Echographic Visualization of Lesions of the Living Intact Human Breast*

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The purpose of this report is to show that the nature of lesions or tissue abnormalities of the living, intact human breast can be determined by the use of pulsed ultrasound. The study is not necessarily directed toward cancer detection and is not necessarily intended to replace existing technics of detection and diagnosis of breast lesions, but rather is aimed at the more fundamental question of whether or not the histological structure of tissue in general can be determined by ultrasonic technics.

The breast was selected as a convenient accessible organ for direct studies on the patient and because of the certainty of obtaining a quick microscopic diagnosis of the lesions. This study is one of the steps toward the examination of less accessible sites.

History

The history of the various technics for using sound energy as a means of examination and detection, applied mainly to industrial and military fields, is described by Carlin (2). There has been a surprising delay in similarly applying sound energy to biology. One reason for the delay has apparently been the difference in outlook between the physicist and the biologist.

The gap was partially bridged in 1947 when Dussik, Dussik, and Wyt, a medico-physicist team in Europe, reported attempts to outline the ventricles of the brain in life (3). The Dussik method is a transmission technic in which sound is driven through the skull from one side and is picked up on the opposite side by a receiver. In this country in 1950 Ballantine, Bolt, Heuter, and Ludwig reported similar attempts to outline the ventricles (1). In 1952 Güttner reported that it is not possible to outline the ventricles by a transmission method because of the interposition of the skull (9), but modification of the existing methods may yet realize the Dussiks' objective.

Another specialized application was made in 1949 by Ludwig and Struthers (12). Using commercial ultrasonic flaw-detecting equipment (5), they showed that gallstones and foreign bodies buried in the muscles of dogs could be detected. These workers stated the opinion that the multiple reflections which they obtained from the soft tissues were too erratic to be of practical value. They suggested, however, that refinements in technic might make the detection of tumors possible. The principle of their method was to drive sound into the dogs' tissues and to detect echoes returning from the junctions between the inserted materials and the muscles.

In February, 1950, Wild reported studies directed toward the measurement of biological tissue elements and the detection of tissue irregularities (14).

The ultrasonic examination of tissues in terms of cellular composition presents formidable problems, both technical and biological. Because of the small dimensions of tissue elements, high frequencies were considered necessary in order to obtain good definition. At high frequencies, with the consequently shorter wave lengths, tissues could no longer be considered homogeneous by the physicist. Worse yet, as far as could be foreseen, the range would be limited at high frequencies.

Since a suitable refined apparatus for preliminary exploratory tissue studies had already been developed by the U.S. Navy for purely military purposes during World War II, the senior author was able to apply biological technics without much specific knowledge of the extremely complex electronic apparatus, operating at a frequency of 15 million cycles per second and timing intervals as short as one millionth of a second.

Preliminary studies by Wild (14) applying biological methods appeared sufficiently encourag-

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ing to warrant experimental application to stomach cancer tissue. Experimental work by French, Wild, and Neal (6, 8) on fresh post mortem brain tissues pointed to the possibility of detecting and diagnosing brain lesions after operative removal of a portion of the skull. Harmlessness of the apparatus was confirmed with animals (7) and by application to the senior author's arm (15). Two cases of living, intact, human breast lesions were correctly forecast before biopsy (15). The application of the method to a living brain lesion was recorded (13, 18) and was followed by a series of 21 cases from the living human breast (17) which gave further evidence of the diagnostic accuracy of the method.

Wild and Reid (16) reported the development of a pictorial method of visualizing living tissues with their original apparatus. Howry (10), using a similar picturial method, reported visualization of the structural elements of the mid-forearm.

Terminology

Wild and Reid suggested the general term, "Echography" for the whole subject of examination of biological tissues by means of ultrasonic echoes (16), regardless of the methods used for displaying the information obtained. The basic electronic machine was called the "Echograph," the applicator units (probes) "Echoscopes," and the records "Echograms." A uni-dimensional echogram (such as those in Chart 2) is the display of echo amplitude versus depth, i.e., along one dimension of the tissue. A two-dimensional echogram (such as those in Figures 1–7) is a map of echo intensity over a plane, i.e., a cross section extending into the tissue. This terminology allows further expansion into a third dimension (17).

Principle of the Echograph

The principle of the instrument is basically simple. The interrelationship of the components of the electronic system is shown in Chart 1.

