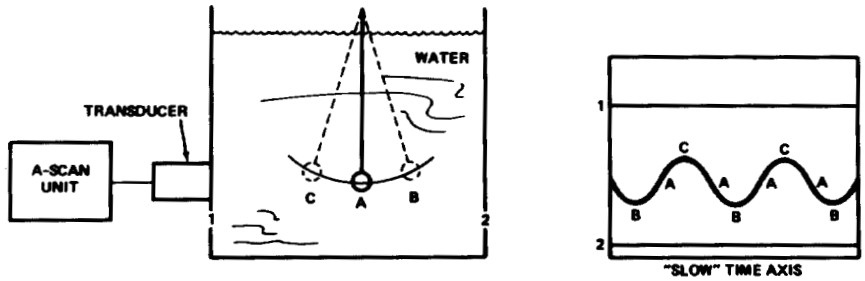

Fig. 7. Elements of an *M*-mode system and display of a moving pendulum.

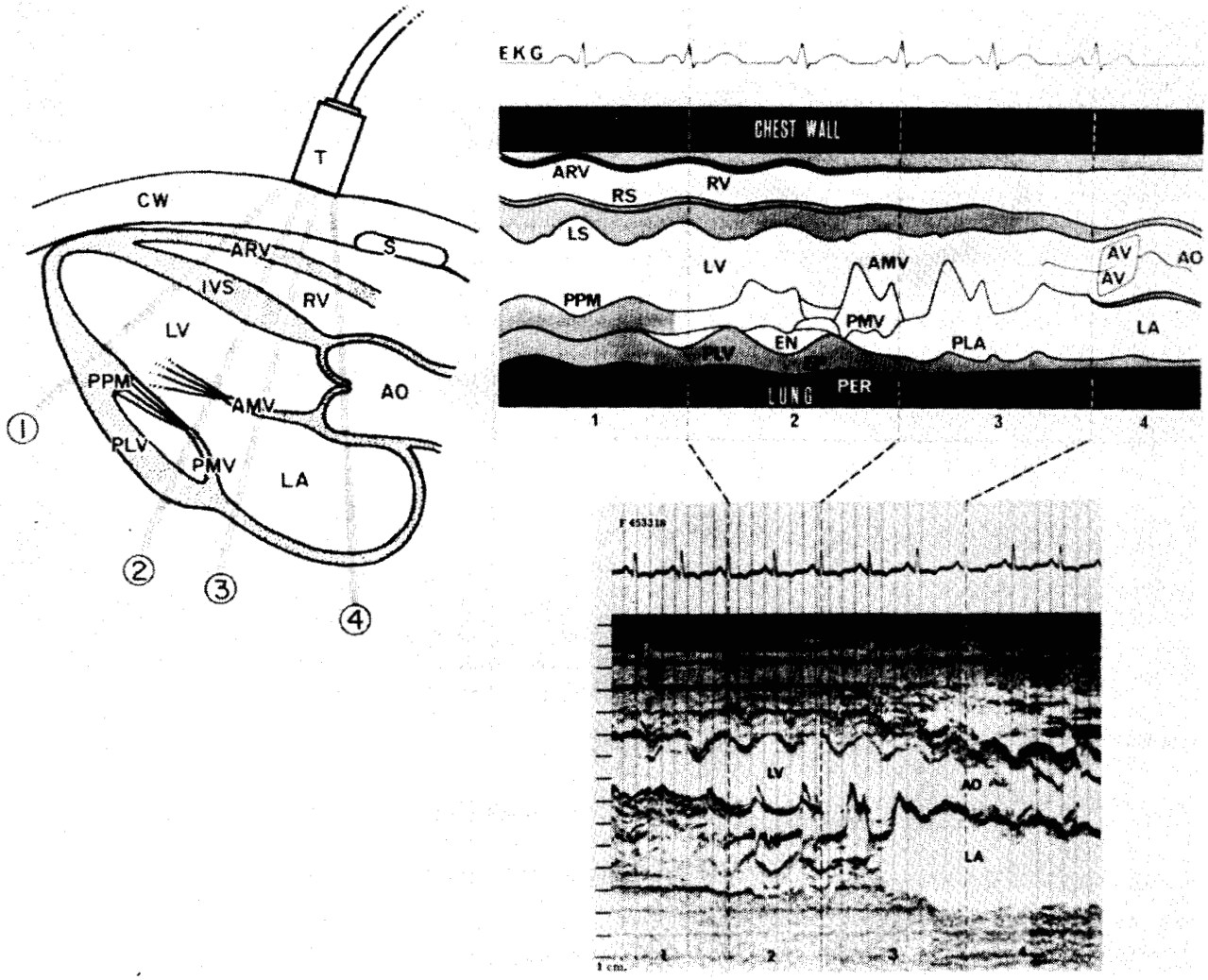

Fig. 8. Human heart section and *M*-mode display of heart structures for each of 4 indicated transducer directions. T, transducer; EKG, electrocardiogram; CW, chest wall; S, sternum; ARV, anterior wall of right ventricle; RV, right ventricle; IVS, interventricular septum; RS, right ventricular septal wall; LS, left ventricular septal wall; LV, left ventricle; AO, aortic outflow tract; AV, aortic valve; PPM, posterior papilary muscle; AMV, anterior mitral valve leaflet; PMV, posterior mitral valve leaflet; PLV, posterior wall of left ventricle; LA, left auricle; EN, endocardium of the left ventricle; EP, epicardium of the left ventricle; PER, pericardium. (With permission of Dr. H. C. Feigenbaum, Prof. of Medicine, Indiana University School of Medicine).

produce a Doppler shifted backscattered signal. The velocity is determined from the standard Doppler formula

$$v = \frac{\Delta f c}{2 f \cos\theta} \tag{4}$$

where Δf is the frequency shift, f is the frequency of the transmitted wave ($f \gg \Delta f$), c is the sound velocity in the medium, and $\cos\theta$ is the angle between the wave axis and the velocity vector.

The primary use for Doppler ultrasound is in obstetrics, particularly for monitoring the fetus during a high risk delivery [211]–[213]. Recently, this technique has also been used for measurement of ankle blood pressures by detecting the stoppage of blood flow when a cuff is inflated as in a conventional arm measurement. Measure-

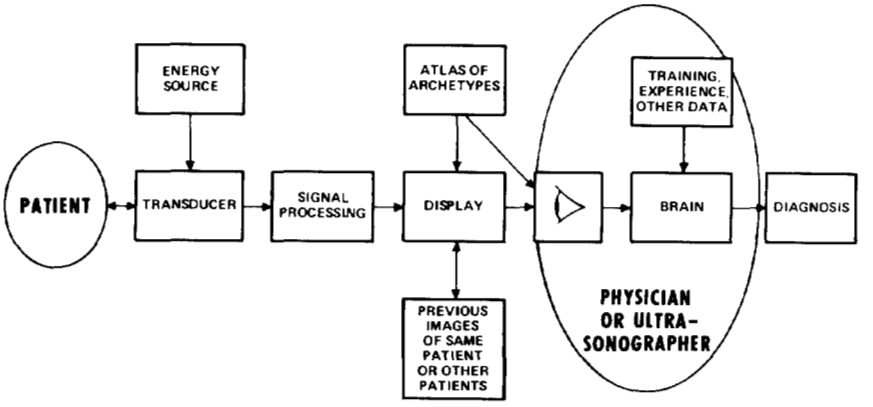

Fig. 9. The diagnostic information system concept.

ment of blood pressures in each extremity is a method for rapid assessment of the vascular system.

