SOUND WAVES with frequencies greater than 20,000 cycles per second are above the limits of sound audible to the human ear and, therefore, are designated as ultrasound. Over the past several years ultrasonic irradiation has been widely employed as a form of treatment in physical medicine.1 Concurrently, other uses of ultrasound have been developed that utilize the particular transmission characteristics of these mechanical waves. Although ultrasound differs from light in being propagated more easily through a liquid or solid than through a gas, its transmission in a suitable medium is similar to light in many respects. It may be directed in a relatively straight beam with considerably less tendency to scatter than that characteristic of lower frequency audible sound, but demonstrates reflection and refraction similar to light. A beam of impulses traversing an acoustically uniform medium will have a portion of its energy reflected if it strikes the boundary of a medium having different acoustical impedance. The acoustical impedance of any substance is determined by the product of its density and the velocity of sound in the substance, and the proportion of ultrasound that is reflected at any interface is directly related to the magnitude of the difference of the acoustic impedance of the two media. Since the angle of reflection is determined by the angle of incidence of the beam, maximum return of reflected waves to the point of origin will occur when the reflecting surface is oriented at a right angle to the longitudinal path of the ultrasonic waves.

Piezoelectric crystals of the type used to generate ultrasonic vibrations from electrical energy can conversely be activated by ultrasound and convert the mechanical waves into electrical impulses suitable for recording. If the velocity of sound in a medium is known, the position of a reflecting surface can be determined by recording the interval between the emission of an ultrasound pulse and the return of the echo to the source. If the ultrasound transducer is rotated, a field may be scanned in the plane of direction of the ultrasonic beam. This “echo-ranging” technic has been well established as the sonar method for the location of underwater objects and mapping of the ocean floor.

The application of the reflected ultrasound technic to medical diagnosis has been undertaken by many workers over the last several years. Ludwig and Struthers2 found that gallstones and other foreign bodies that had been buried within dog muscle could be located by ultrasound. Subsequently, the technic has been employed to study tumors of the breast,3 and to define soft-tissue structures of the extremities, neck, liver, spleen, and kidneys.4 The normal brain reflects a distinctive midline echo. Displacement of this echo from the midline position has been used to diagnose space-occupying lesions within the skull.5-7 The ultrasonic visualization of the light-opaque eye and other structures of the orbit has been undertaken.8 Pulsed ultrasound scanning of the abdomen is being investigated as a possible adjunct in the diagnosis of cysts, solid tumors, ascites, and in the location and measurement of the fetal head in utero.9

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Reflected Ultrasound in the Assessment of Mitral Valve Disease

By Claude R. Joyner, Jr., M.D., John M. Reid, B.E.E., M.S., and James P. Bond, B.S.
Block, diagram of the ultrasound transmitter, receiver, and the recording equipment employed in these studies.

All of these diagnostic applications of pulsed ultrasound have been concerned with the location or delineation of stationary structures within the body. It is also possible, however, to record the motion of a structure moving to and from the ultrasound transducer, provided the orientation of the reflecting surface is close enough to a right angle to the longitudinal path of the sound beam to reflect a detectable echo to the piezoelectric crystal. The location of the reflecting surface relative to the ultrasound source can be determined at any moment by measuring the time lapse between transmission of a short pulse and the return of the echo. With a transducer designed to emit many short pulses of ultrasound per second, and receive the echoes between transmissions, a nearly continuous record of motion can be obtained.

Edler and Hertz\(^9\) introduced this method for recording cardiac motion in 1954. Their initial impression that the technic might have particular application in the clinical evaluation of mitral valve disease was expanded in the subsequent report of Edler and Gustafson.\(^11\) They described a rapidly moving echo that could be recorded when the ultrasound transducer was aimed toward the heart from the third or fourth left interspace, 1 to 4 cm. lateral to the sternal border. This moving structure was located about 6 to 8 cm. from the anterior chest wall and had a range of motion of about 2 cm. in the anterior-posterior plane. The curve of motion had a consistent characteristic pattern in normal persons with a distinctive distortion of the pattern in patients with mitral stenosis. This method was then undertaken by Effert, Erkins, and Grosse-Brockhoff,\(^12\) who recorded curves appearing identical to those described by Edler. A typical double-peaked curve was found in normal subjects; a distinctive plateau-like distortion of the curve was found in mitral stenosis. The technic has been adopted by other workers in Europe who have essentially confirmed the findings of Edler and Effert.\(^13,14\)

