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U. S. NAVAL SUBMARINE MEDICAL CENTER

Submarine Base, Groton, Conn.

REPORT NUMBER 508

THE FEASIBILITY OF USING PULSED ULTRASOUND TO DETECT THE PRESENCE OF IN VIVO TISSUE GAS BUBBLES

by

John H. Sutphen
Lieutenant, MC, U.S. Naval Reserve

Bureau of Medicine and Surgery, Navy Department
Research Work Unit MF011.99-9003.01

Released by:

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COMMANDING OFFICER
Naval Submarine Medical Center

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SUBMARINE MEDICAL RESEARCH LABORATORY
U.S. NAVAL SUBMARINE MEDICAL CENTER REPORT NO. 508

Bureau of Medicine and Surgery, Navy Department
Research Work Unit MF011.99-9003.01

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SUMMARY PAGE

THE PROBLEM

To review the properties of ultrasound and to investigate the feasibility of using pulsed ultrasound to detect **in vivo** bubble formation.

FINDINGS

The use of pulsed ultrasound to detect tissue bubbles was found to be promising. Bubbles of the order of 0.5 mm to 1.0 mm were consistently detectable. Certain technical problems were encountered. These are discussed in the paper in depth and are basically considered to be amenable to certain modification of some of the present techniques.

APPLICATIONS

Actual physical detection of **in vivo** bubbles represents a significant advancement over observation of their resultant physical signs and symptoms. Ultrasound can give the researcher an objective answer as to when, where, and how much embolization is taking place. This more precise detection in turn can lead to more accurate decompression schedules and possibly even individualized decompression. It may also become a valuable tool to unlock the etiologic factors operational in tissue/gas bubble physiology.

ADMINISTRATIVE INFORMATION

This investigation was conducted at the Submarine Medical Center and reported by the author in partial fulfillment of requirements for qualification as a Qualified Submarine Medical Officer. It was selected for publication as a Submarine Medical Research Laboratory report, designated as Report No. 508, MF011.99-9003.01, in order to make the material available in the literature of submarine medicine and for use in the School of Submarine Medicine at the Center.

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ABSTRACT

To know the precise moment at which a gas bubble forms in a tissue could be of considerable value to researchers and clinicians involved in the study of decompression sickness and air embolism. The observation of clinical signs and symptoms as an end point lends a certain vagueness to the actual events occuring within the tissue itself.

This thesis is designed to familiarize the reader with the basic properties of ultrasound and to investigate the feasibility of employing pulsed ultrasound to obtain echoes from tissue air bubbles.

The results indicate that pulsed ultrasound as employed in the reflectoscope is capable of detecting individual bubbles in the tissue continum. The technique is of course not without its shortcomings and technical difficulties. These problems are discussed and recommendations are made for their solution.

ACKNOWLEDGEMENTS

I wish to express my utmost appreciation to Edward Smith, a student at Albany Medical College, for his tremendous aid in the experimental phase of this study. In addition, I wish to extend my thanks to L. B. Roberts of Ohio State University for his technical assistance and his devotion to all of his students in general. Both Mr. Smith and Mr. Roberts were serving as Ensigns, MC, USNR, under the Cadet Program #1915, at the Submarine Medical Center during the summer of 1967, while I was conducting this study.

My gratitude is also extended to the Submarine Medical Research Laboratory, Submarine Medical Center, Naval Submarine Base, Groton, Connecticut, for providing the necessary surgical equipment and photographic equipment.

John H. Sutphen
Lieutenant, MC, USNR

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THE FEASIBILITY OF USING PULSED ULTRASOUND TO DETECT THE PRESENCE OF IN VIVO TISSUE GAS BUBBLES

INTRODUCTION

A tremendous amount of work has gone into the preparation of the current decompression tables and treatment schedules for air embolism and decompression sickness. These efforts however have been based on empirical observations of "end point," laborious calculations and "guesstimation" of suitable safety factors. Just when an animal becomes a "bent animal" is based largely upon when the animal presents the characteristic signs and symptoms of the "bends." At the time of initial symptomatology there is little doubt that bubbles are in fact present. There does however remain a certain degree of uncertainty and confusion as to whether prior to the occurence of physical signs there may have been tissue bubble formation. If this is the case there is a latent period between the bubble genesis and their collection or recruitment in a sensitive area. The implication here is that perhaps the symptoms and not the bubbles themselves have been the target of our treatment. It would be desirable to have a knowledge of exactly what is going on bubblewise in the tissue itself and whether the symptoms that are seen are the manifestations of the embolus or from the resultant edema. A similar case can be argued for air embolism.

It is the purpose of this paper to present a method of directly monitoring tissue bubble formation and disposition in the affected area. The properties of pulsed ultrasound appear to be promising in this mission. A discussion of the basic properties of ultrasound, the instruments used, and a simple laboratory study are integrated into an investigation of the feasibility of this technique.

BACKGROUND

Ultrasound, Basic Principles

Ultrasound is defined as mechanical radiant energy with a frequency beyond the upper limit of perception of the human ear. The upper threshold frequency of human hearing is generally placed at 20,000 Hz. It is essential to have a good understanding of the properties of sound as well as ultrasound to understand why it lends itself so readily to **in vivo** tissue investigations.

Sound propagates in basically two wave forms, longitudinal and transverse. Longitudinal waves propagate in any material possessing bulk elasticity. They therefore can be transmitted through most media; gases, liquids, and solids, in various degrees. (Figure 1.). Transverse or shear waves on the other hand are more limited as to available media. They can travel only in a medium that possesses elasticity of form (Figure 2) and accordingly are propagated in solids and near solids.

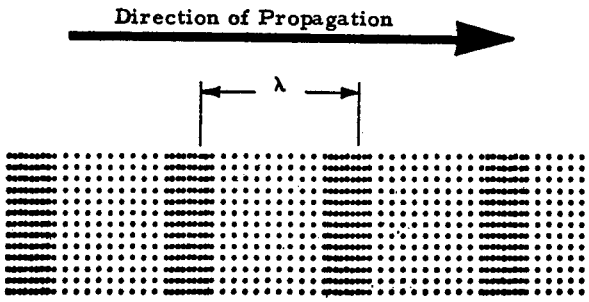


Figure 1. Particle Motion for a Longitudinal Wave

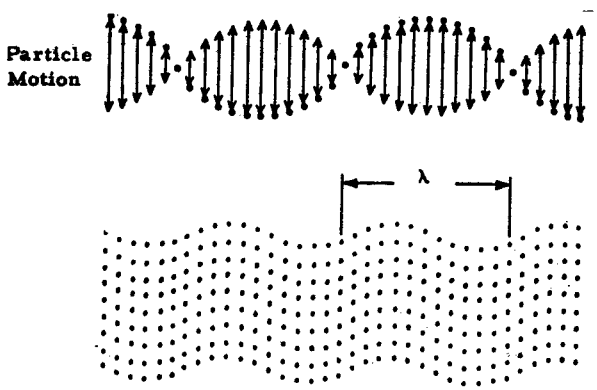


Figure 2. Particle Motion for a Shear Wave

It might be more clear to state that longitudinal waves can travel in soft tissue, tissue fluids, and bone. Shear waves may be seen only in hard objects such as bone.

Sound velocity is dependent upon the elastic properties and the density of the medium. Shear waves travel at substantially lower velocity than longitudinal waves, usually about 30% to 70%. Sound velocity is not appreciably influenced by frequency provided that the elastic properties and the density remain constant. In diagnostic work it is unlikely that any parameter other than temperature change has much effect on the sound velocity in a particular tissue. Temperature produces an effect due to the density change that is associated with it. Sound velocity may be calculated using equations 1 through 3 in Appendix A.

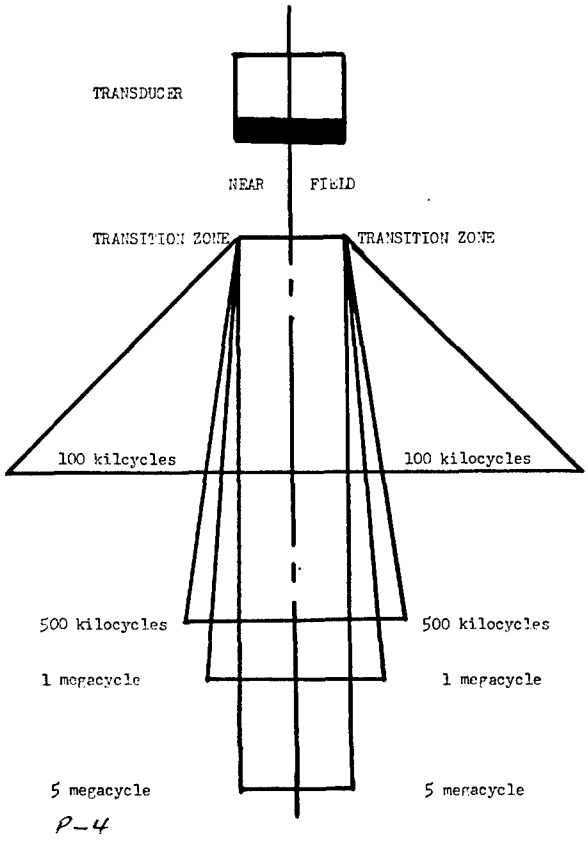


Figure 3. Far Field Beam Divergence Patterns for Frequencies of 100 KHZ to 5 MHZ for a Circular One Inch Diameter Crystal. Medium is Water at 20 Degrees Centigrade.

Audible sound has essentially no beam characteristics. As the frequency of sound increases, the more it tends to collimate into a beam. The mathematical expression for this property is shown in equation 4. The angle of divergence is directly proportional to wavelength. A diagram demonstrating beam divergence as a function of frequency is shown in Figure 3. It may be seen from this figure that there is essentially no beam divergence at 5mHz.

Owing to its beam characteristics ultrasound has many useful applications. It can be focussed, refracted, and reflected. These properties are a function of the relative acoustic impedances of the tissues at either side of an interface. Acoustic impedance is the product of the density and the sound velocity of the substance. The fraction of incident sound that is reflected or transmitted at an interface is a function of the impedance mismatch of the two media and the angle of incidence. Calculation of the corresponding reflection and transmission coefficients is accomplished using equations 5 and 6. The angles of refraction at the interfaces obey Snell's law as expressed in equation 7. It is interesting to note that echoes have been detected, amplified, and recorded with reflection coefficients of 0.01%. A table of useful sound parameters of some common materials is presented in Table I.

Attenuation of sound in a medium depends upon the distance from the transducer as well as the attenuation coefficient. The mathematical expression of the relationship is found in equation 8. The attenuation coefficient is a function of the frequency and, being exponential, exerts a pronounced effect on the transmission of sound. The higher the frequency the greater the energy loss of the beam over a given distance. As the frequency drops, the beam property disappears, and resolution is lost. The frequency selected for a given purpose therefore depends upon whether the investigator desires to merely detect a discontinuity or to describe it in detail as to its physical form. Low frequencies are for high sensitivity and lower resolution. High frequencies are for high resolution at the expense of sensitivity.

The Reflectoscope

The instrument largely responsible for the recent interest in diagnostic ultrasound is an outgrowth of metallurgical nondestructive testing. The instrument is appropriately called the ultrasonic reflectoscope. It is essentially an ultrasonic sonar tranceiver.