V. THE SYSTEMS APPROACH

Ultrasound has reached its present position in medicine based largely on technology and concepts developed during the 1950's. As new technology is introduced, we believe it is useful to evaluate the diagnostic process in terms of unified system concepts. Such techniques for analysis must necessarily include the physician and/or technologist as an integral part of the system and would be valid for virtually all medical instrumentation including X-ray, nuclear medicine, and ultrasound. A diagram presenting this diagnostic information system concept is shown in Fig. 9.

Too often in the past, system design concentrated on the transducer and signal processing to the exclusion of the physician who, like all humans, is an image-oriented person. Such an attitude resulted in the physician being required to adapt his perception processes to the machine. Appropriate system design, on the other hand, should have a data format that includes the physician as an effective part of the diagnostic system. In order to develop ultrasonic systems that satisfy the full spectrum of medical users, we feel that the following specific criteria must be satisfied.

1) Ultrasound must provide new or additional diagnostic information not readily available by other means.

2) The information derived should be as quantitative and repeatable as possible in such a complex structure as the body.

3) Image interpretation should be possible with minimal additional training beyond that currently given to cardiologists, obstetricians, gynecologists, radiologists or any other medical specialists.

4) The system should be interactive in the sense that the physician or technologist is able to easily control the data acquisition from the patient, as well as the signal processing and display to fit the diagnostic situation.

5) The patient should be subjected to minimal personal discomfort and hazard, and the equipment should be designed to accommodate a wide range of body sizes and shapes.

6) Equipment must be highly reliable and low enough in cost to be widely used.

Generalizing these criteria, the idealized requirements for any diagnostic system can be stated quite simply. A diagnostic system should evaluate the patient's state of well being, and, if necessary, identify the site of any malfunction or disruption of normal body processes. The success with which ultrasound meets these criteria will determine its ultimate usefulness in medicine.

VI. NEW DIAGNOSTIC TECHNIQUES PRESENTLY UNDER INVESTIGATION

In the past, medical ultrasonics relied on technologies developed for other applications (see Table I). Moreover, pulse-echo equipment presently used in the clinics can be broadly classified as essentially similar to that available twenty years ago. Fortunately, pulse-echo ultrasonic researchers are now beginning to use the sophisticated data acquisition, signal processing, and display schemes developed for sonar and radar. Even more encouraging is the fact that some of the research now in progress is developing new technologies for medical ultrasonics that are addressing some of the problems uniquely associated with diagnostic medicine. The field offers an open proving ground to many technologies developed for other applications and provides a host of challenging and important problems that are unique to medicine and biology. We divide our review of new ultrasonic diagnostic techniques into three areas: 1) pulse-echo work, 2) Doppler ultrasound, and 3) holographic or holographic-type processes and acoustic "imaging" systems. Although pulse-echo research will be discussed in more detail than the other areas, many of the pulse-echo developments are applicable to both Doppler and holographic techniques. This review is not intended to be comprehensive, but merely indicative of the type of research activities now in progress.

Developments in Pulse-Echo Ultrasound

In reviewing pulse-echo developments, it will be convenient to divide these research activities into three categories: 1) display techniques, 2) resolution improvement techniques (including beam focusing and transducer ar-

rays), and 3) processing techniques. Obviously, any successful diagnostic system must incorporate improvements from each of the three areas.

1) Display Techniques: Perhaps improvements to the display are the most easily implemented in present pulse-echo ultrasound systems. Considerable echoamplitude information is lost in present clinical systems because of the restricted dynamic range of the recording device, which is usually the storage tube of an oscilloscope and/or Polaroid film. Although the acoustic transducer used in diagnostic work has the capability of measuring reflections over a range of pressure amplitudes in excess of 100 dB (a factor of 100 000), an intensity modulated oscilloscope can only display about 20 dB (a factor of 10), while Polaroid film has a dynamic range of only about 10 dB. Thus, with present instrumentation, it is necessary to make a number of scans at different gain settings since only a limited dynamic range can be displayed in any one scan. To display both large and small echoes simultaneously, it is necessary to compress the whole range of echo amplitudes to match the dynamic range of the display unit. The echograms obtained with such an amplitude compression technique are usually termed gray scale images. The usefulness of gray scale echography has been demonstrated for obstetric scanning [173] as well as for the detection of various liver diseases [214]. Several commercial firms are now offering their own form of gray scale imaging, and evaluations are beginning to appear in the literature.

Although gray scale echography may, in many cases, provide a better means of data presentation, the technique is still fundamentally limited by the dynamic range of present recording devices including the ability of the human eye to distinguish various shades of gray. To improve the dynamic range of the display, a number of workers [215], [216] have suggested using a color presentation that has been appropriately encoded to the echo-amplitude. One system presently used can display twelve colors and has a dynamic range of about 36 dB. This system apparently shows promise for the diagnosis of breast lesions [216].

Further improvements in the display dynamic range probably require digital rather than analog techniques. For example, a technique for digitizing two-dimensional analog signals [217] has been used to analyze pulse-echo ultrasonic data [218], [219]. Although the primary interest in analyzing the pulse-echo data was in presenting three-dimensional displays of ultrasonic data, this work also indicates how digital techniques can be used to improve the display dynamic range. Furthermore, this work suggests the importance of combining computer technology with medical ultrasonics and demonstrates how additional important information can be obtained by simply displaying the data in a more appropriate fashion. It should be noted that clinical ultrasound, unlike nuclear medicine and X-ray, has yet to take full advantage of computer technology. No doubt future ultrasonic systems will take full advantage of computer processing, not only for the display of images, but also for the analysis of acoustical signals.

2) Resolution Improvement Techniques: Present ultrasonic systems generally use a plane-piston source transducer for producing a beam of acoustic energy [220]. The axial resolution is determined by the transducer material and construction details [221], [222], by the electrical and mechanical loading [223], and by the acoustic properties of the target. In general, since the attenuation in the target increases with frequency, the operating frequency is selected as high as possible while keeping within signal-to-noise restrictions. In addition, a compromise must be made between axial resolution and transducer sensitivity. It is quite practical, without an appreciable sacrifice in sensitivity, to produce a transducer that is sufficiently damped so that only three to five cycles of the resonant frequency are generated when a voltage spike is applied to the transducer. Although most commercially available transducers have relatively good axial resolution, at least in comparison with typical azimuthal resolution values, further improvements in axial resolution can be made. Experimental studies [230], [231] have recently succeeded in producing broadband sources, which have almost attained the theoretical limit for axial resolution. In the near field [224] of such an unfocused beam, pulse stretching due to unequal path lengths is unavoidable [225], [226]. A transducer with an acoustic lens [227], [228] can be used to eliminate this problem at the focal region of the beam. However, axial resolution is a secondary problem in most ultrasonic systems presently in use.