An electronic clock (1) times the bursts of sound energy (60–1,000 c.p.s.) and starts the traces on the face of the cathode-ray tube (center). The transmitter (2), upon receipt of the pulses from (1), creates electrical impulses to excite the piezoelectric crystal (3) in the echoscope. The pulses of electrical energy, converted to pulses of sound energy at the crystal (3), travel into the tissues in a narrow beam. The series of echoes returning from the tissues are received by the same crystal, quiescent between pulses, and are amplified by unit 4 to deflect the traces on the cathode ray tube as shown in Chart 1 (center).

The construction of the echograph has been described in more detail elsewhere (11, 13).

Uni-dimensional Echography

Chart 2 is a comprehensive representation of the way in which some "meaning" has been obtained from the echo-patterns which appeared confusing to other workers (10, 12). The left half of the chart contains a series of drawings concerned with a hypothetical lesion of the breast. The right half shows similar data concerning normal breast tissue.

The pulsed sound beam leaves the piezo-electric crystal O, passes through the water contained in the echoscope, through the rubber membrane and skin, and into the breast tissue at A. The beam passes into the lesion at B and leaves the lesion at C.

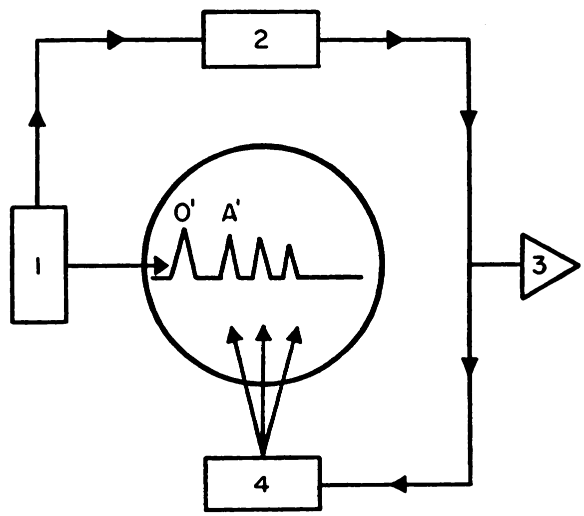


Chart 1.—Diagrammatic drawing of the operation of the echograph.

The resulting echogram No. 1 is shown with the echo from A shown at A′, and similarly for the other letters. Since the sound velocities in various tissue elements are nearly identical, the distances between echoes on the echogram are closely proportional to the distances between the sound reflecting structures in the tissue.

If the velocity of sound in tissue is known, the size of a lesion can be calculated if recognizable definitive echoes are produced, such as B′ and C′. The portion of the echograms representing the water column (O′A′) is constant and is deleted from the subsequent echograms. The signal at D′ represents the limit of depth.

As the sound pulses enter the tissue, very strong echoes are produced (A′B′) which exceed the present linear range of the machine so that the separate echoes from the water-membrane-skin-tissue interfaces are not distinguished. Fortunately, it is not necessary to be able to identify indi-