One of the most important components of the reflectoscope is the transducer. The transducer acts to change electrical energy to mechanical energy or **visa versa.** Certain crystalline substances exhibit the piezoelectric effects, that is they can change pressure (mechanical energy) into electrical energy. These substances have a rather ideal property therefore to act both as a transmitting source and as a receiver of acoustic energy. There are two categories of piezoelectric substances- naturally occuring and synthetic. Quartz, lithium sulfate, and Rochelle salt fall into the first group. The modern, synthetic polarized ceramics include barium titanate, lead zirconium titanate, and lead metaniobate. In diagnostic ultrasound, the latter group seem to perform better than the naturally occuring crystals. The crystal is set into vibration by a pulse of radio frequency energy lasting 2 microseconds or less. After the crystal has given off its short burst of vibrations it becomes a receiver for a period long enough to receive the echoes. The cycle repeats itself from 100 to 600 times per second. The transducer is therefore in the receiving mode 99.97% of the cycle. These sound pulses are transmitted to the tissue where they propagate away from the transducer until they meet a discontinuity of acoustic impedance such as bone, fat, lung, etc. where an echo is reflected back to the transducer.

At the same instant that the sound pulse leaves the transducer a horizontal sweep is initiated across the face of an oscilloscope. When an echo is received by the transducer it is amplified and fed to the vertical deflection plates of the oscilloscope. Accordingly a vertical spike is produced on the sweep. The distance from the transducer to the tissue discontinuity is therefore proportional to the length of the oscilloscope sweep. The sequence of the above electronics is illustrated in Figure 4. This type of display is known as the "A" mode. This display is the one used in this experiment.

There are several other display modes available in the reflectoscope. It may be operated in the through transmission mode with a separate transmitting and receiving transducer. This mode may also be modified to receive the echoes that return to points other than that of the transmitter. A separate transmitting and receiving crystal are required for this operation.

TABLE I

SOUND PARAMETER OF SOME COMMON MATERIALS

Material	T °C	V_L cm/sec x 10^5 (mm/μsec)	V_T cm/sec x 10^5 (mm/μsec)	ρ gm/cm³	Z = ρc gm/cm² sec x 10^5
1. Air	0°	0.331	--	1.29 x 10^{-3}	0.00042
2. Water	20°	1.483	--	.998	1.48
3. Water	25°	1.495	--	.997	1.49
4. Saline (0.154 mil)	25°	1.504	--	1.005	1.51
5. Glycerin	20°	1.923	--	1.26	2.42
6. Methyl Alcohol	20°	1.123	--	0.799	0.889
7. Soft Tissue (human) average	37°	1.54	--	1.06	1.63
8. Bone	37°	3.48	--	1.8	6.26
9. Acrylic Plastic		2.68	1.1	1.18	3.16
10. Polystyrene		2.35	1.12	1.056	2.48
11. Aluminum		6.25	3.10	2.71	17.2

T= temperature in degrees centigrate

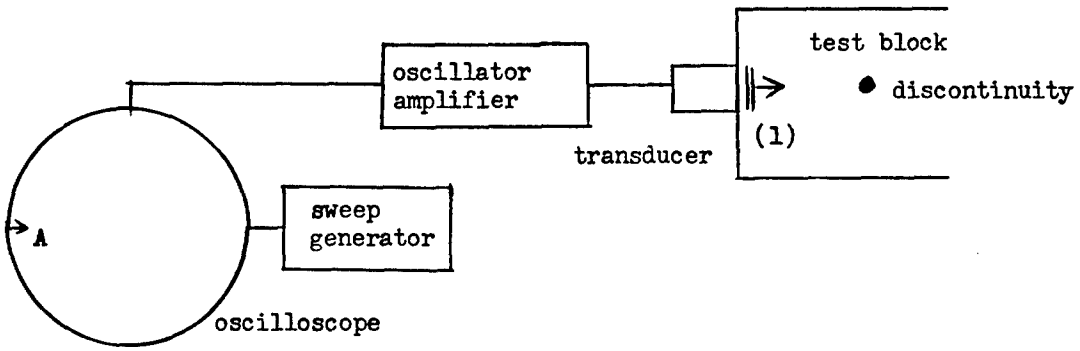
V_L= velocity of longitudinal waves in cm/sec x 10^5

V_T= velocity of transverse waves in cm/sec x 10^5

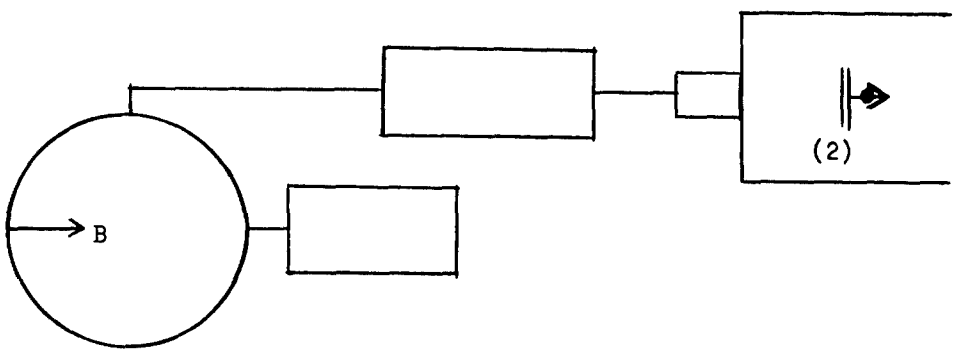
ρ= density in gm/cm³

Z= acoustic impedance in gm/cm²sec x 10^5

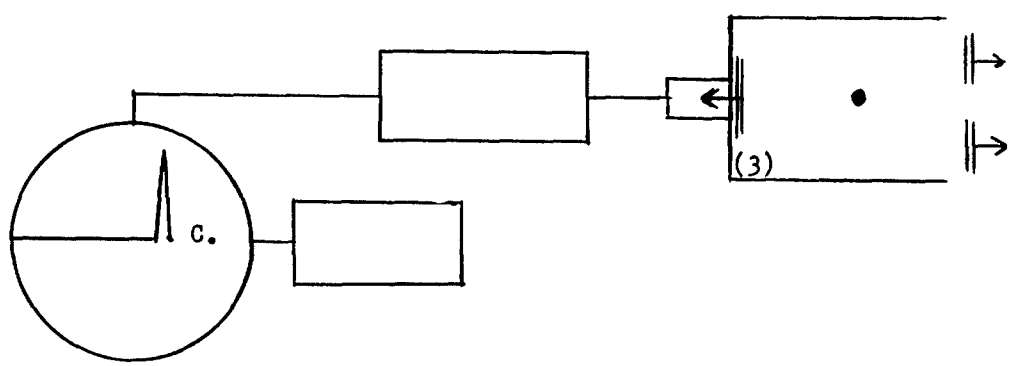
Perhaps the most promising method of display for biological scanning is the "B" mode. In this mode an actual pictorial plot is represented on the cathode ray tube. The "B" mode transducer position is varied in a line across the area to be recorded. Each transducer position corresponds to a separate sweep origin. The sweep is intensity modulated so that wherever an echo is received a dot appears on the corresponding oscilloscope sweep. An illustration of the "B" mode is shown in Figure 5.



(1) Sound pulse generated as transducer begins travelling through test block.
A. At same time CRT horizontal sweep is initiated.

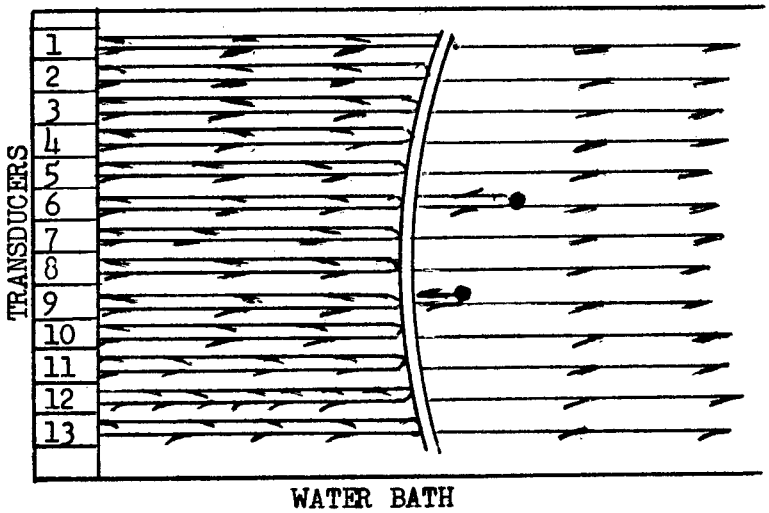


(2) Sound pulse travels to position (2)
B. In same time CRT has advanced to position B.

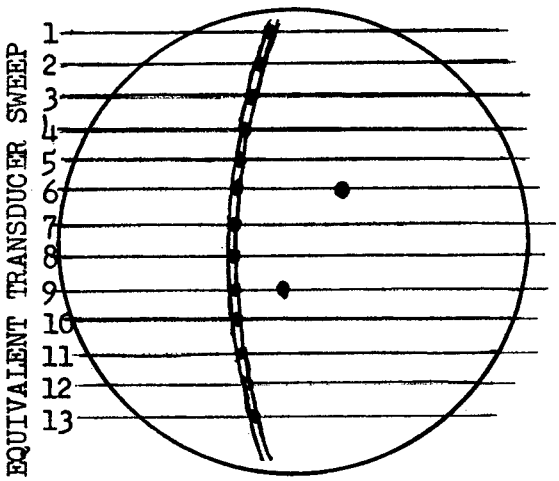


(3) Portion of sound pulse has been reflected from discontinuity, received by transducer and amplified to produce vertical spike on CRT.
C. In the time that it took for the sound pulse to travel to the discontinuity and return to the transducer the sweep has advanced to position C. The length of the CRT sweep is therefore proportional to depth of the discontinuity in the test block.

Figure 4. — Reflectoscope Display in Mode "A"



TEST OBJECTS IN WATER BATH SHOWN IN RELATIONSHIP TO TRANSDUCER ARRAY.



CATHODE RAY TUBE DISPLAY WITH VARIOUS TRANSDUCERS SYNCHRONIZED TO A CORRESPONDING SWEEP POSITION

Figure 5. — Reflectoscope Display in Mode "B."

In the mode "B" display multiple transducers (or a single moving transducer) are required. In effect, for each transducer position there is a corresponding different sweep origin. If each sweep begins as its mated transducer sends its sound pulse, then the distance travelled by the pulse-echo will be proportional to the horizontal sweep distance. In the "B" more, however, the echo is NOT seen as a vertical potential spike on the CRT screen, but rather as an increase in the intensity of the electron beam. Hence, where there is an echo, there will be a dot on the screen. The confluence of dots outlines a video image. The resolution of the system is determined by the number of transducers used and the number of separate associated sweeps.

Ultrasound in Medical Diagnosis

The potential value of medical ultrasonics was recognized as early as 1942 when Dussik (1) attempted to use sound as a means of producing an "x-ray" type picture. His experiments utilized the transmitter-receiver concept. A transmitting transducer was placed on one side of the head and a receiver on the opposite side. His hopes were to demonstrate a decrease in sound intensity in the penumbra of the third ventricle. Unfortunately Dussik lacked the modern tools to execute his experiment and his efforts were largely unsuccessful. The experiment did however outline many of the technical advances that would be required for perfection of the technique.