Azimuthal resolution, on the other hand, is fixed by diffraction considerations and is a real limiting factor in ultrasonics. Using the Rayleigh criterion, the diffraction-limited resolution in azimuth at the focus of a circular transducer with a lens is given by [232]

$$w = 0.61 \frac{\lambda F}{a} \tag{5}$$

where F is the focal length of the lens, a is the transducer radius, w is the beam radius at the focus, and λ is the acoustical wavelength. With a focal length of 20 cm, a transducer radius of 4 cm, and a wavelength of 0.75 mm (corresponding to a frequency of 2 MHz in water), the resolution is 4.6 mm (or twice the beam radius). This is at the focus, however, and the resolution falls off rapidly at points away from the focus.

For many applications it is desirable to compromise azimuthal resolution in favor of increased depth of field. In this case, known as weak focusing [229], the ultimate resolution is not achieved, but a reasonable value is obtained over a much larger penetration range. Typically, a beamwidth of 1.2 cm may be obtained over a range from 20 to 30 cm by using a transducer having a diameter of 3.5 cm, a radius of curvature of 2.5 cm, and a resonant frequency of 2 MHz. This beamwidth may be optimized for different ranges and transducer radii and can be further reduced by increasing the frequency.

For situations in which azimuthal resolution cannot be

compromised, strong focusing can be employed in conjunction with range gating so as to display only those echoes that are close to the focus. The transducer must then be moved in range so that the focal region explores each point of the target. The time to make a compound scan with such a device is rather lengthy and is determined by mechanical considerations [77], [82], [233].

A system using strong focusing with azimuth and range resolution on the order of one sound wavelength has been developed and is in clinical use [77], [82], [233]. This system uses a computer-controlled rapid mechanical scan pattern with automatic mechanical adjustment of the focal region to all depths in the tissue being scanned. Scan times are on the order of a few minutes for a complete picture with high resolution and compensation for attenuation due to tissue depth. The computer provides the capability for true integration of echoes from a given point when viewed from many angles. Following the scan and processing, the image is displayed and photographed on Polaroid film. This instrument provided the basis for a wide range of transducer and software developments, as well as serving as a system for investigations of tissue visualization in the brain [65], [82], [83], [234], [235], breast [79], [148], [151]–[156], and liver [76]–[78], [148]–[150].

Sharp focusing over an extended axial range has been obtained through electronic focusing of an annular transducer array [236], [237]. For focusing on transmission, it is necessary to use appropriately delayed pulses to excite each of the annular rings. For example, if five focal ranges are to be used, it is necessary to transmit five differently focused pulses to cover all of the penetration range. With a 5-cm depth of field in each range, this gives a total range of 25 cm, and the repetition rate for a line could be as high as 1 kHz.

For focusing on reception with the annular array, the received signals must be delayed. This may be achieved digitally or with analog delay lines. Dynamic focusing using only a single transmitted pulse together with continued adjustment of the delay times has been demonstrated to achieve virtually perfect focus over a wide axial range [238], [239]. Further improvements in resolution are possible through a combination of focusing methods.

Since the reflections from tissue at ultrasonic frequencies are primarily specular, the received echo pattern varies considerably with small changes in transducer beam direction. With manually scanned *B*-mode systems, the appearance of the echogram can be altered considerably by changing the scanning pattern (see Section IV). One of the effects of specular reflection is that the system dynamic range must be very large to retain the small scattered component reflected from inclined interfaces. This, in turn, accentuates artifacts attributable to beamwidth, beam sidelobes, and multiple reflections within the examined structure. Some limitations of specular reflection can be overcome by using a wider transducer aperture, which allows reflected energy from a more inclined surface to be received. Obviously, the use of a wide aperture transducer requires focusing if the azimuthal resolution is to be retained. Shading or apodizing the transducer is another method to reduce beam sidelobes and increase system dynamic range.

The effects of specular reflection can also be minimized by using a higher sensitivity and displaying echoes scattered from within the tissue structures. Through logarithmic compression and nonlinear allocation of the gray scale, specular echoes are allowed to saturate the display, while weak echoes are displayed normally. Differences in echo texture can then be used to indicate interfaces between structures [148], [173], [240], [345]. Although this technique has the advantage of providing information about the tissue structures themselves, it can display artifact echoes arising from multiple reflections and beam sidelobes. Alternatively, omnidirectional scanning [82] can be used in an extension of compound scanning to obtain a specular highlight echo from each interface.

Present techniques for scanning moving structures such as the heart require the clinician to precisely and rapidly move a single transducer. To allow moving cardiac structures to be displayed continuously and in real time, an ultrasonic scanner having an array of twenty fixed elements has been devised [241]. Fast electronic switching from one element to another and appropriate display of the echoes result in the instantaneous and continuous display of a moving structure. The dynamic focusing system mentioned previously is also being used for heart scanning [239]. An alternative approach to heart scanning uses a high-speed mechanically moved transducer to produce sector scans of the heart [242], [243].

More sophisticated techniques such as electronic sector scanning [244], [245] and synthetic aperture processing [246]–[249] are also being developed for diagnostic medicine. These and other techniques originally developed for sonar and radar applications offer the potential of extremely high resolution.

3) Processing Techniques: Just as innovative transducer design and sophisticated computer software will increase the resolution capabilities of present ultrasonic systems and will allow the clinician to manipulate the ultrasound data in an effective and efficient manner, processing of ultrasonic signals will allow this modality to make additional advances within the next decade. Various signal processing procedures should allow specific and quantitative information to be extracted from ultrasonic signals that currently appear qualitative and imprecise.

Some of the more fundamental implications of signal processing have originated in communication theory. Using the results of this formalism, an acoustic measurement technique has been developed in which the transmitted signal has a predetermined frequency spectrum with the equivalent of a time tag to each frequency component [101], [174], [250]. Since the frequency spectrum of the time-delayed signal is reconstructed after either transmission or reflection, the technique is known as time delay spectrometry. In its present configuration the transmitted signal is swept in frequency over a wide bandwidth while

the received signal is passed through a narrow-band tracking filter synchronized with the transmitted signal but with an appropriate time delay to allow for propagation between the source and the receiver. The method not only provides the complete complex spectrum with amplitude and phase, but signal components due to longer path lengths are suppressed because their spectrum time tags are rejected. Thus the technique allows multiple reflections and scattered signals to be removed, and it transforms the received signal into a more appropriate form for further analysis.

As was mentioned in Section III, several workers have keyed scattering from biological tissues to specific tissue types and disease states. Unfortunately, the scattering process is not well understood and very few experimental measurements are presently available. However, it appears that scattering can be considered to be a property of tissue which, like absorption and velocity, is amenable to direct measurement [164]–[168]. Presumably, knowledge of the scattering would provide additional information important to making a differential diagnosis. Some preliminary scattering experiments have indicated a relationship between normal and infarcted tissue [146]. Thus a spectrum analysis of scattering from heart tissue may provide a technique for differentiating between normal and infarcted myocardium.