Our investigation was therefore undertaken to develop suitable echo-ranging equipment in this country, and further to evaluate the validity of the method in cardiac diagnosis. The studies in human subjects were undertaken after the equipment was determined to have a negligible acoustic power output, and after preliminary examinations in dogs had demonstrated that satisfactory curves of motion could be obtained.

**Method**

**Equipment**

Figure 1 is a block diagram of the apparatus. The transmitter generates a short electrical pulse that is converted by a barium titanate transducer into a 1-microsecond burst of ultrasound having a frequency of 2 megacycles per second. Immediately after emission of the ultrasonic pulse, the transducer becomes inactive and in receive condition to be mechanically activated by returning ultrasonic echoes. The receive period lasts for 499 microseconds until the transmitter operates again. The control timer repeats this sequence 2,000 times each second. Therefore, the transducer transmits ultrasound only during 1/500 of each second. The acoustic power output delivered by our equipment has been measured directly and found to be less than 0.012 watts per cm.\(^2\).

Echoes returning to the transducer during the receive period are converted into voltage pulses, which are amplified by a receiver and projected upon the screens of two oscilloscopes. An open-face oscilloscope is used to observe the echo pattern during recording. The ultrasound pattern and a simultaneous one-lead electrocardiogram are permanently recorded upon continually moving
35-mm. film from the face of a dual-beam oscilloscope. The echo displayed on the oscilloscope is superimposed upon a linear time base sweep, which starts at the time of transmission. This linear sweep is calibrated in centimeters of tissue between the transducer and the reflecting surface based upon a mean sound velocity of 1,540 M./sec.\textsuperscript{13} A graph of distance as a function of time is thus obtained by moving the recording film at right angles to the horizontal time base sweep and echo display.

**Recording Technic**

The recording area for cardiac motion is limited to that portion of the chest through which an ultrasound beam may be directed without encountering the multiple air-tissue reflecting interfaces of lung tissue. The radiating surface of the transducer is one-half inch in diameter, so that it may be applied in an intercostal space to avoid reflection and absorption of the ultrasound by the ribs. Records are obtained with the subject in a supine position. In most cases, a fast moving echo is best obtained with the transducer applied in the third or fourth left interspace 1 to 4 cm. lateral to the border of the sternum. In a few subjects with thick chests or markedly enlarged hearts, a better tracing is obtained from the fifth interspace.

**Results**

Records were obtained from 25 normal volunteers, all of whom showed a consistently similar echo wave. The characteristic normal echo pattern is shown in figure 2. The electrocardiogram is displayed at the top of the record and one-second time markers are automatically recorded on the bottom of the film. The first white line beneath the electrocardiogram represents the skin surface of the anterior chest. Succeeding echoes from above downward indicate reflections from structures deeper within the thorax. The vertical scale near the middle of the record indicates depth in centimeters from the anterior chest wall. The moving echo with which we have been especially concerned is located at a depth of 5.5 to 8.5 cm. in this subject and has a range of anterior-posterior motion far greater than that of any other reflecting structure. Motion toward the top of the film indicates motion forward, toward the anterior portion of the chest. Motion in the opposite direction represents regression posteriorly in the chest. The configuration of this curve is identical to that reported in normal subjects by Edler and Effert, who suggested in their initial reports that this echo was reflected from the anterior wall of the left atrium.\textsuperscript{10-12} Subsequent to these reports, however, accumulated evidence indicates that the quickly moving echo is reflected from the anterior leaf of the mitral valve. Certainly the reflecting structure is located anterior to the cavity of the left atrium, since multiple-layered echoes of large, laminated, left atrial thrombi have been found to fill the area just posterior to the moving curve.\textsuperscript{16} Edler et al.\textsuperscript{17} passed a needle through the thorax of cadavers in the same plane and direction as that previously taken by the ultrasound beam. After coursing through the anterior wall of the right ventricle, right ventricular outflow tract, interventricular septum, and upper portion of the left ventricular cavity, the needle usually passed through the anterior leaflet of the mitral valve before entering the left atrium from which exit was