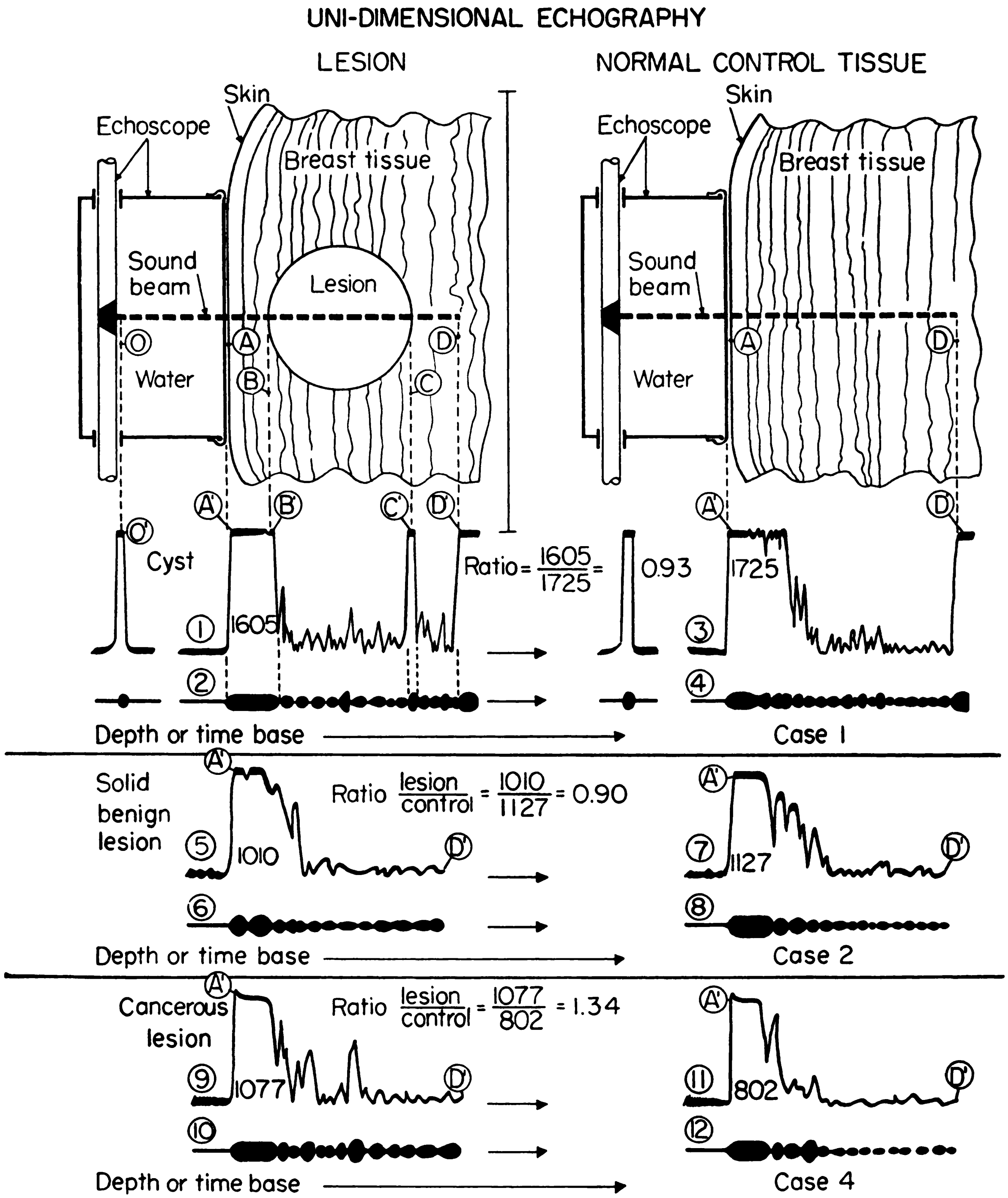


CHART 2.—Representative uni-dimensional echograms

vidual echoes in order to use the information contained in the echogram.

Technic of Biological Control of Uni-dimensional Echograms

Inherent in experimental biological method is the concept of controlling systems in such a manner that all variables except one are held constant. Thus a second echogram (No. 3) is recorded through normal breast tissue *without alteration of the controls of the echograph.* Since there is a case to case alteration of the controls, *it is not valid to compare echograms from case to case.*

The echogram pairs of the first two living breast lesions examined (15) showed recognizable differences subjectively. Later it was found (17) that a series of nineteen pairs of echograms taken from palpable breast lesions and control tissue could be

Lesions		Agreement with biopsy
Malignant	20	19
Benign	21	19
Total	41	38

Chart 3.—Summary of uni-dimensional echographic and biopsy findings on breast lesions.

compared objectively. The area under each echogram represents the amount of sound returning from the tissue. This area is calculated for each echogram by projecting the original records onto paper ruled in both directions and by counting squares. The area ratio of the tumor echogram to the control echogram is determined for each pair. A ratio of less than one was obtained in nearly all the eight lesions subsequently found to be nonmalignant at biopsy. The ratio was greater than one in all the eleven lesions subsequently declared malignant by the pathologist.

Drawings of typical pairs of echograms from other cases are also shown in Chart 2. Echogram 5 of a solid, nonmalignant, fibromatous nodule is compared to the normal control number 7. Similarly, Echogram 9 of a cancerous nipple is controlled by the normal Echogram 11.

Reference to Echogram 1 will show a signal C′ which came from the far side of the cyst because of the relatively greater acoustical difference between the liquid in the cyst and the tissues. In all the other similar echograms, however, signals between A′ and D′ could not be definitely identified in the living subject. (Experimentally it is possible to identify some echoes [18].)

It should be emphasized that it is invalid to compare echograms from case to case.

The results of extension of the original unidimensional series of breast lesions up to the time of preparation of this report are shown in Chart 3. The single error in the malignant group occurred in a case where both breasts were atrophic so that no normal breast tissue was available for control. The two errors in the nonmalignant group were in cases of fibrocystic disease affecting both breasts, making the control technic likewise invalid.