As shown in Section III, it would appear that many types of normal and abnormal tissue can be uniquely classified in terms of their acoustic properties. If such a classification scheme proves to be feasible, it would be highly desirable to have a noninvasive technique for making such identification. A recently proposed technique [97], [251]–[256] offers a means for quantitatively and noninvasively measuring tissue acoustic properties at any appropriate anatomical site within the body. The method uses time-domain deconvolution of appropriately shaped acoustic impulses and their echoes to obtain the impulse response as a function of acoustic travel time. The integral of the impulse response can then be analytically related to various physical parameters such as the specific acoustic impedance. The technique is termed impediography since the impedance is measured as a continuous function of position. The acoustic mapping made with impediography —whether a simple *A*-scan plot of impedance versus distance or an impedance profile of an arbitrary cross section—is termed an impedogram. In preliminary experiments, impediography has been able to detect impedance transitions on the order of 1% behind a section of human skull bone. The signal processing procedures used with impediography allow the removal of multiple reflections produced by large impedance changes such as between skull bone and brain tissue.

Although the determination of impedance may, in many cases, be sufficient to differentiate between tissue types, impediography also allows the acoustic attenuation to be measured as a function of acoustic travel time, provided the transmitted as well as the reflected impulse response functions can be obtained. In certain physiological structures, knowledge of the attenuation may be more important to tissue identification than knowledge of the impedance. For example, the impedance transition between gray and white brain matter is only about 0.1%, whereas the change in the acoustic attenuation is two orders of magnitude larger.

Developments in Doppler Ultrasound

Improvements in instrumentation utilizing the Doppler effect for measurement of flow and for mapping are being undertaken in relatively few centers, although the technique is in widespread use for nonmapping applications. By far the major research effort in this field is directed toward the study of blood circulation to the brain. Doppler techniques have the potential of being able to examine a common site of flow obstruction, such as the carotid artery bifurcation in the neck, as well as being able to determine the effects of arterial constriction on blood flow.

Continuous Wave Doppler: Perhaps the major problem with continuous wave Doppler systems is that frequency changes are received from every moving reflector. Since all body tissues, especially those near the larger arteries or the heart, are in continual motion, the reflected signal will contain information from many structures. Moreover, since each structure is moving with a different and changing velocity from other structures, the frequency changes in the reflected signal are very complex. For this reason it is essential to restrict the received signal to a smaller region or restrict the frequency changes recorded to a predetermined magnitude or range. The former can be achieved with highly directional beams, generators, and receivers so arranged that their field patterns intersect only in restricted regions, or by pulsing and time-gating the system [257], [258].

A combination of these techniques has been developed and has already resulted in the production of tomographic angiograms in two planes of the carotid artery bifurcation as well as other vessels [259]. In this system the frequency shifts are presented as a *B*-scan display so that tomograms of the region of rapid arterial flow are produced. The possibility of using this technique to study cerebral circulation is actively being pursued. Even if Doppler ultrasound becomes only an auxiliary to the commonly used dye-contrast radiography, it would still be quite useful since mapping allows positive separation of the flow in the internal and external branches of the carotid artery.

Another problem in Doppler ultrasound is the requirement for accurate knowledge of the direction of flow with respect to the ultrasonic beam (θ in (4)). Instrumentation to measure vessel cross section in two axes and to simultaneously measure the Doppler shift is being developed [260]. These Doppler techniques are obviously applicable to many other areas of the body and to different clinical problems. For example, one area presently under study is the post-operative assessment of saphenous vein by-pass procedures done to correct stenotic (constricted) coronary arteries [261].

Pulsed Doppler: Although continuous wave Doppler

systems can measure the velocity of a moving object if the surrounding structures are stationary, they are not capable of providing range information or of determining the motion at an arbitrary distance from the probe. Fortunately, it is possible to separate the Doppler signals generated by a number of moving targets with a range-gating technique in which the frequencies of the echoes collected at an arbitrary range are compared with that of a reference oscillator that is itself gated to provide the transmitted pulse [261], [262]. Such range-gating procedures are usually termed pulsed Doppler techniques and should provide the impetus for the development of new diagnostic procedures directed toward detailed and quantitative measurements of blood flow.

Random Signal Doppler: Random signal Doppler is a relatively recent innovation in ultrasound, taking advantage of signal processing procedures available with large bandwidth signals. Conceptually it has its origin in noise radar, but the application to ultrasound and biological tissues accentuates some problem areas not so prevalent in the radar case. In a conventional coherent wave pulsed Doppler system, the bandwidth-pulse duration product is approximately 1.2. Hence, it is not possible to simultaneously obtain good range and velocity resolution. In a random signal pulse Doppler system, on the other hand, the transmitted signal is derived from wideband Gaussian noise, which permits a large bandwidth-duration product and, therefore, alleviates range and velocity ambiguities. This correlation method is still in its formative stages with respect to studies in living tissue [111], [112], [263]–[267].

Developments in Acoustical Imaging Systems Including Holographic [334] *Techniques*

Although *B*-scanners produce pictorial representations of the location of reflectors and scattering sites in the body, they do not "image" in the generally accepted optical sense. We choose to call these devices parameter mapping, or simply mapping systems. This category would include even sophisticated signal processing schemes such as impediography or time delay spectrometry if they are scanned to map a region.

Acoustical "imaging" had its origin in some early work involving a vacuum tube that uses an electron beam to raster scan the back surface of a large resonant piezoelectric disc [102]. A water coupled acoustic wave incident on the front side of this disc produces a charge distribution corresponding to maxima and minima in the acoustic field. This charge pattern then modifies the secondary electron emission, which is collected and used to intensity modulate a TV monitor. This original device, known as the Sokolov tube, together with acoustical lenses, produced the first dynamic images of biological structures and still represents a potentially useful tool for medical diagnosis [103], [335], [336].

Another contribution to acoustical imaging was the use of liquid surface levitation caused by an ultrasonic wave incident on a water-air interface [337]. Once again the imaging was done with an acoustical lens. A Schlieren optical system was used to transfer this acoustical image to the optical domain for viewing. The original system was only able to detect edges, since the Schlieren optical system acts as a high-pass spatial frequency filter.

Liquid surface levitation has recently been revived and greatly improved [338]–[341]. An off-axis acoustic reference source was added as a spatial carrier frequency to allow the true acoustical image to be passed by the Schlieren system. The idea presumably originated in the concept of off-axis optical holography. It has been shown that a dynamic reference wave is made unnecessary by placing a wire grid near the interface [268]. This produces the same spatial carrier as the acoustic reference and allows true imaging with an acoustic lens.

Recently, a new optical detection system to produce acoustical holograms was demonstrated [269]. This system records the amplitude and phase of the fringe pattern of an acoustical wave scattered from an object incident upon an interface. As in optical holography, this acoustical hologram can be reconstructed with a laser to yield an optical image of the acoustical object. With this method of reconstruction, only one transverse plane of the three-dimensional image is viewed at a given time. This is due to the wavelength disparity between the ultrasound (1 MHz) and the laser light, together with the requirement that the entire 30 cm diameter acoustic aperture must be used simultaneously for good resolution. The luxury of trading resolution for parallax is not available in acoustic holography as in optical holography.