While Dussik was at work in the medical field, others were applying ultrasound to the field of non-destructive testing. Flaws in metals proved to be relatively easy to detect when ultrasound was transmitted into a steel plate. Flaws, abrupt changes in density, and impurities produced recordable echoes. The concept of the pulse-echo instrument was developed here. This reflectoscope relied not upon the transmitted sound intensity recorded at the opposite side of the material but rather upon the reflected echo intensity. A more complete treatment of the subject of non-destructive testing using ultrasound can be found in reference (2).

In 1956 a Swedish neurosurgeon, Leksell, (3) was able to convincingly demonstrate lateral shifts in the midline structures of the brain due to space occupying lesions. He used the reflectoscope principle and correlated his findings with the anatomy of the brain itself. His work was the first to awaken the medical profession to the tremendous potential of ultrasound. Since Lekell's original paper, there have been several large clinical series substantiating his work (4-7). All of these investigations deal primarily with shifts of the third ventricle/septum pellucidum complex due to space occupying lesions. The "echoencephalogram" has become commonplace in many emergency rooms throughout the world as a rapid, atraumatic screening procedure for subdural hematoma, brain abscess, brain tumor, cysts, and various forms of hydrocephalus.

As early as 1954, interest was aroused in the field of cardiology (8). Again the activity was begun in Europe. Edler and Hertz (9) introduced a method of recording ultrasonic echoes from the anterior leaflet of the mitral value. Since these early studies, numerous investigators have corroborated and extended these cardiac findings (10-13). In an article by Segal **et al** (14), 125 patients, of which 50 served as normal controls, were extensively examined correlating electrocardiogram, phonocardiogram, catheterization, and cineradiocardiogram with the echocardiogram. In only five patients were they unable to show the expected pattern. Each of the five had pulmonary emphysema with some degree of chest deformity. In patients with mitral stenosis they were able to show definite slowing of the movement of the leaflet. In addition, they could correlate its motion with sounds, electrical activity, and the actual dynamics of the cardiac cycle. Both the "A" mode and a modified "B" mode, sometimes known as the "T-M" mode, were used in this experiment. The "B" mode was the more fruitful of the two, in that it provided a time-displacement plot which lent itself readily to analysis of the resultant wave forms.

Due to the heart/lung interface at the posterior pericardial margin, it is quite easy to obtain echoes from this interface. In pericardial effusion this distance is increased. Investigators have been able to demonstrate pericardial effusion by this technique (15). It is conceivable that this method might be modifiable to also demonstrate cardiac hypertrophy.

Holmes **et al** (16) were able to demonstrate various somatic and visceral tissues utilizing the "B" mode display. In their work they first made ultrasonic "somagrams" of laboratory animals and then correlated these with the actual anatomy by frozen cross-sections made at the level of the corresponding transducer scan. Echoes were produced at tissue interfaces. Using this technique they were able to demonstrate convincing outlines of organs such as stomach, spleen, kidneys, liver, and spinal column. Howry and Holmes (17) subsequently published an excellent article which gives the reader a panorama of uses of diagnostic ultrasound in the diagnosis of abdominal diseases. They were able to show excellent scans of human liver, kidneys, and bladder. Figure 6 is a poor copy of one such scan of a urinary bladder, before and after catheterization. Their pictures of hepatic abscesses, hepatic cirrhosis, and kidney cysts are not as clear as radiographs but are far more definite than radioisotopic scans. These investigators also have been able to obtain other human anatomical features such as carcinoma of the breast, gallstones in situ, and numerous cross sections of arms, legs, necks, etc. (18-20). It is interesting to peruse these soma-

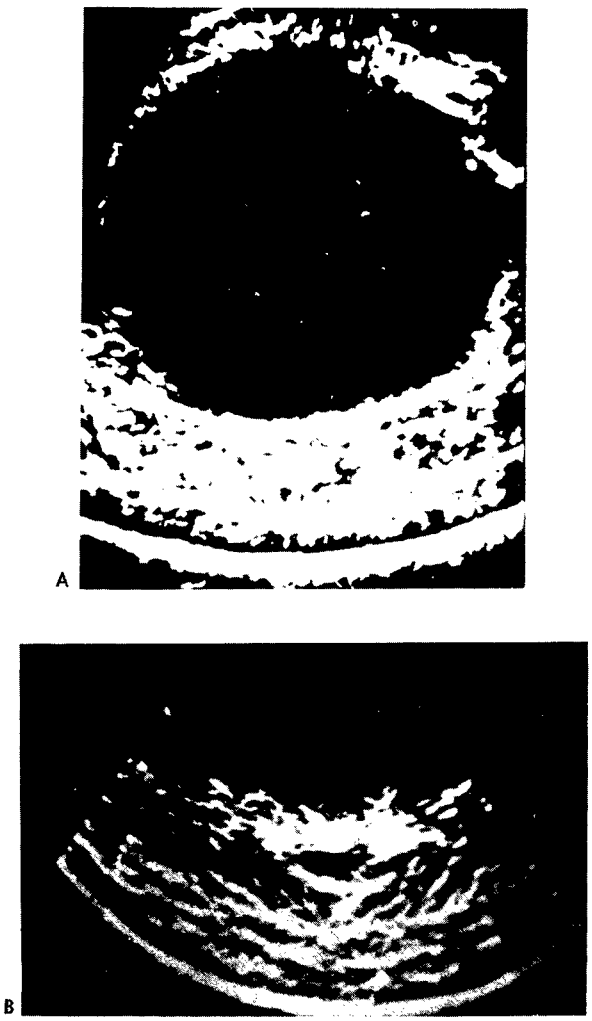


Figure 6 A and B. Somagrams of Bladder Region of a Patient Before and After Remival of 500CC's of Urine by Catheter. in A, Distended Bladder (Spherical Gray Area) is Well Outlined.

grams to get a feeling of the quality of current ultrasonic scanning techniques.

The methods used by Howry and Holmes have found acceptance in the fields of obstetrics and gynecology (21). The gradual curves of the maternal abdomen and the fluid filled uterus lend themselves well to transducer coupling and sound transfer to the fetus in the gravid uterus. The "B" mode scan gives an outline of fetal head and to a lesser extent the skeleton. Biparietal diameters, growth rates of the fetal head, predicted fetal weights, etc. can all be reasonably calculated using ultasonics (22). Using the "A" scan, Winters (23) was able to detect the presence of intrauterine contraceptive devices in 45 of 47 patients examined without the use of x-ray. Using a miniature transducer fixed to the tip of a rubber glove positioned in the posterior vaginal fornix, he directed the sound beam across the uterus. When an IUD was encountered by the beam an echo was produced which then appeared as a "blip" on the reflectoscope screen.

With the development of special-purpose transducers, ultrasound was adopted by other medical specialties. Some of the more interesting as well as rewarding experiences have been in opthalmology. Figure 7 is a rather poor reproduction of a scan made by Dr. Gilbert Baum of the normal eye. It was published in references (24) and (25). Considering the relative densities of the tissues of the eye and the clarity of present ultrasonograms, it appears that ultrasound will have a promising future in diagnosis of eye pathology. Bronson (26) has been successful in using the "A" mode to locate intraocular and extraocular foreign bodies. There are several advantages of using ultrasound in preference to x-ray for foreign body detection. First of all, it will detect many types of objects that are radiolucent. Secondly, the eye is relatively more easily accessible to the ultrasonic transducer than it is to the x-ray tube/film combination. There are also certain advantages to the magnifying effects of the ultrasonogram as well as the geometrical advantage of presentation of a transverse cross section of the globe on the cathode ray tube.

As a final illustration of the usage of diagnostic ultrasound, Austen and Howry (27), used it to detect bubbles in the extracorporeal loop of a cardiopulmonary bypass in a dog. Loose particles and bubbles entering the blood stream in such procedures can produce severe and long lasting neurological deficits. Visual inspection of the arterial line is not as accurate or dependable as a constant ultrasonic scan.

Figure 7. Ultrasonogram of Human Eye. Tremondous Loss of Resolution Due to Copying.

EXPERIMENTAL PROCEDURE

Introduction

In the previous section of this paper many well documented applications of diagnostic ultrasound were discussed and in some cases illustrated.

Referring to Howry's work (18, 19, 20), reasonably strong echoes could be obtained from many soft tissue interfaces. Echoes were always received from soft-tissue/bone interfaces. Reflections from the bladder-wall /urine interface shown in Figure 6 had reflection coefficients of about 0.15%. For the soft-tissue/bone interfaces the coefficients approximated 34.5. These values were computed from equation 5, Appendix A, and the values of acoustic impedance tabulated in Table I. Using this same method the reflection coefficient for soft-tissue/air comes out to be 100.0%! It would therefore seem logical to assume that detection of such a discontinuity would be almost a certainty. This thesis attempts to lend some some insight into the practical aspects of detection of these bubbles.

The first portion of the project was aimed at studying air bubbles in a model medium. Three separate transducers were tested for their ability to detect air bubbles generated from a glass diffuser immersed in a water-filled plexiglass tank.

Detection of intravascular and extravascular bubbles was the object of the second phase of the experiment. Several coupling techniques were attempted on rabbits.

The rabbits proved to be difficult animals to work with and in the third part of the experiment a dog was used instead of a rabbit. Recordings of intracranial emboli were made on this animal.

Phase 1.—Tank Studies

In this section of the experiment a large plexiglass tank filled with water was used for familiarization with the reflectoscope, transducers, cathode ray tube/camera assembly, coupling agents, and techniques of microscopic bubble generation.

The apparatus is shown in Figure 8. The reflectoscope was a modified Sperry* UM 715 with a 5N pulser-receiver unit and a preset sound velocity selection switch cailbrated to the average velocity of sound in soft tissue. A plywood adapter was constructed to accommodate the Tektronix** C-12 oscilloscope camera to the reflectoscope. Using Polaroid*** black and white film, ASA 3000, the ideal camera settings were f5.6 at 0.1 sec. The following were the settings used as parameters set into the reflectoscope:

1.	Sensitivity	X1 with vernier at 0.2
2.	Pulse Length	¼ to ½ turn clockwise
3.	Reject	0.1 turn clockwise
4.	Sweep	Internal preset
5.	Markers	Calibrated to 1 cm/division
6.	Mode	A scan
7.	Sweep Delay	Adjusted for best representation

A rather limited search was made to find a coupling agent. Common laboratory items such as petrolatum, glycerin, surgical lubricant, SAE 30 machine oil, lanolin, and water were tried. There was little difference in the coupling characteristics of these compounds. Surgical lubricant§ seemed to be the most convenient to handle and was chosen for use in the animal experiments. SAE 30 machine oil was used for the tank study.