Two-dimensional Echography

An alternative electronic method of presenting the information, based on radar principles, was developed which gives information in two dimensions instead of one (16). The type of uni-dimensional echogram described above is changed in such a manner that the signals produced by the echoes from the tissues are recorded in the echogram as spots of light with intensity or brightness which varies with the strength of the signals, or "loudness" of the echoes. The alternative "intensity modulated" uni-dimensional echograms (even numbers) are drawn in Chart 2 beneath the corresponding "amplitude modulated" echograms. The signals are deliberately exaggerated in width to simulate intensity changes. It will be noted at once that information has been rendered more difficult to evaluate, but an advantage has been gained. If the sound beam is now moved through the tissues to successive positions (up and down in Chart 2) a series of echograms could be obtained from the tissues which could be placed side by side and which would differ according to the position of the sound reflecting interfaces of the tissues.

The result of such a series of echograms from a cyst, placed side by side, is shown in Figure 1. The skin contour has been charted A′, and the cyst has been directly revealed. An instrument was constructed (16), and two-dimensional echograms were obtained of kidney tissue and of a tumor in a living subject. Echograms of a malignant breast tumor were reported in the living subject with the same instrument (17). The first instrument gave valuable information for the construction of a second improved body-surface two-dimensional echoscope shown in section in Chart 4.

The instrument was designed to produce a reciprocating motion of the transducer (B) within an elliptical water chamber (H), thus keeping the sound beam normal to the axis of reciprocation throughout the range of movement.

The tube on which the transducer is mounted is sealed into the water chamber by means of "O" rings and is driven back and forth at constant velocity by a dual-direction screw rack (C) turned by the motor (A).

Coupled to the reciprocating mass is the rectilinear potentiometer (E) from which a signal is taken to position the scanning line on the face of the 12DP7 cathode-ray tube. The information received from the moving transducer causes the scanning line to brighten at points along its length so as to draw out the image of the tissue structure.

The 15-mc. quartz crystal is connected to a matching network (G) by a flexible coaxial cable (F). A photograph of the actual echoscope is shown in Figure 8.

The conclusions drawn from preliminary unidimensional studies were that nonmalignant tumors of the breast returned as much sound or less than did normal tissue at comparable depths in the tissues. Conversely malignant tumors returned more sound than did normal tissue at comparable depths. Therefore, provided that the sound beam could traverse the tumor completely from normal tissue to normal tissue, a tumor of either type should be revealed by two-dimensional echography. The nonmalignant tumor would be recognizable as an area of less bright signals occuring at the same depth as brighter normal areas on either side. The malignant tumor would appear as an area of brighter signals occurring at the same depth as much less bright normal surrounding signals. A cyst would be clearly outlined because of the structureless liquid content. The following cases were taken from current clinical studies.

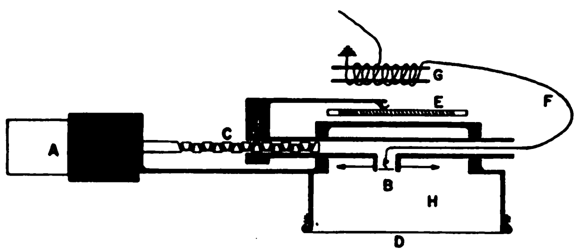


CHART 4.—Schematic drawing of the two-dimensional echoscope.

CLINICAL CASES SHOWING THE RESULTS OF TWO-DIMENSIONAL ECHOGRAPHY

Case 1.—Mrs. D., age 34, presented for echography with a lump in the left breast above the nipple 2–2½ cms. in diameter. The two-dimensional echogram of the lesion is shown in Figure 2. An immediate diagnosis of a cyst (nonmalignant) was made. This diagnosis was confirmed at biopsy on the following day.

Case 2.—Mrs. A., age 36, was referred for echography with a hard lump 2–3 cm. in diameter under the areola near the left nipple. The skin was not involved. The two-dimensional echogram is shown in Figure 3. The group of low-intensity signals under the broken line Y, occurring on the high intensity background, can be seen where the sound beam swept through the lesion. The control echogram of normal tissue showed a uniform overall signal intensity as shown in a typical normal echogram, Figure 5. The uni-dimensional echographic area ratio was 0.90, showing nonmalignancy (17). Biopsy revealed the lesion as nonmalignant (fibroma).

Case 3.—The patient (Miss S., age 43) was referred on July 21, 1953, for echographic examination of a breast nodule 1 cm. in diameter, first noticed 2 weeks previously. The nodule was situated in breast tissue under the margin of the areola at 10 o'clock in the left breast. The skin moved freely over the nodule. The two-dimensional echogram of the nodule in this case is shown in Figure 4. The tumor can be recognized at (Z) as a group of high intensity signals occurring at a depth in which almost no signals are returned from the normal surrounding tissue. The unidimensional ratio was 1.2, indicating malignancy (17). A cancer (scirrhus carcinoma) was found at biopsy.