Acoustic arrays made up of a line or a matrix of electronically scanned discrete hydrophones are one of the other important developments in acoustical imaging. One such linear array, currently being developed, uses coated acoustical lenses together with an ingenious counter-rotating prism system for scanning the image across the array [270]. Matrix arrays of piezoelectric [271] and electrostatic [343] transducers are also being developed. This system is scanned electronically and has the capability of acting as a transmitter. This array could be used with acoustic lenses or holographically with computer or optical reconstruction of the received acoustic amplitude and phase distribution.

Bragg diffraction imaging using ultrasound has also been demonstrated and has potential for medical diagnosis [272]–[274]. Early work in this area showed problems at the 1–5 MHz frequencies commonly used in medical diagnosis. Recently, the use of more sophisticated detection schemes has somewhat removed this limitation. In summary, acoustic imaging is a very active research frontier that should provide new and useful medical systems in the near future.

VII. THERAPEUTIC ULTRASOUND

At present, therapeutic ultrasound is used primarily in physical medicine. A large body of clinical information exists regarding prescribed safe and effective dose levels in terms of acoustical intensity and irradiation time [275].

Therapeutic instruments are capable of delivering acoustical intensities on the order of several watts/cm^2. Depending on the circumstance, irradiation periods can range up to ten minutes. The transducer is usually hand held and moved about in contact with the desired body region. Although this modality has been in existence for some forty years, the applications have yet to be exhausted. For example, wound healing time may be reduced through application of ultrasound [41], [276]. Evidence also suggests that transport rates of macromolecules across biological membranes can be increased by ultrasound [277]; what role this effect might play in assisting a chemotherapy agent in a selected body region remains to be investigated.

High intensity focused ultrasound can be used to produce tissue selective lesions. This effect has been extensively investigated in brain tissue, and the method has been used in experimental animal work [20], [21], [278]–[281], [292], [297] as well as in several human clinical studies [64], [132], [282]–[286]. Other body tissues, including liver [33], [34], [42], muscle [129], [287], spinal cord [288], peripheral nerve [288], [289], and blood vessels [130] have also been studied. Implementation of this precise surgical modality in brain requires the removal of overlying skull bone with a simple appropriate prosthesis inserted in its place. Subsequent internal brain lesioning procedures are conducted through the intact scalp. Lesions of any desired size or shape to match the neural structure of interest are generated from a multiplicity of individual small lesions [31], [126], [127], [290], [291]. Of considerable interest is the fact that an ultrasonically generated lesion in brain can be detected by ultrasonic visualization means [234].

VIII. ADDITIONAL BIOMEDICAL APPLICATIONS OF ULTRASOUND

In addition to serving as a noninvasive diagnostic tool and as a therapeutic agent, ultrasound has many other biomedical applications. One of the more interesting of these applications is the acoustic microscope [104]–[109]. Although the concept was proposed over twenty years ago, it is only recently that a practical, operating device has been available. The apparatus is shown schematically in Figure 10. The generator produces 100 MHz plane waves that pass through the specimen. The transmitted wave, which carries spatial information about the specimen, strikes a plastic mirror angled at 45° to the direction of sound propagation and causes a dynamic ripple on the mirrored surface. These ripples, in turn, cause periodic angular deflections of a focused laser beam, which is reflected off the mirror. This angularly modulated reflected light beam gives rise to an electrical signal in a photodiode when half the beam is intercepted by a knife edge. This signal is proportional to the angular displacement of the mirror and, therefore, to the local pressure amplitude of the sound. The focused light beam is rapidly scanned over a selected area of the mirror in synchronization with a conventional television monitor. The signal from the photodiode modulates the intensity of the display. The photodiode signal may also be applied to a phase detector and compared with an electronic reference signal so that an acoustic hologram is displayed on the television screen. Typical results, shown in Fig. 11, compare the simultaneous acoustical and optical imaging of a live drosophila larva (100×). Resolution in both the optical and acoustical pictures approaches 1.5 μm.

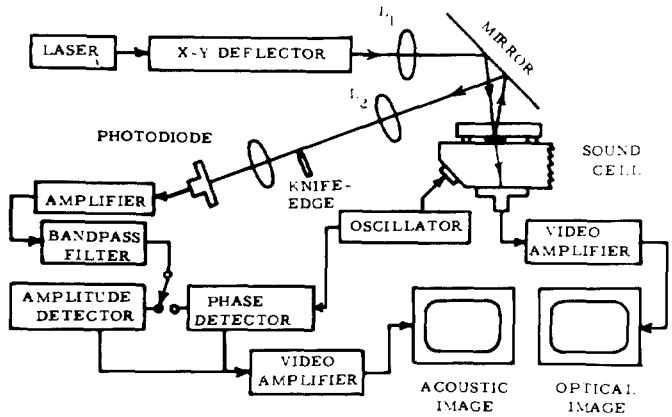

Fig. 10. Elements of an acoustic microscope system.

Further developments in this field will hopefully produce an acoustic microscope operating in the GHz frequency range with resolution comparable to that at the limit of the optical microscope. High frequency acoustic examination of biological tissue can provide unique information about the physical state and the structural components of tissue. Elasticity and density are parameters assessable through acoustic impedance, whereas structural and thermal relaxations, as well as the conformal states of the macromolecular components of tissue, cause changes in the ultrasonic absorption.

Another biomedical application of ultrasound involves the invasive insertion of a transducer to take measurements that cannot be obtained noninvasively. Ultrasonic transducers can be miniaturized so that they can be built into catheters for insertion into selected body regions such as the heart, rectum, and blood vessels. In some cases these approaches are considered acceptable for human clinical work, while in other cases the methods can be used primarily in animal experiments to elucidate aspects of structural motion or flow. For example, fine details of structural motion in the dog heart have been elucidated by such a miniaturized system [311].

IX. SAFETY OF ULTRASOUND

All techniques for medical diagnosis and/or therapy can involve risks if improperly used or if adequate equipment calibration standards are not applied. Many techniques involve danger even in the best hands. The question of risk versus benefit may enter into the medical decision as to what specific modality to apply in a particular case. Ultrasonic methods are attractive for diagnosis because of their noninvasive nature and their apparent safety. This apparent safety rests on data from experimental