Three separate transducers* were tested for their ability to detect the bubbles generated in the plexiglass tank. A 3/4 inch diameter, 5mHz; a 3/4 inch, 2.25mHz; and a 1 inch and a 3/4 inch, 1mHz transducer were each coupled to the plexiglass tank and compared as to their abilities to detect the bubbles generated (Figure 9). The bubbles were generated from a ground glass diffuser immersed in the plexiglass tank. Detergent was added to the water in the tank until bubble size reached a minimum diameter. The bubbles were generated at about 15 cm from the transducer surface and had an average diameter of 0.4mm. Figure 10 shows a close-up

*Sperry Products, Division of Automation Industries, Danbury, Conn.
**Tektronix Corp., Portland, Oregon.
***Polaroid Corp., Cambridge, Mass.
§Comfort Mfg., Chicago, Illinois

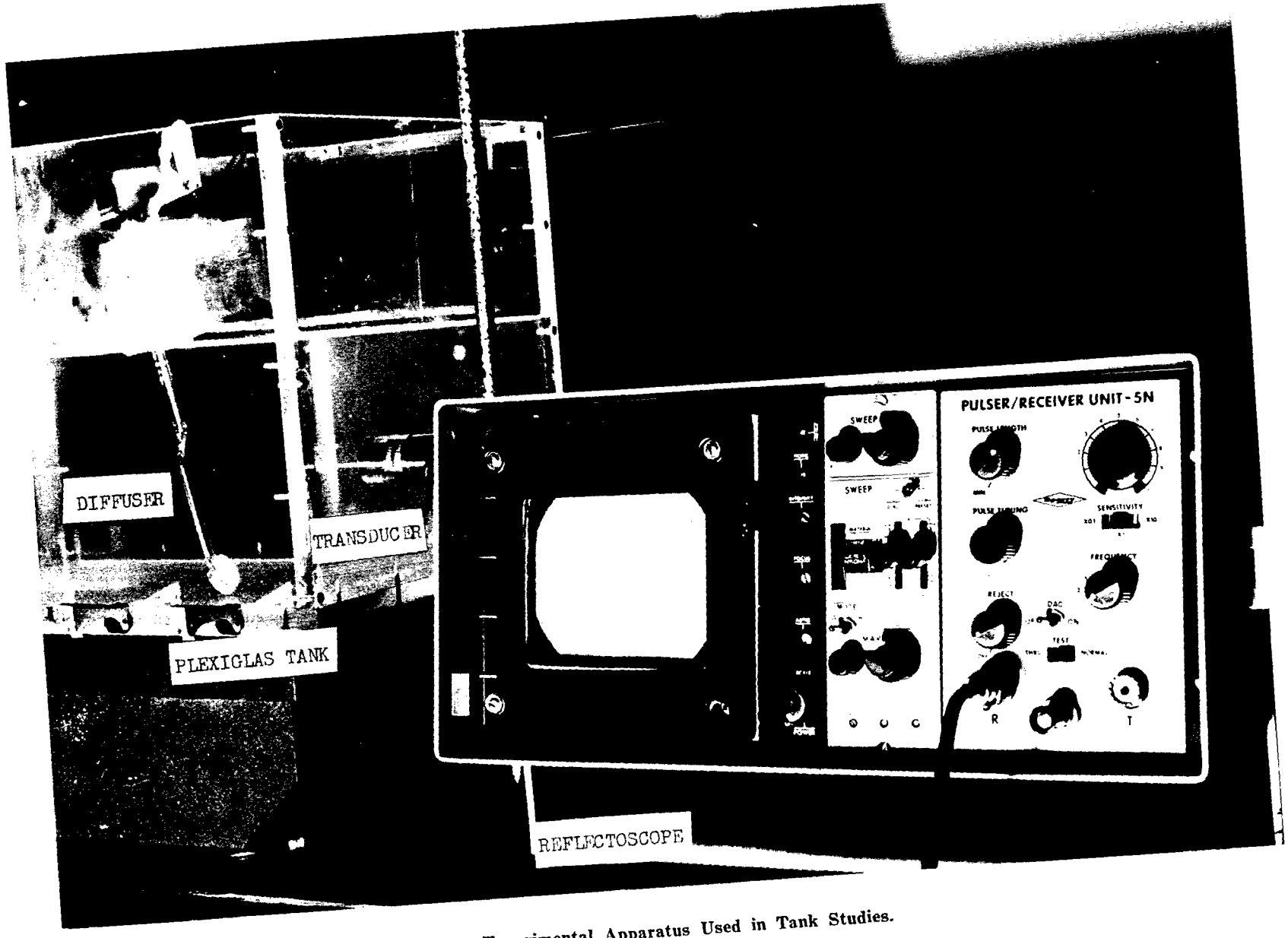


Figure 8. Experimental Apparatus Used in Tank Studies.

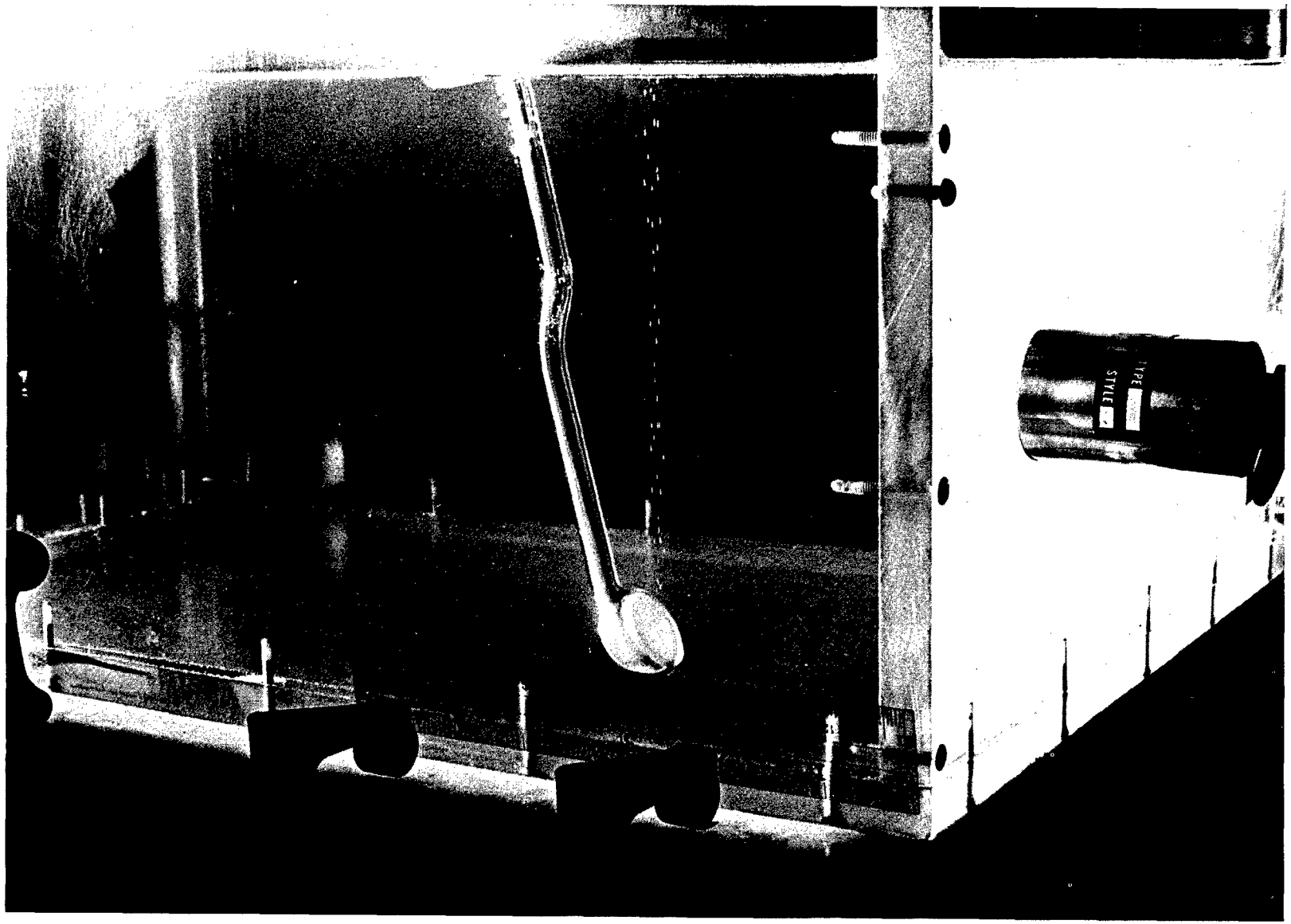


Figure 9. Close Up View of Transducer/Tank Complex in Tank Study.

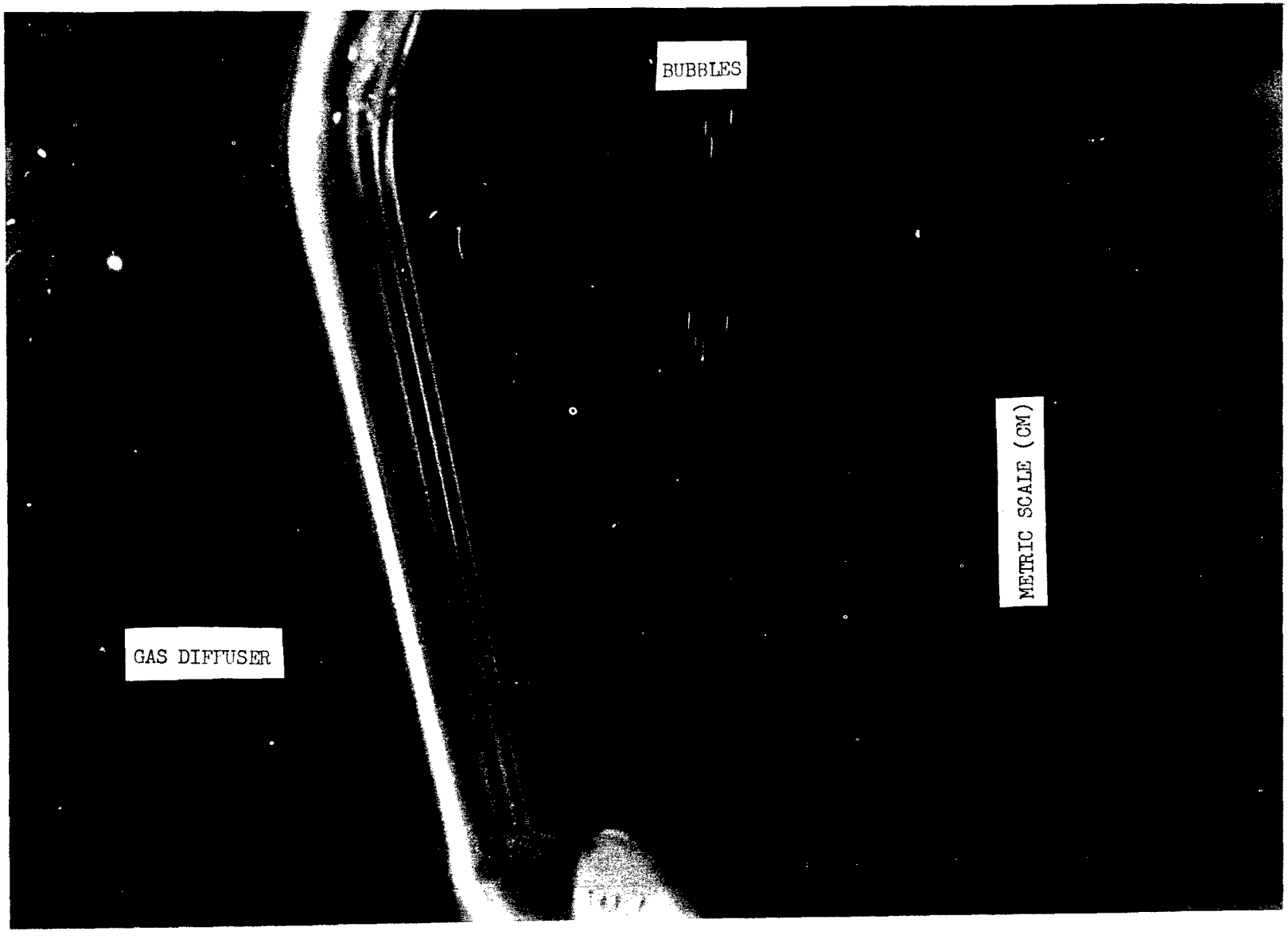


Figure 10. Close Up View of Diffuser, Bubbles, and Scale.