Case 4.—The patient (Mrs. J., age 70) complained of redness and soreness of the left nipple of 5 days duration. Examination revealed a slight enlargement, redness, and firmness of the left nipple as compared to the right nipple. A clinical diagnosis of inflammation of the nipple was made. Echography was carried out on May 16, 1953. The two-dimensional echograms obtained by sweeping the sound beam through the affected left nipple and the normal right nipple are shown in Figures 6 and 7, respectively. The nipples can be seen outlined. A group of high intensity signals can be seen in echogram No. 6 at (V) not present in the echogram of the normal nipple No. 7. The uni-dimensional echograms of this case are shown in Chart 2. The ratio was 1.34. The echograms were demonstrated and the tumor declared malignant at the centennial meeting of the Minnesota State Medical Association, May 18, 1953. On May 23, 1953, the diagnosis was confirmed by biopsy (scirrhus carcinoma). The tumor was 7 mm. in diameter. The two echograms in this case are shown greatly enlarged in Figures 9 and 10.

DISCUSSION

It should be stressed that the two types of presentation of data, the graphic or uni-dimensional, and the pictorial or two-dimensional, are two methods by which the final output of the echograph is revealed to human perception. The output of the echograph is represented by the graph of voltages, which voltages are proportional to the "loudness" of the echoes, plotted against time, as seen in the uni-dimensional echogram. This voltage-time graph is the basis of all types of presentation. Differences in the more than sixteen possible ways (4) of using the basic output of the echograph arise in the uses made of the information as to the *position* of the crystal. The "pictorial" two-dimensional echogram is dramatically direct, and there is thus a strong temptation to ignore disadvantages such as the loss of detail and to overlook the value of the uni-dimensional echogram, less obvious though actually containing more information. The two methods are complementary, and both types of echograms are taken routinely in each case in the current breast studies. Uni-dimensional echography, because of its relative technical simplicity, made possible the preliminary data, which in turn justified the construction of the considerably more complex two-dimensional apparatus.

The area beneath the uni-dimensional echogram can be electronically determined instantaneously, and comparisons can likewise be made so that skill in interpretation can be eliminated once the basic data are compiled for a given application.

Relevant echographic studies up to the present have been directed towards establishing whether or not it would be possible to detect tissue irregularities of sufficiently small size to make early detection of cancer possible and further whether the histological nature of tissue irregularities could be determined in terms of malignancy and benignancy.

By selecting the highest available frequency (15 megacycles) as a starting point for studies in spite of apparent range limitations, the authors believe that they have made possible the early detection and diagnosis of irregularities of tissue structure of sufficiently small size to be of value in the control of cancer, at common sites within the body, such as the upper and lower gastrointestinal tract, accessible from the mouth and anus, respectively, the cervix uteri, and prostate. Instruments for preliminary studies at these sites have already been constructed and will be reported on, together with results, in due course. Palpable tumors accessible from the skin at sites such as the breast and probably the thyroid can be diagnosed *in situ* with the echoscope described here. It must be stressed that no specific attempt has yet been made to *detect* unsuspected lesions at any site.

A great deal of acoustic and electronic development will be necessary to determine whether very small foci of abnormal tissue can be detected from the skin. Such detection of very small abnormalities will make practical examination of patients on a mass basis. Much less developmental work will

Typical two-dimensional echograms obtained from the living breast in the current studies are shown. Echogram Number 1 is oriented with the depth axis horizontal to facilitate comprehension of the transition from uni-dimensional (Chart 2) to two-dimensional display. The rest of the echograms have the depth axis vertical. The letters A′–D′ superimposed upon the echograms correspond to those in Chart 2.

FIG. 1.—*Echogram 1* from Case 1 has been modified artificially to show how a series of intensity modulated uni-dimensional echograms (Chart 2, No. 2) when placed side by side reveal the structure of the lesion.