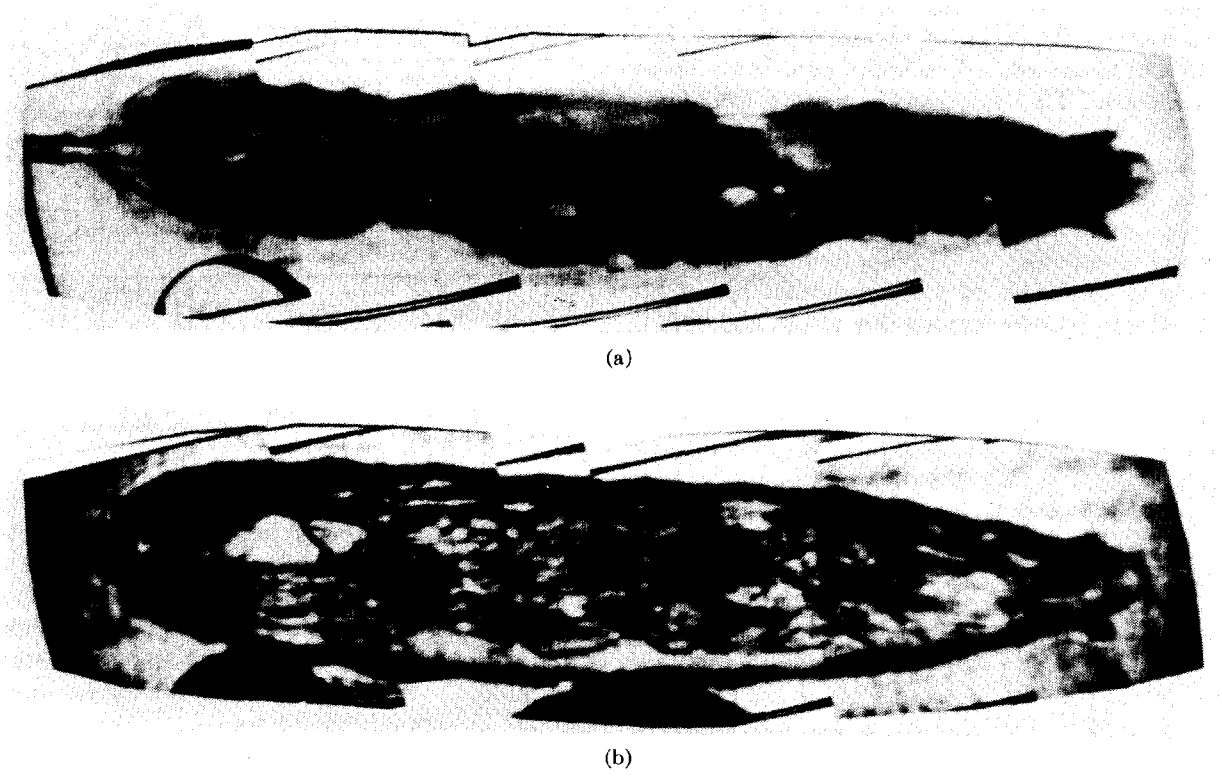

Fig. 11. Acoustic microscope image of living larva. A, optical image; B, acoustical image (magnification 100×).

animal work and over twenty years of extensive human clinical experience.

Acoustical intensity thresholds for lesion production in the brains of experimental animals have been extensively studied. These quantitative measurements used histological as well as function endpoints. The results are summarized in Figure 12, which is the threshold for histologically observed lesions in the gray matter of monkey, cat, and rat brains. This curve describes the conditions for lesion production from a single sound burst in 50% of the irradiation exposures using a statistical analysis [309]. Equation (7) describes this 50% curve where I is the intensity in watts/cm² and t is the pulse length in seconds:

$$\log_{10} I = 2.57 - 0.448 \log_{10} t. \qquad (7)$$

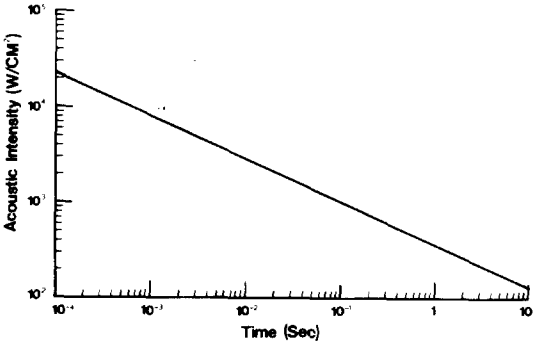

Fig. 12. Acoustical intensity and time duration of the single exposure required to produce histologically observable lesions in central nervous system tissue of cats, monkeys and rats [309].

Generally, three mechanisms are considered to be important over the range of this curve. The most readily demonstrable mechanism is thermal in nature and involves raising tissue above a lethal level due to absorption of acoustic energy [310]. For intensities below several hundred watts/cm², the computed and measured temperature rise, starting from a base temperature of 37°C, is sufficient to produce the observed lesion. It is apparent from the slope of (7) and from measured and computed temperature rises that other mechanisms are involved as the exposure times are decreased. Cavitation involving microbubbles, as opposed to gross effects involving tissue tearing, is under investigation. It has been demonstrated, however, that ultrasound can produce its effects on central nervous system tissue when hydrostatic pressure is applied; this presumably eliminates the possibility of cavitation. Other possible interactive mechanisms have been lumped into other mechanical effects. In addition to classical elastic effects such as fatigue or fracture, these effects could be associated with forces producing molecular changes. These could lead to such things as changes in membrane permeability to bioactive chemical constituents such as enzymes. Either reversible or irreversible changes could occur. None of these effects, either collectively or individually, have been completely studied for any tissue or organ system. Histological studies of the interaction of ultrasound and tissue have also been conducted on the liver [34], [42], blood vessels [130], and muscles [129], [287]. A more complete understanding of the interactive mechanisms is one of the challenging areas of research in ultrasound.

Functional changes have been used to study and assess

the interaction between ultrasound and brain tissue. In one study, reversible suppression of electrical activity in the visual pathway in the cat was observed under conditions that did not produce an histologically observable lesion [128].

Apart from studies seeking to elucidate the nature of interactive mechanisms, there have also been studies directed to the area of toxicity because of the increasing usage of ultrasound in medical practice [293]–[307], [344]. Although toxicity studies rely heavily on an understanding of the interactive mechanisms between ultrasound and tissue, it is not necessary to thoroughly or completely understand the fundamental nature of the phenomena in order to appropriately use the interactive effects for investigation. In medicine it is required that possible toxic effects be studied along with clinical evaluation procedures. Greatest attention has been centered on the reproductive system since effects there could be rather severe with respect to an individual offspring (teratogenic effects) and successive progeny (mutagenic effects). Effects of ultrasound on biological systems in test tubes can be profoundly different from effects seen in the living body so that extrapolation from *in vitro* data to possible *in vivo* effects is highly speculative. It is highly desirable to study toxic effects in animal models that mimic human anatomy and physiology as closely as possible. At the same time, extreme care in collecting human clinical data is required so that accurate intercomparisons between human and animal data can be made. Different organs and tissues will undoubtedly have different levels of susceptibility to change by ultrasound. The general trend towards higher toxicity thresholds as acoustic pulse length is decreased produces advantages for system design. Improvements in signal-to-noise ratios can then often be produced with higher acoustic input levels. Little is known, however, about possible cumulative effects of repetitive sequences with pulses of extremely short duration [42], [280], [304], [308]. The relative significance of peak and average acoustic intensities in producing interactive effects is also an area of ongoing research.

Several literature surveys on interactive effects have been published [297], and inferences have been drawn with respect to their possible relevance to medical practice [307]. With the present lack of definite information in most tissues, it is too early to establish definitive ultrasound toxicity thresholds. Suffice it to say that as of the present time, there are no data available from any clinical source that indicate that presently used levels of diagnostic ultrasound are unsafe for humans [306]. This does not imply that there is no urgent need for toxicity and basic mechanism studies; in fact, quite the opposite is true since these studies will serve as the basis for new generations of ultrasonic devices, as well as provide information of immediate value to the human clinical areas.