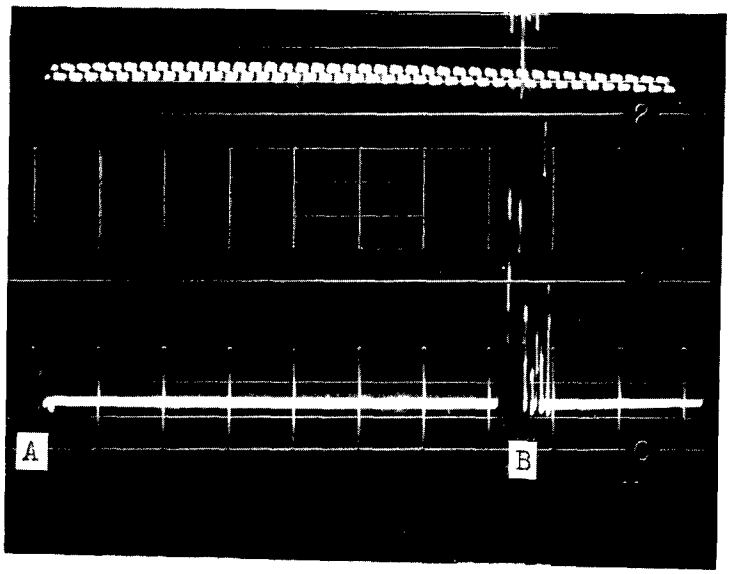


Figure 11. Tank, No Bubble Formation. "A" is Initial Transducer Complex. "B" is Echo Complex from Opposite Side of Plexiglass Tank.

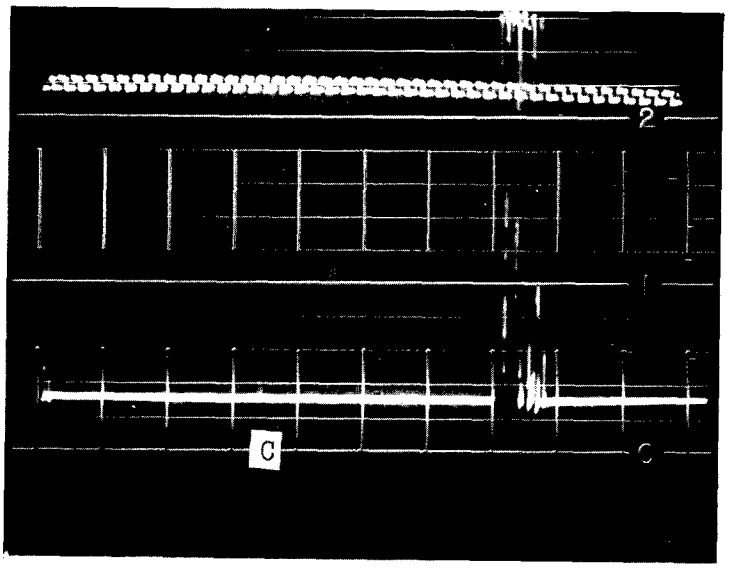


Figure 12. Same Situation as in Figure 11 with Echo "C" Shown From Volley of 0.4 MM Bubbles. Transducer is 5 MHZ.

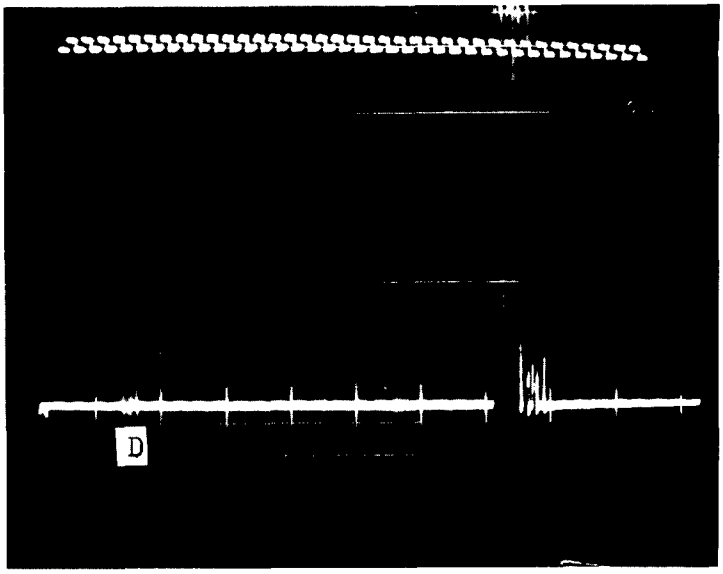


Figure 13. Tank, Echo "D" is From Volley of 00.4 MM Bubbles. Transducer is 1 MHZ.

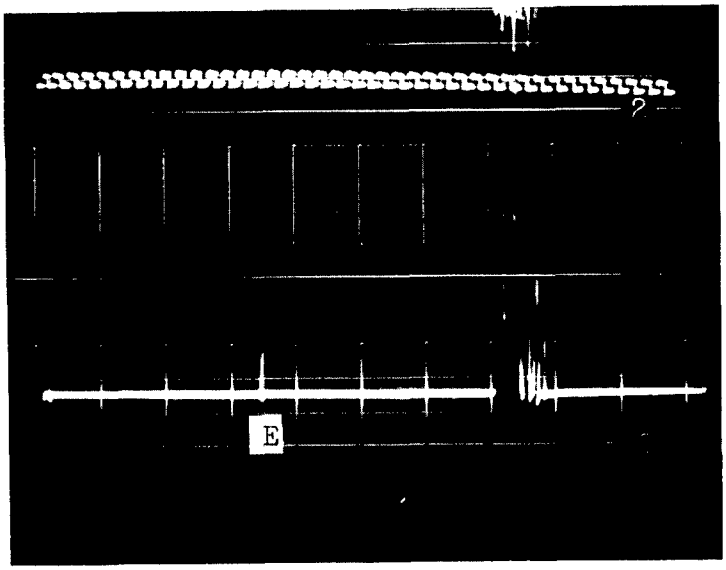


Figure 14. Tank Echo "E" is From Single Bubble 0.4 MM Diameter. Transducer is One MHZ.

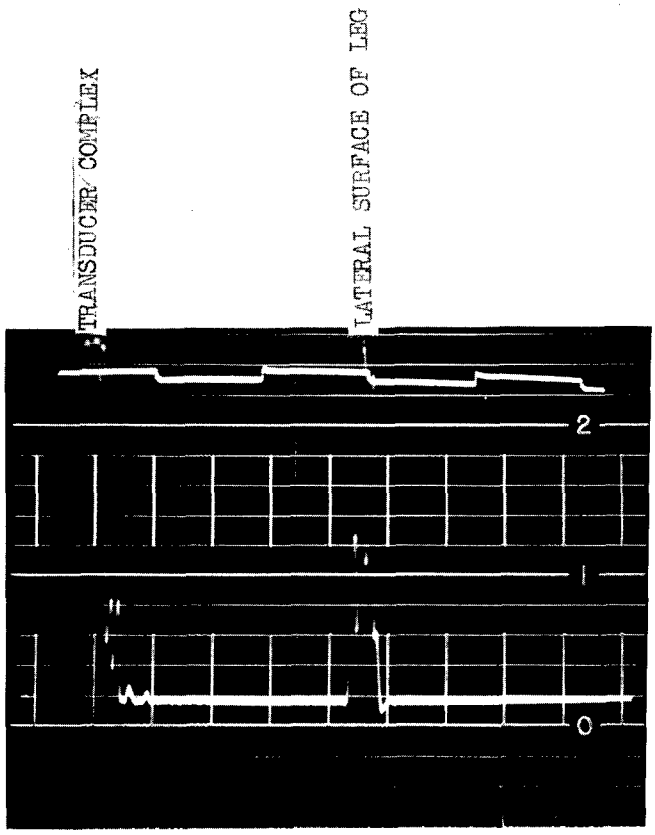


Figure 15. Cross Section of Hind Leg of Rabbit No. 1. Pre-Injection.

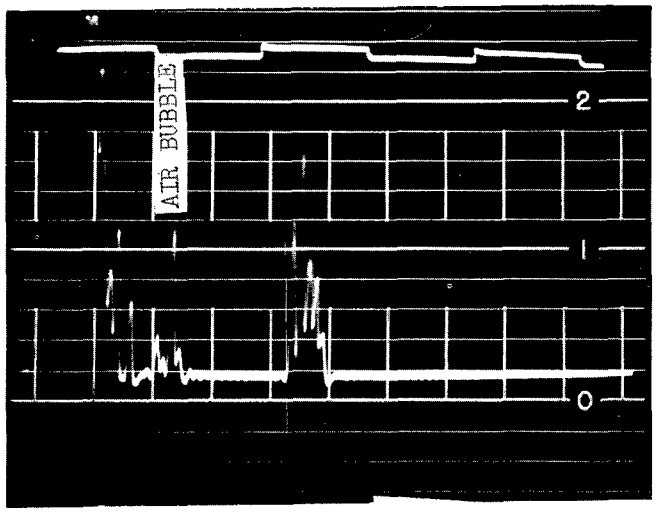


Figure 16. Same Cross Section, Post-Injection.