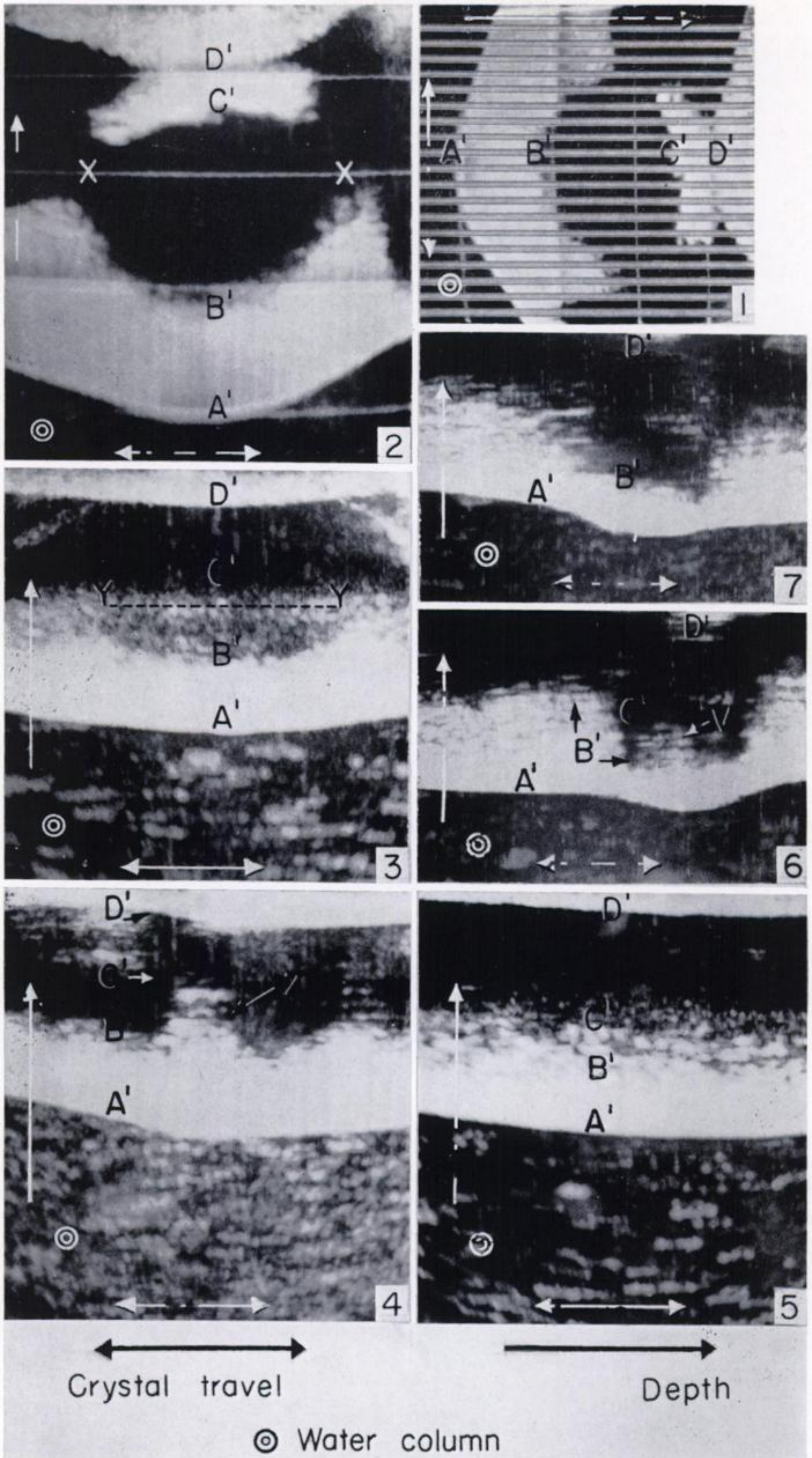
FIG. 2.—*Echogram 2* is the actual echogram of the cyst in Case 1 as produced by moving the intensity modulated uni-dimensional trace through the tissues. It will be noted that echoes were not returned from the side walls of the cyst, *X–X*.

FIG. 3.—*Echogram 3* was obtained from Case 2. The lesion (fibroma) was revealed under the broken line *Y–Y*.

FIG. 4.—*Echogram 4* from Case 3 shows the cancer at *Z*.