X. STANDARDIZATION IN DIAGNOSTIC ULTRASOUND

Figure 13 shows the diagnostic ultrasound environment and its interrelationships. At each link in this environment, standards of one form or another are needed. In the research area, however, (shown in dotted lines in Figure 13) standards may actually inhibit growth. After twenty years of use, very little has been done with the vital, yet unglamorous, subject of standardization in diagnostic ultrasound.

Figure 14 shows organizations currently involved in standards work in the United States. The International Electrotechnical Commission (IEC) is included since it is the parent world standards organization. The IEC Subcommittee 29D (Ultrasonics Working Group on Medical Applications) is currently circulating a draft standard entitled "Methods of Measuring the Performance of Ultrasonic Pulse-Echo Diagnostic Equipment." This document will be evaluated in hospital clinics in 1974 before final adoption.

Other organizations shown in Fig. 14 are also involved in standardization in one way or another. Those shown with a dotted line are acting in an advisory capacity although there is a possibility that some standards could eventually become law, subject to enforcement by the Food and Drug Administration. This is especially true when medical device legislation passes in the Congress of the United States.

There are basically three types of standards: 1) fundamental standards, 2) engineering standards, and 3) user-oriented operational standards.

1) Fundamental Standards

Measurements of fundamental quantities such as the peak and average acoustic intensity in an ultrasound beam are often very difficult to perform. However, such measurements are presently being made at a number of institutions and should soon result in calibrated secondary standards for engineering measurements. There is no unanimity about the best method for measuring ultrasound intensity. Currently, the following techniques are being examined [327], [328], [332].

Radiation Force: a method for measuring average intensity which uses the change in force (typically measured in micrograms) recorded as the deflection of a reflecting or absorbing target with incident ultrasound [312]–[314].

Calorimetry: a classical method for measuring average power using the change in temperature due to ultrasound absorption in a fluid [315]–[317].

Capacitive Transducers: a method for measuring both peak and average intensities using the modulation of the spacing of a charged parallel plate capacitor by an incident sound wave [318]–[320].

Transducer Reciprocity Calibration: a well-known method in sonar which allows a simple measurement of peak and average intensities provided the reciprocity parameters are known and are not seriously complicated by the near field diffraction pattern [321]–[323].

Optical Diffraction: a method for measuring the peak and average intensity using the Debye–Sears effect [325], [326], [333].

Since no single technique is clearly superior, it seems certain that some combination of these methods will re-

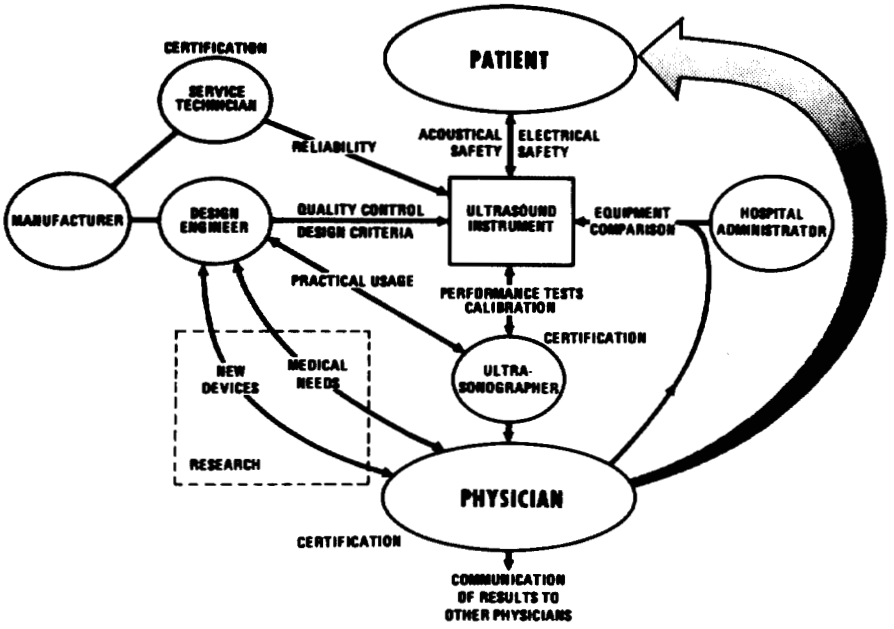

Fig. 13. The diagnostic ultrasound environment.

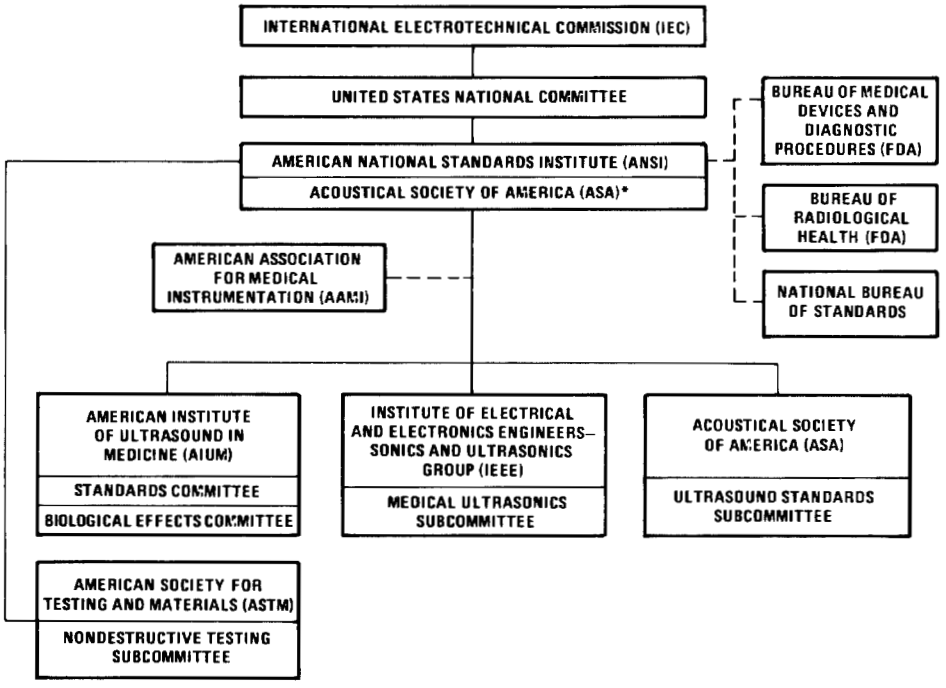

Fig. 14. Groups actively participating in ultrasound standardization. The American Society for Testing and Materials Committee is included because of the great similarity between the two fields. * The Acoustical Society Subcommittee comprises the ANSI Committee.

sult in calibrated secondary standard piezoelectric transducers for research and engineering measurement. Such a transducer should have a resonance frequency much higher than the frequencies being measured so that its frequency response is essentially flat in that region. Another very important requirement, which has unfortunately been neglected in much published experimental work, is that the diameter of the transducer and its supporting structure must be much less than a wavelength, i.e., a fraction of a millimeter at low MHz frequencies. This small size is required to avoid diffraction and reflection effects that perturb the field being measured [324]. If this condition is not met, a diffraction correction must be made for accurate results.