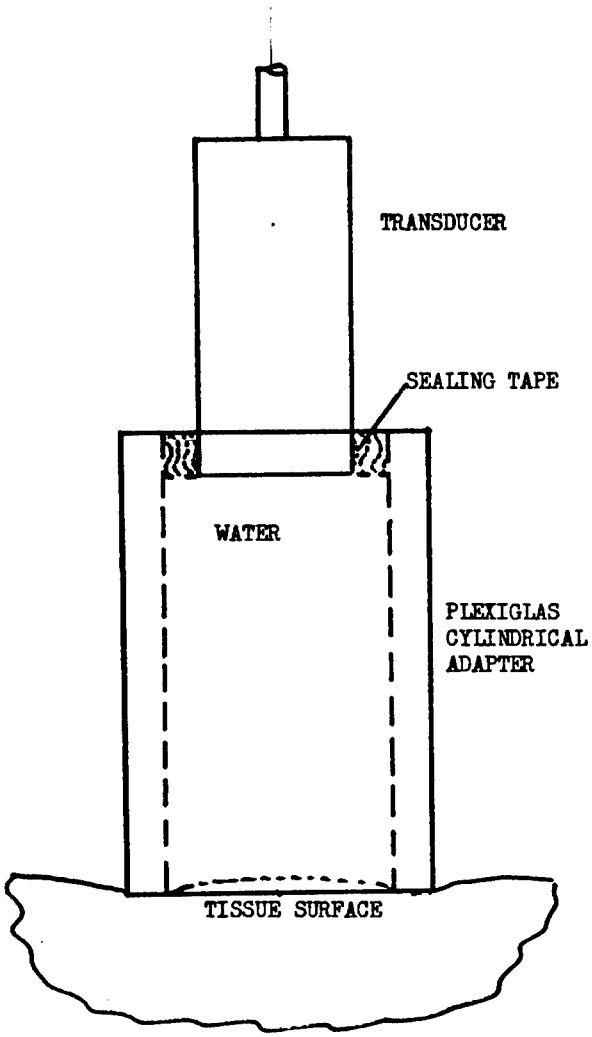


Figure 17. Spacer/Adapter Diagram. Plexiglass Cylinder is Filled with Water to Couple Transducer to Tissue Surface. This Technique Separates the Transducer Complex from the Skin Echo.

view of the generator, a centimeter scale, and the bubbles. The sound beam from the 5mHz crystal was drastically attenuated by the water but nevertheless did provide an echo (Figure 12). Attenuation of the sound from the 1mHz transducer was much less than with the 5mHz as may be seen by comparing Figure 12 and 13. Figure 11 is a blank and Figure 14 is an echo from a single bubble as seen with the 1mHz transducer. The 2.25 mHz transducer as might be expected lay somewhere in between. Inasmuch as resolution, a function which increases with frequency, was of minor concern, and sensitivity, a function which is less attenuated at lower frequencies, was of primary concern, the 1 mHz transducer was chosen as the transducer of choice for the **detection** of bubbles.

The water-filled tank was chosen as a test system because of the similarity of the relative acoustic impedances of soft tissue and water (1.63×10^5gm/cm^{2}sec vs. 1.51×10^5 gm/cm^{2}sec, respectively). Water also presented a continuous medium thus eliminating artifacts introducable by density changes.

From this phase of the experiment it appeared that if stereotaxis could be maintained between the transducer and the target bubbles, bubbles of 0.4mm diameter could be constantly observed with the 1mHz transducer.

Phase 2.—Rabbit Studies

This part of the experiment involved the deliberate innoculation of air into a piece of living tissue by intramuscular or intra-arterial injection. The 3/4 inch, 1mHz transducer was coupled to the shaven skin of a rabbit thigh in several different ways. Four sibling rabbits weighing from 7 to 8 pounds were used in this phase of the experiment.

Rabbit no. 1 was a seven pound female. It was anesthetized with sodium pentobarbital. The hair on the medial aspect of the right hind leg was shaved. The transducer was then mounted in a fixed position on the medial aspect of the thigh, being coupled to the skin with surgical lubricant (see section on tank study, phase 1.). Figure 15 is the ultrasonogram before the injection of air. Figure 16 is the same scan after the injection of 9 cc's of air. A distinct spike is seen in the vicinity of the intramuscular bubble.

Rabbit no. 2 was an 8-pound male. It was prepared in the same manner as the first rabbit. In this experiment however, an effort was made to dissociate the transducer wave complex from that of the proximal skin. This

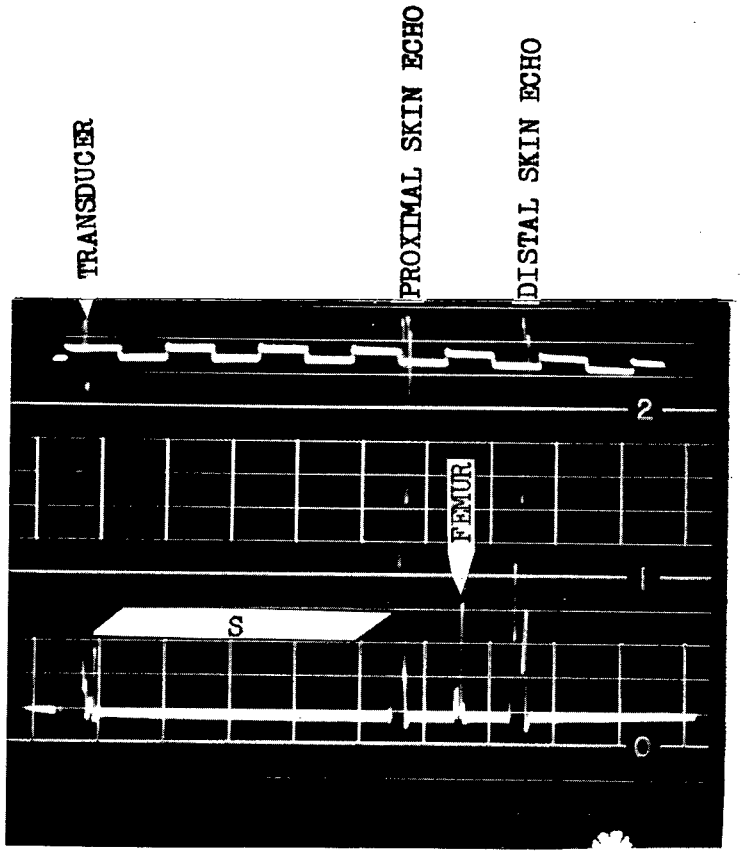


Figure 18. Pre-injection Film Rabbit No. 2. Distance "S" Represents Distance From Face of Transducer to Proximal Skin Echo.

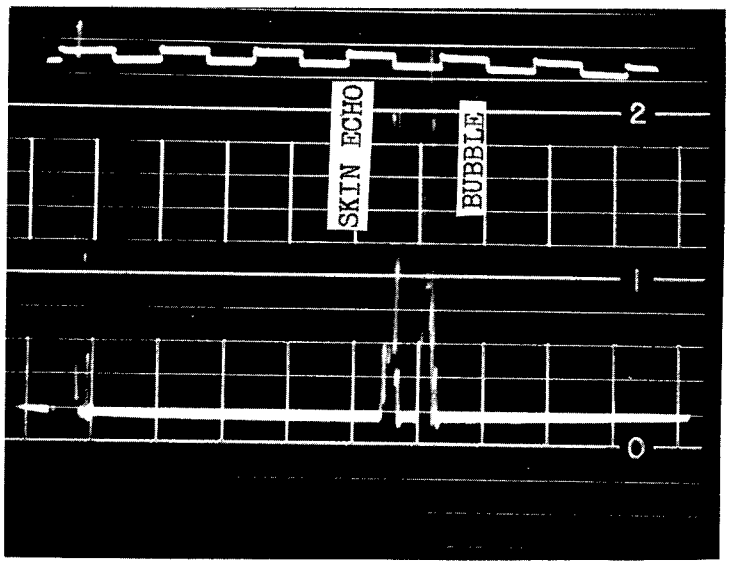


Figure 19. Post-Injection Film, Rabbit No. 2. Intramuscular Bubble Echo Obscures Distal Skin Echo.

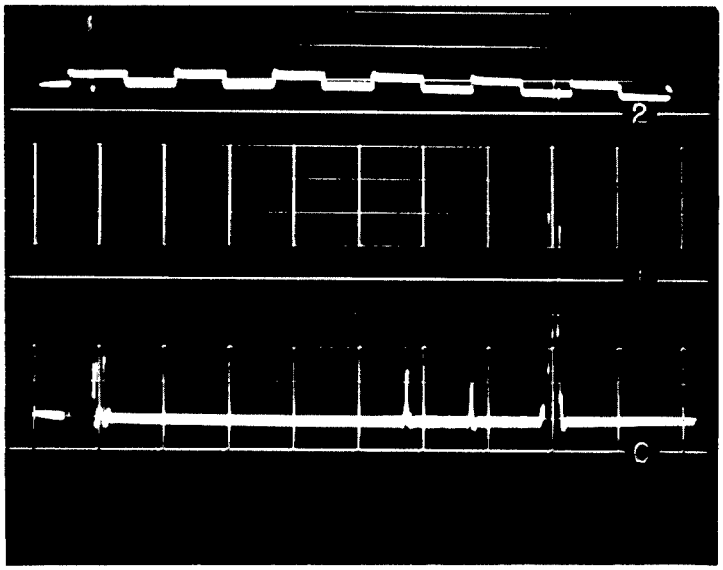


Figure 20. Ultrasonogram Prior to Intra-Arterial Injection in Rabbit No. 2. Note Similarity to Figure 18.

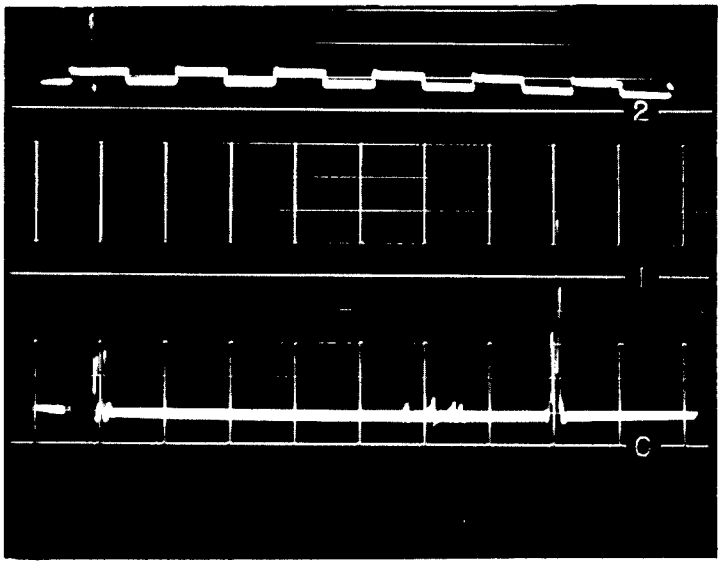


Figure 21. Post-Injection Film of Rabbit No. 2. Intra-Arterial Air Injection. Loss of Intensity on First and Fourth Spikes are Due to Slight Loss of Stereotaxis. Bubbles are Represented by the Second and Third Spikes. Reflection of Distal Skin is Preserved.

separation was achieved by placing a spacer between the surface of the transducer and the skin. A diagram of this spacer is shown in Figure 17. Figure 18 is the pre-injection film. Figure 19 is the same profile after the injection of 5cc's of air. The significant spikes on the recorded picture are described on the figures. Following the intramuscular the right femoral artery was isolated and a small (circa 0.1mm ID) catheter was passed up the artery into the abdominal aorta. At this point the rabbit died. With the catheter in place, 5cc of air was injected. There was no alteration of the CRT trace. The rabbit was posted at this point. The aorta, heart, and major arteries and veins were filled with air. No air however passed below the catheter into either iliac arteries. The aorta was then clamped at the diaphragm and the transducer replaced on the left femoral area. Five more cc's of air were then injected into the aorta. This air passed readily into the left femoral arterial tree. The pre- and post-injection profiles are shown in Figures 20 and 21 respectively. Post mortem examination of the left iliac and femoral arteries confirmed the presence of intravascular air emboli as well as the previously injected intramuscular air.