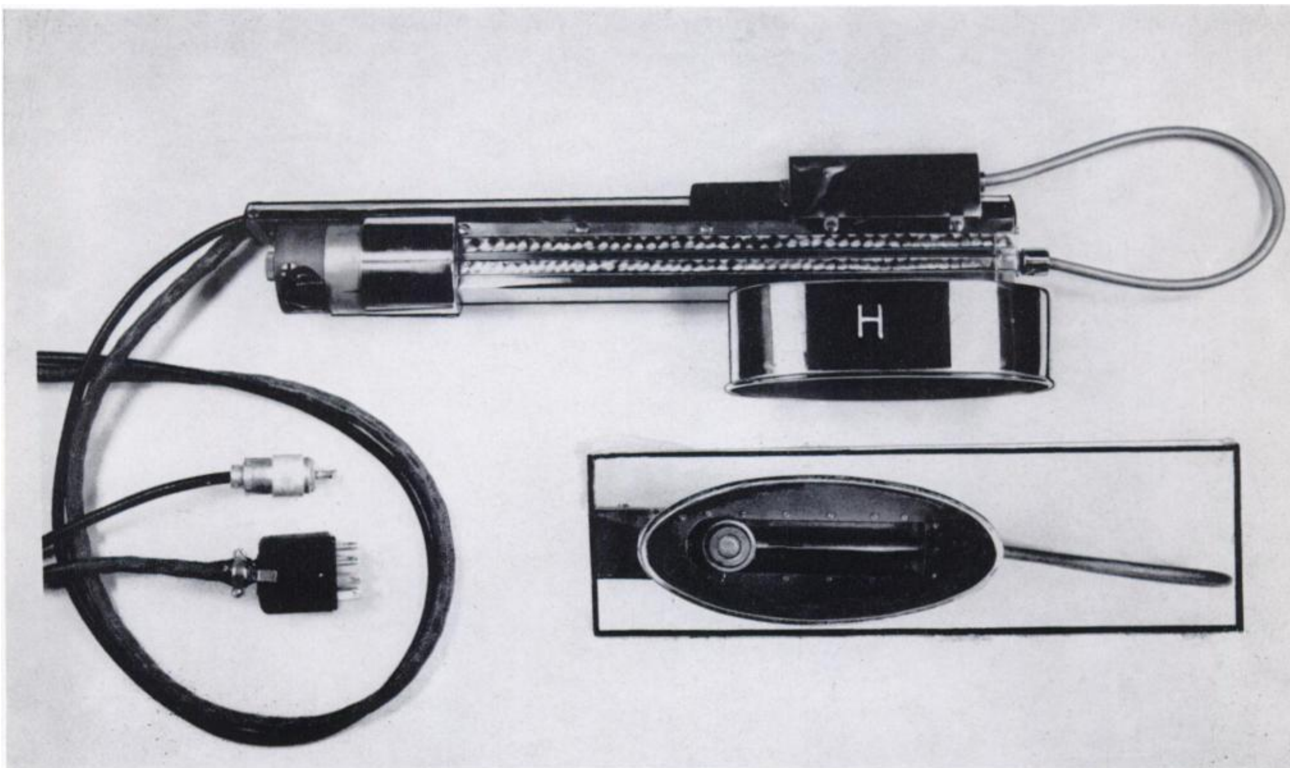
FIG. 5.—*Echogram 5* is a representative echogram from normal breast tissue.

FIGS. 6 and 7.—*Echograms 6 and 7* show a comparison between the echograms of the affected nipple (No. 6) and the normal nipple (No. 7) in Case 4. The cancer was revealed by the white area *V* within the nipple not present in the normal nipple. The echograms are approximately life size.



D'
C'
X
X
B'
A'
2
A'
B'
C'
D'
1
D'
B'
A'
7
D'
C'
Y
Y
B'
A'
3
D'
C'
B'
A'
6
D'
C'
B'
A'
4
D'
C'
B'
A'
5
Crystal travel
Depth
Water column

FIG. 8.—A photograph of the two-dimensional body-surface echoscope is shown opposite. The water chamber is shown at *H* The inset shows a view into the water chamber with the crystal in the base to the left. The crystal travel is 6.5 cm.