2) Engineering Standards

These standards are normally intended for measurements on subsystems to be performed by manufacturers and calibration centers. Traditional engineering methods and standards for measuring gain, bandwidth, noise level, electrical leakage, etc., are available. With the exception of the ultrasonic transducer and its radiation pattern, this

area of standardization is well advanced, although the measurements can become tedious and, therefore, may be neglected unless mandated by law.

3) *User-Oriented Operational Standards* [329]–[331]

Methods for checking the performance of complex ultrasound systems on a daily or weekly basis may literally be a matter of life or death. Whereas an oscilloscope out of calibration may mean the repeat of a test for an engineer, it may result in missed diagnosis with irretrievable results for the physician.

Standards for use by the hospital technologist must be simple and easy to use since they will often be used by people with little or no background in science or engineering (in many larger hospitals, biomedical engineering technicians are just now filling this gap). The test must use a simple low cost device and should test the whole system as a "black box" to avoid manufacturers' complaints. The traditional method in medicine is to employ a "phantom" or a standard object to be scanned.

One such phantom, the "standard 100 mm test object" (Figure 15), is currently being developed by the American Institute of Ultrasound in Medicine Standards Committee. This phantom has also been incorporated into the IEC draft standard. It consists of 0.75-mm diameter stainless steel rods arranged in a geometrical pattern. Figure 16 is a *B*-scan of this test object taken with linear scans with the transducer at three different angles. In addition to providing a recognizable image, the test object is useful for depth and azimuthal resolution measurements and spatial calibration. Note that the transducer beamwidth does not allow resolution of the bottom rods. One of the major goals of this phantom is to enable *B*-scans from different laboratories to be compared, and it is hoped that reproduction of such a scan would be required for publication.

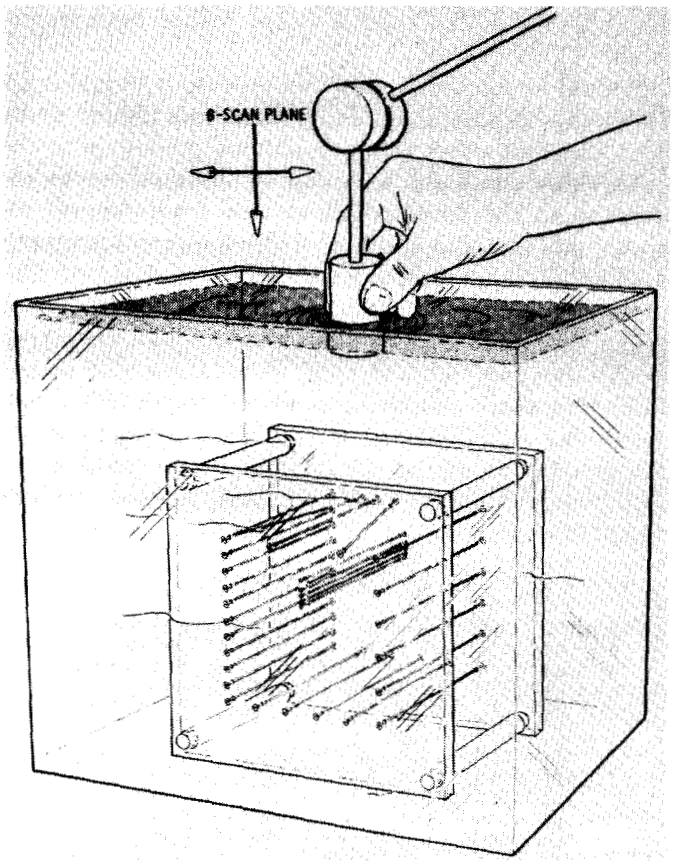

Fig. 15. Standard 100 mm test object—American Institute of Ultrasound in Medicine.

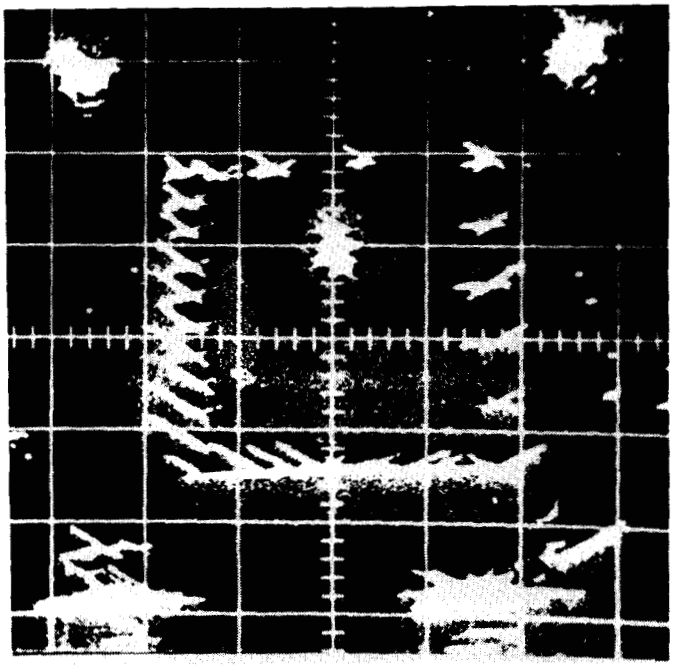

Fig. 16. *B*-scan of standard 100 mm test object.

CONCLUSION

Ultrasound has now established itself as a useful medical modality, both in diagnosis and therapy. Technological advances of the last two decades are now finding their way into ultrasonic systems and can be expected to have a major impact in the near future. Moreover, medical ultrasonics has recently developed into a field of research specialization that is addressing some of the unique and important problems of diagnostic medicine. New technologies are being developed which, in the future, will greatly influence clinical medicine as well as many areas of science and engineering. These new technologies are making their major contribution in the diagnostic area and are centered primarily around methods for obtaining real-time images of high resolution and for quantitatively measuring and differentiating tissues.

As new advances are made in diagnostic ultrasound, similar progress is expected in therapeutic ultrasound. For example, low intensity ultrasound may find new applications in wound healing and as a chemotherapy catalyst. High intensity focused ultrasound offers considerable potential as a noninvasive surgical modality. The combination of low intensity ultrasound for diagnosis and tissue differentiation with high intensity ultrasound for surgery offers the prospects for a major advance in clinical medi-

cine, which even few science fiction writers have anticipated.

Medical ultrasonics is a rapidly growing field and is on the verge of making a significant impact on clinical medicine. The field offers an open proving ground to many technologies developed for other applications, gives inspiration to the development of new technological advances, and provides a host of challenging and important problems that are unique to medicine and biology. The future of ultrasound in medicine depends upon talented people from medicine and the physical sciences working in close collaboration and upon the emergence of a new breed of research scientist trained in both medicine and engineering and dedicated not to the technology of destruction but rather to the preservation of life and humanity so that "man will not merely endure: he will prevail."*

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