Rabbit no. 3 was an 8-pound female. This animal was prepared as in the previous experiments. A cutdown was made in the right femoral artery and a tiny catheter advanced to the abdominal aorta. Heparin was added to the catheter and a 5cc syringe was attached to the base of the catheter. The transducer with the spacer attached was then placed against the medial aspect of the left thigh. The water in the spacer served as the couplant. The apparatus was then anchored securely to a heavy ringstand. After a control film was taken, 5cc's of air were injected into the aorta. The resultant bubble spikes were seen on the CRT screen but due a time lag they were missed by the camera. A repeat injection of 4cc's was then attempted and the camera caught several of the passing bubbles. The rabbit succumbed after this injection. Post mortem showed that there were indeed bubbles throughout the arterial and venous systems. There were many bubbles in the brain and heart presumably from retrograde flow up the aorta and through the heart. The recordings made are shown in Figures 22 and 23.

Rabbit no. 4 was an 8-pound male. It was prepared as were the previous three. In addition 2cc's of 1% xylocaine were infiltrated into the area of the arterial cutdown. This measure proved to be of remarkable value in decreasing the rabbit's response to local stimulation and also decreased the dosage of sodium pentobarbital required from 200mg to 90 mg. The arterial cutdown was then made into the right femoral artery and the catheter inserted to the level of the bifurcation of the aorta. The transducer with the attached spacer was then mounted on the medial aspect of the left thigh and anchored by a clamp to a ringstand. The pre-injection photograph is shown in Figure 24. The first 5cc injection of air was largely missed except for residual air trapped in some of the smaller arteries. Figure 25 demonstrates these. Figure 26 was taken at the time of injection and consequently caught many of the emboli as they passed beneath the transducer on their trip downstream. There seemed to be no loss of stereotaxis in this phase of the experiment and as a result it was felt that this portion of the study was quite accurate.

Phase 3.—Dog Study

It was felt after the results of the rabbit studies that a significant amount of information might be gained from attempting to detect cerebral gas embolism in a larger animal. (An attempt was made to do this in the rabbit, but relative size of the cranial structure caused such a profusion of secondary and tertiary echoes that the bubbles themselves were obscured.)

A 35-pound beagle dog was anesthetized with 10cc's of Sedasol. A local infiltration of 1% xylocaine was made in the area of incision of the cervical skin. The right carotid artery was then isolated and a heparinized 18 ga polyethylene catheter inserted into it. The animal was then placed in a prone position and the scalp shaved from the zygomata to the midline occipital protuberance and forward to the anterior margins of the orbits.

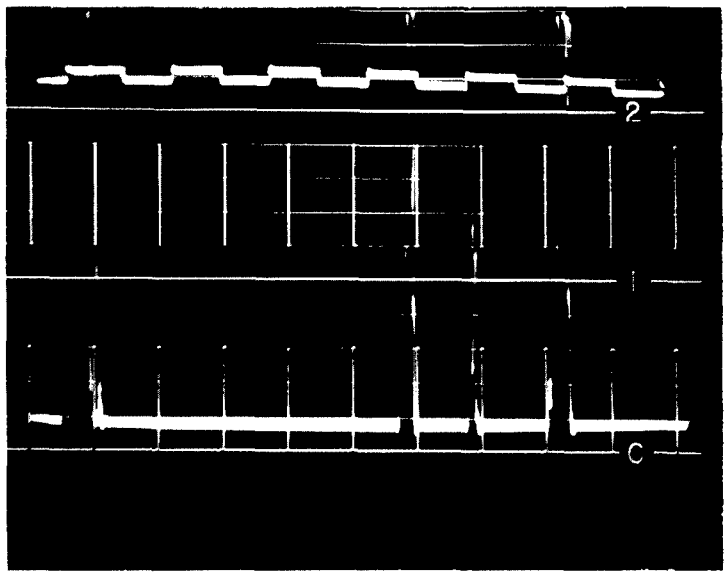


Figure 22. Pre-Injection Film, Rabbit No. 3.

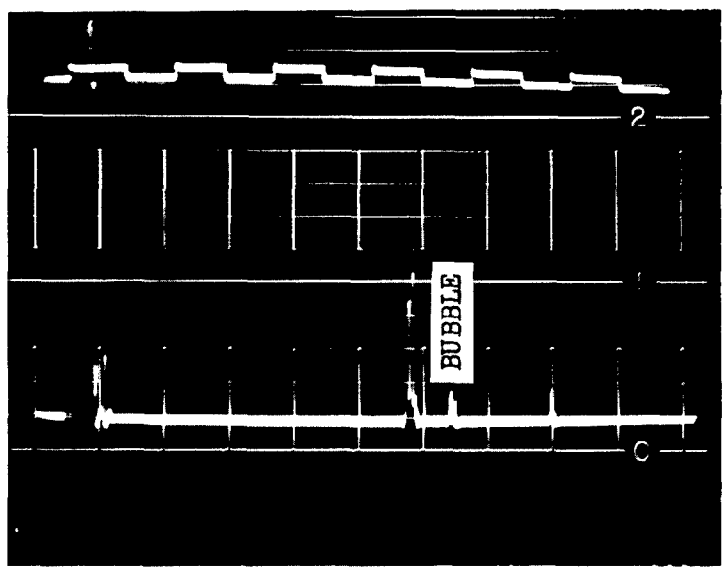


Figure 23. Post-Injection Picture of Above. Amplitude Decreases are Due to Slight Loss of Stereotaxis. Note the Presence of Bubble Echo and Position of it Relative to the Skin and Bone Echoes.

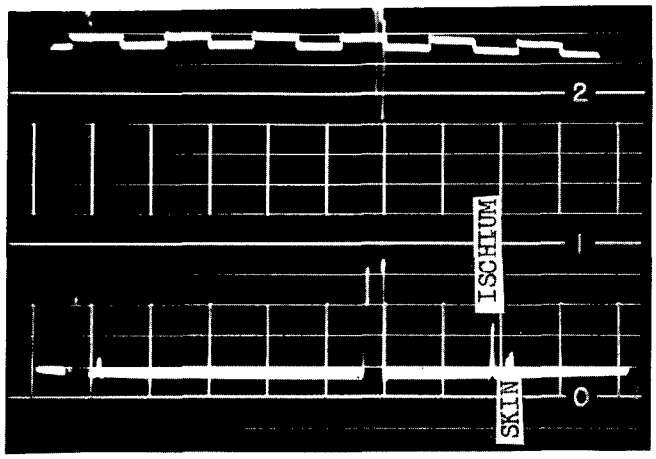


Figure 24. Rabbit No. 4 Pre-Injection. Spikes at Right are Ischium and Skin.

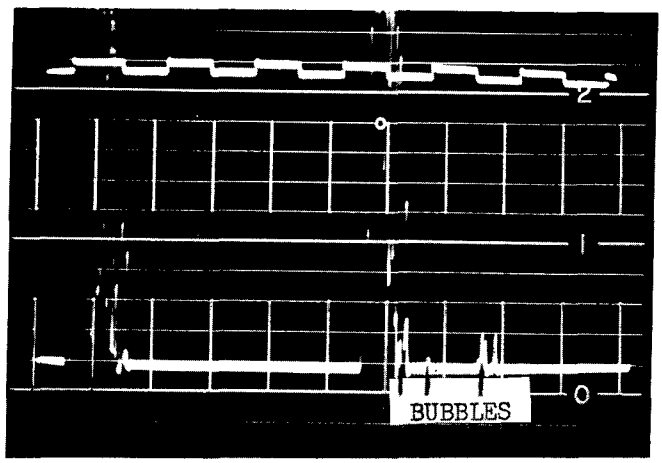


Figure 25. Post-Injection of 5 CC's of Air into Left Iliac Artery.

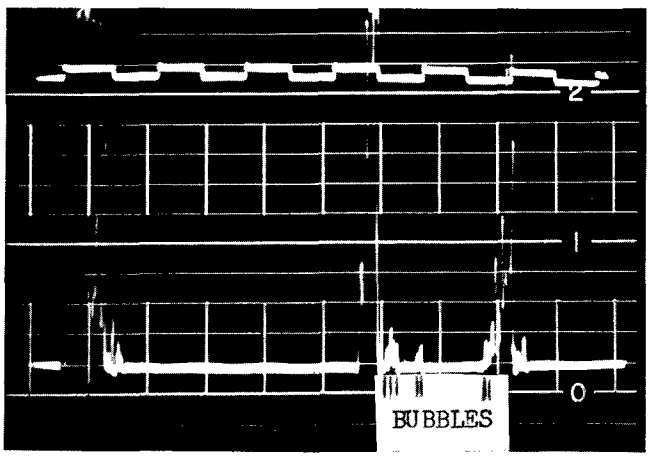


Figure 26. Post-Injection of Another 5 CC's of Air into Left Iliac Artery.

The 1mHz transducer with and without the spacer was placed in a variety of trial positions on the skull. The best echoes were obtained by placing the transducer without the spacer at the crest of the zygoma at its anterior-posterior midpoint. The axis of the transducer was then directed across the brain toward the opposite external auditory meatus. Figure 27 is the ultrasonogram of this path prior to embolization. One and one-half cc's of air were injected into the carotid artery. The transit of the bubbles was missed by the camera but was witnessed by the reflectoscope operator. A second shot using 5cc's was then slowly infused and the camera was triggered earlier than with the 1½cc shot. The results are shown clearly in Figure 28. The dog died after this injection and was subsequently posted. Figure 29 shows a photograph of the left side of the brain around the middle cerebral artery. Bubbles may be seen in the middle cerebral artery as well as some of the smaller arteries. The depth of the bubbles as determined by the reflectoscope were then compared to the depth measured by a centimeter rule. The experimental error between the two measurements was within 5%. In Figure 29 the instrument seen in the upper part of the photograph is the tip of a Kocher clamp. Using this object for reference, the largest bubbles may be seen to be 1.0mm in diameter. From the reflectoscope pattern it is obvious that some smaller bubbles are also being detected. There was no readily available means of correlating the location of these spikes with the distance to the bubbles themselves.

It seemed therefore, despite the unusually complex curvatures of the dog's cranial vault and the relatively confined geometry of the vault, that echoes of extremely small bubbles were being displayed on the reflectoscope screen.

DISCUSSION

Despite the fact that bubbles could be detected in all of the animals embolized, it was felt that these results would have been more meaningful if a larger test animal had been used. The thickness of the thigh of a rabbit (circa 3cm.) and the relative sizes of the anatomical structures and their positions made the positioning of the transducer difficult. Slight loss of stereotaxis amplified inconsistencies. The diameter of the arteries made embolization difficult, inasmuch as the diameter of the catheter approximated that of the rabbit's aorta and tended to obstruct flow into the legs. The technique of arterial cutdown was also quite tedious, due to the size of the femoral artery. An animal with a thigh diameter of 5 to 10 cm or greater would have been more satisfactory for this study.

There is no question that the "B" mode or a modification thereof would have superior to the "A" mode. Beam alignment would not have been so critical. In the technique used, any loss of stereotaxis between the pre- and post-injection phases required duplication of the entire procedure. Had it been known in which direction the beam drifted, correction might have been possible. Utilization of the "B" mode could have cut down considerably on the time required to place the transducer properly. It was largely unknown in the "A" mode whether the transducer was actually sounding the anatomic area that indeed corresponded to the area of the highest bubble density. Similarly bubble dispersion could not be studied in adequate detail. These events, as well as the final steady-state equilibrium, would be nearly impossible without the "B" mode. The single transducer would have to be in too many places at too many times in too small of an interval. The ideal device for **detection** as well as **localization** of emboli would be a modified "B" mode display or perhaps some form of sector scan.