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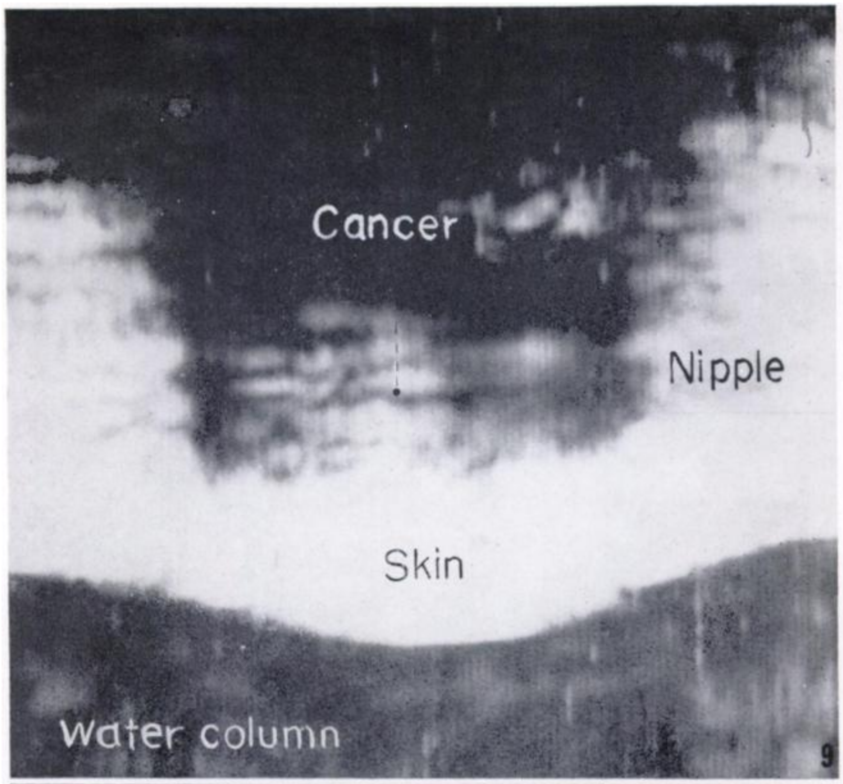
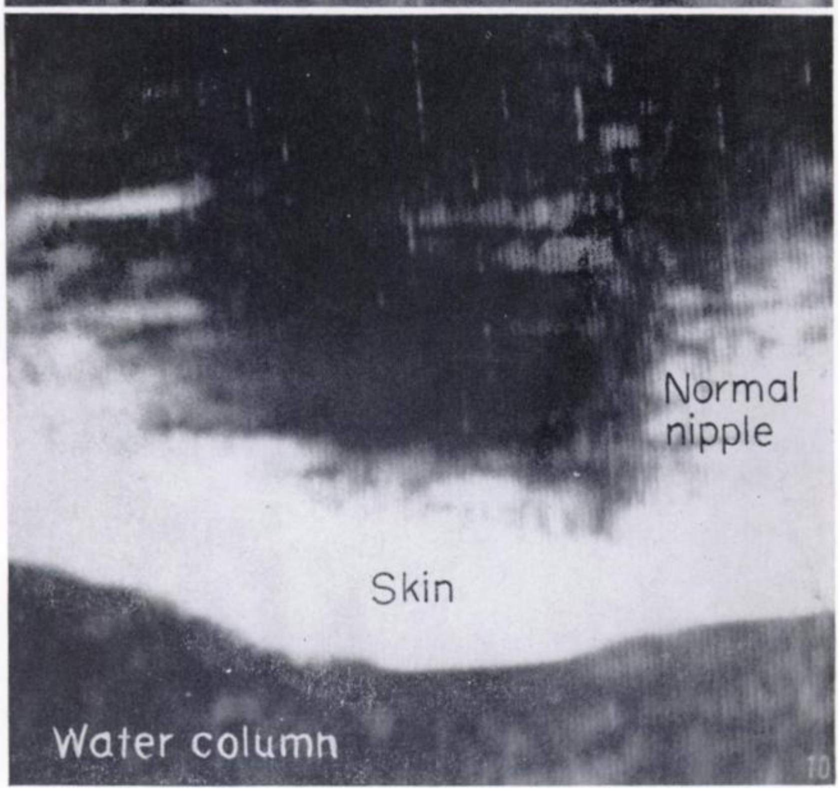
FIGS. 9 and 10.—Greatly magnified echograms of the nipples in Case 4 are shown. The component intensity modulated uni-dimensional echograms can be seen vertically.


Cancer
Nipple
Skin
Water column
9


Normal
nipple
Skin
Water column
10

be necessary for mass internal detection and diagnosis. The operation of the crystal in a liquid-filled enclosure, necessary for internal studies, was achieved at the beginning of the studies in 1949.

Biological technics have disadvantages as seen from the physicist's frame of reference. Physical technics appear impossibly precise to the biologist. Standardization of sound phenomena has always presented a challenge to the disciplines of physics. Sound phenomena do not seem strange to the biologist who rarely, if ever, works to exact standards and who is keenly aware of the deficiencies of his technics. Can physics "measure" the esthetic output of an orchestra as do the human ear and brain? Ultrasound has become at least one common meeting place for the two disciplines.

SUMMARY

A study is reported of the examination of lesions of the living, intact, human breast using a pulsed ultrasonic reflection technic. Terminology is based on the word "echo," e.g., Echograph, Echogram, and Echoscope.

Two of many possible ways of revealing the final output of the echograph to human perception are described: uni-dimensional echography, comparable to a needle biopsy, and two-dimensional echography, or pictorial visualization of tissues in a plane. The relationship of the two methods is described.

Examples are given of both types of echogram taken from current clinical studies. The results of uni-dimensional studies up to the time of preparation of the report are given, to show how the echograph can diagnose the histological nature of lesions.

The position of this study in the approach to mass examination at suspected cancer sites, such as the breast, thyroid, upper and lower gastrointestinal tract, cervix, and prostate, is discussed.

What is believed to be the first actual visualization of a cancer within the nipple was achieved (Figs. 9, 10).

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