There are basically two varieties of "B" mode displays currently used in ultrasonic diagnosis. One method utilizes a single transducer which moves in a linear track thereby scanning a slice of tissue. The other consists of a fixed linear array of many transducers which are sequentially activated by a switching assembly. In both of these methods the position of the activated trransducer is synchronized with the y axis sweep origin of an intensity modulated horizontal scan. A multiple transducer array with high speed electronic switching would be far more expensive but would provide a more accurate, simple, and rapid scanning procedure. There is a

problem however with any linear scanning array. If the echoing surface begins to curve away from normal to the sound beam, the reflected signal does not return to the transmitting transducer and therefore the echo is lost.

The transducers could be arranged in a circular array. This could be accomplished by placing a single transducer on a circular track and synchronizing its orbital position with a centripetal polar CRT scan, similar to a radar scope display. As an alternative, multiple transducers could be placed in a circular array around the patient and an electronic switch could then scan these different transducers. The output signals would then be displayed on a centripetal polar scan. Using this circular array, an entire sweep of 300 transducers could be made every 0.5 seconds. If the number of transducers were halved the sweep frequency could be doubled and so on.

The question of course arises, what type of coupling could be used with the "B" mode scanners? Direct coupling to the skin could be attempted with the multiple transducer technique but this would require individual biases to be applied to each polar sweep origin. In addition, there are inherent advantages in having a distance of homogeneous material for the sound to traverse before encountering the tissue surface. The distance acts to isolate the transducer and near zone beam artifacts from the near surface of the test object thereby eliminating the "noise"

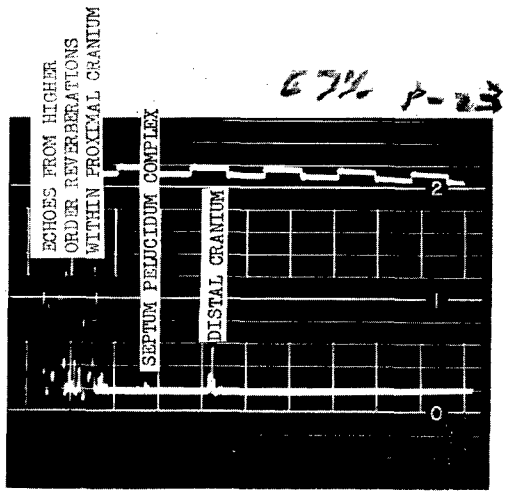


Figure 27. Ultrasonogram of Transcerobral Scan Prior to Injection of Air into Carotid Artery.

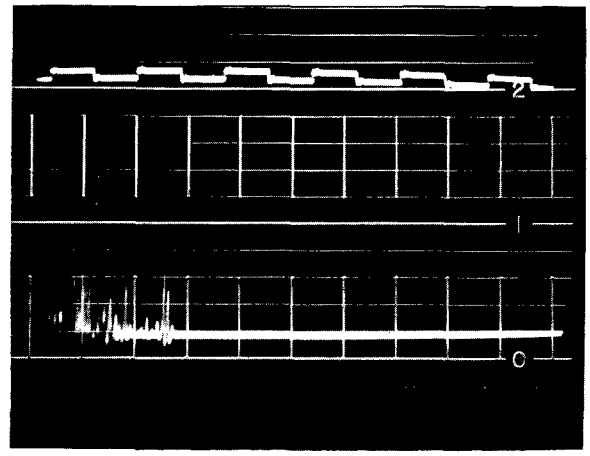


Figure 28. Post-Injection Film of Above Animal. Essentially all Spikes are Bubble Echoes. Distal Cranial Echo is Lost Due to Attenuation of Sound by Bubbles.

associated with the transducer/tissue interface. This technique also makes subcutaneous objects of interest easier to visualize. Coupling in such an instance is usually attained by immersing the test object or patient in a water bath. A problem arises in the case of a lacerated or severely injured part being immersed or if scans are to be made about the face. One solution to this problem is to fashion polyethylene bags or adhesive plastic surgical drapes into custom-fitting pools and tanks about the area to be kept dry. Reference (17) gives a description of such techniques as used by Howry and Holmes in some of their work. Some variation of their method would be adaptable to the study of **in situ** bubble investigation.

Another problem that arose in the experiment was the maintenance of stereotaxis. In order to study a given part of the animal with the "A" scan, that part had to be completely immobilized relative to the transducer through both the control phase and the embolization phase of the experiment so that an accurate comparison of the two films could be made. Various devices have been described to achieve this. Most of them rely on mechanical fixation to bony prominences, grooves, etc. The techniques, needless to say, are rather traumatic if the patient is required to spend more than fifteen minutes in such a

vice-like device. If more extensive data were available in the basic ultrasound/anatomical relationships, fixation need not be so critical.

Due to the three degrees of freedom indigenous to the beam of the "A" scan, the search for familiar tissues can be exhausting and reproducibility a near impossibility. One degree of freedom is eliminated by virtue of the geometry in adopting the "B" mode. Inferences are more easily made from the planar representation of the "B" scan. Similarity of this display with an actual anatomical cross section facilitates one's getting one's bearings from familiar structures. Positioning is still important in the "B" mode, however, but to a much lesser degree.

Ultrasound is in its early childhood. It is evident that it will have a trying adolescence prior to the realization of its full potential. It must be studied and compared to the normal anatomy and physiology to establish itself in the diagnostic armamentarium. It has already shown its capacity to detect soft tissue discontinuities but needs the same patient research that brought x-ray into our ken.

If more sophisticated ultrasonic instruments were employed in submarine and aviation medicine, more light could be shed on our present decompression tables. Are there actually bubbles present before decompression sickness is manifested by its symptoms? Are our present decompression and treatment tables too long? Is there enough individual variation among divers to warrant separate tables for each diver? What parameters affect bubble formation? What is the disposition of these bubbles? Are there any physical procedures that help guard against decompression sickness and air embolism? Do certain drugs affect bubble formation? Is it possible to monitor affected aviators and divers with ultrasound through their decompression on an individual basis? There are many such questions that need to be answered. Ultrasound may well prove to be the key to their investigation and eventual solution.

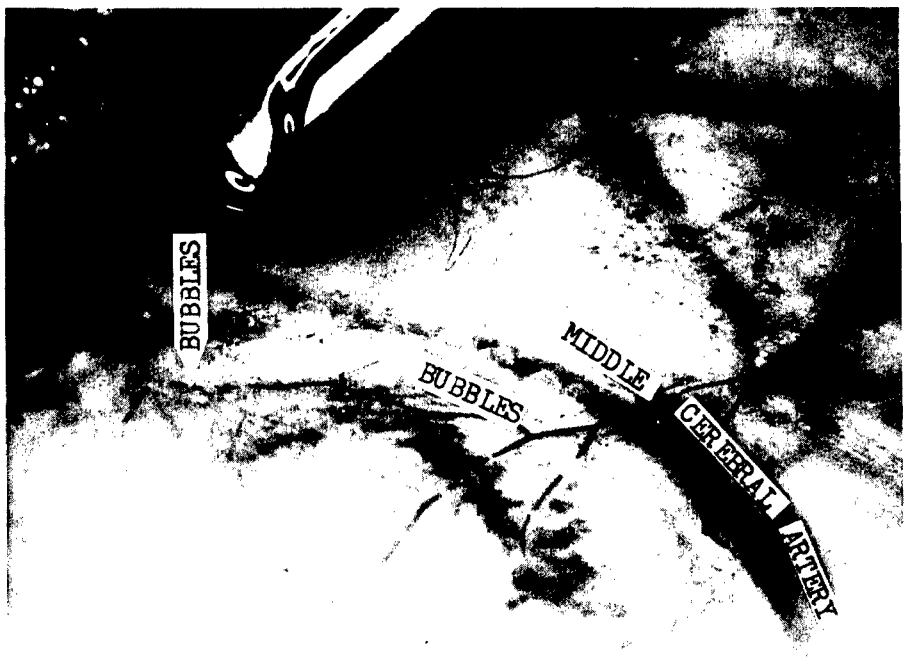


Figure 29. Post Mortem Photograph of Left Parietal Brain Area. Bubbles are Prominent in the Middle Cerebral Artery and Many Tributaries. The Instrument in the Upper Portion of the Picture is the Tip of a Kocher Clamp. Bubbles are About 1 MM in Diameter.

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APPENDIX A

EQUATIONS

1. $V_L = \sqrt{\frac{1}{D\ B_a{}^d}}$ (sound velocity for longitudinal waves in liquids)
2. $V_L = \sqrt{\frac{Y'}{D}\frac{(1-s)}{(1+s)\ (1-2s)}}$ (longitudinal waves in solids)
3. $V_T = \sqrt{\frac{d}{D}}$ (sound velocity for shear wave)
4. $\sin \phi = \frac{1.22\ L}{d'}$ (beam divergence angle)
5. $R_c = \left[\frac{Z_2 - Z_1}{Z_2 + Z_1}\right]^2$ (reflection coefficient)
6. $T_c = \frac{4Z_2Z_1}{(Z_2+Z_1)\ 2}$ (transmission coefficient)
7. $\frac{\sin \phi_1}{\text{si}V_1} = \frac{\sin \phi_2}{V_2}$ (Snell's Law)
8. $I_x = I_0 e^{-2ax}$ (Attenuation of sound intensity)

DEFINITION OF TERMS

V_L	velocity of longitudinal wave
Y'	Young's Modulus of Elasticity (dynes/cm^2)
D	density (gm/cm^3)
B_{ad}	adiabatic compressibility (cm^2/dyne)
s	Poisson's ratio
V_T	velocity of transverse wave (cm/sec)
d	shear modulus of elasticity (dynes/cm^2)
ϕ	angle of divergence (degrees)
L	wavelength (same units of length)
d'	diameter of transmitting crystal
R_c	reflection coefficient
R_T	transmission cofficient
Z_1	acoustic impedance of medium 1 (gm/cm^{2}sec)
Z_2	acoustic impedance of medium 2 (gm/cm^{2}sec)
ϕ_1,ϕ_2	angle of incidence and refraction, respectively
V_1,V_2	velocity of sound in medium 1 and 2, respectively
I_x	intensity of sound at distance "x" from O.
I_O	intensity of sound at initial measuring point in the medium
a	amplitude absorption coefficient
x	distance travelled by sound beam between measurement at I_O and I_O

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13. ABSTRACT

This report concerns a review of the properties of ultrasound and an investigation of the feasibility of using pulsed ultrasound to detect the presence of in vivo tissue gas bubbles. The results indicate that pulsed ultrasound, as employed in the reflectoscope, is capable of detecting individual bubbles in the tissue continuum. The technique is not without shortcomings and some technical difficulties. These problems are discussed and recommendations made for their solution. Possible additional uses for this technique are indicated, when once it has been perfected.

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14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Use of Ultrasound to detect embolism						
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