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made through the posterior atrial wall. In the same report, they described experiments performed on isolated, perfused cow hearts in which mitral valve motion was produced by cyclic variations in left ventricular and left atrial pressure. Echoes having a typical pattern of motion were obtained when ultrasound was beamed through these hearts. Needles passed through these hearts in the direction of the ultrasound beam pierced the anterior leaflet of the mitral valve in a path similar to that found in the cadaver studies. When the anterior mitral leaflet of the cow heart was immobilized by forceps during the pulsing experiment, the moving echo became stationary.

The numerical designations indicated for the different portions of the ultrasound complex in figure 2 follow the system proposed by Effert and associates. Wave 1 follows closely after the P wave of the electrocardiogram and represents motion toward the anterior chest. Following the peak of wave 1, the reflecting surface begins to recede and moves rapidly to the most posterior point (2) just after the inscription of the QRS complex. There is a rather gradual slope anteriorly to form a short plateau (3), which is followed by very rapid motion forward to peak 4. This peak, in early ventricular diastole, represents the most anterior position reached during the cardiac cycle. The curve then recedes quickly, inscribing a sharp slope to the posterior position 5.

Wave 1 is not seen in the presence of atrial fibrillation but small "flutter waves" can be seen in the ultrasound pattern of some patients with atrial flutter. The relation of wave 1 to atrial activity can be seen in figure 3, which was obtained from a patient with incomplete atioventricular block. The ultrasound pattern in mitral stenosis is different from the normal curve. The 90 persons with mitral stenosis whom we have studied have all shown the distinctive, abnormal pattern described by the European workers. The typical configuration is illustrated in figure 4, which is a preoperative record from a 36-year-old woman with mitral stenosis. At the subsequent operation, the stenotic valve opening of this patient was found to be narrowed to an estimated "one-finger" orifice. The distinguishing feature of the mitral stenosis pattern is the delay in posterior motion from peak 4. When this anterior "hang-up" of the curve during ventricular diastole is of an extreme degree, a nearly flat-top plateau complex results. With this very restricted motion, wave 1 will be very small even in the presence of normal sinus rhythm and effective atrial contraction.

Quantitative assessment of that portion of the ultrasound complex which is distorted in mitral stenosis has been undertaken by meas-
Voelcro of motion of 60 patients with mitral stenosis plotted against the mitral valve size determined at subsequent surgery or necropsy. Velocities recorded in 25 normal subjects are plotted on the right of the chart.

During the speed of motion posteriorly from point 4,12,17 During this phase of ventricular filling, the normal curve shows rapid posterior motion as is demonstrated by the steep slope outlined on the last complex in figure 2. The speed of descent from the horizontal level of peak 4 is measured from the slope by reference to the time and depth scales. In this subject, the velocity is 140 mm./sec. In contrast, the restricted motion mitral stenosis produces the gradual slope seen in figure 4. The velocity is reduced to 15 mm./sec. in this patient. The velocity measurements from the records of 25 normal subjects and 60 patients with mitral stenosis are charted in figure 5. The 60 patients presented, from a total of 90 cases of mitral stenosis studied, are those in whom the size of the mitral valve was determined at operation or postmortem examination after the ultrasound record had been made. The 30 patients not plotted on the chart were either studied only following mitral valve surgery or have not yet been operated upon. Since most of the mitral stenosis patients represented in figure 5 had valvulotomy performed by a closed technic, the size of the valve orifice is presented as estimated by the palpating index finger.* The velocities measured ranged from 85 to 160 mm./sec. in normals and between 2 and 35 mm./sec. in individuals with mitral stenosis. Therefore, no mitral stenosis patient showed a velocity faster than 35 mm./sec., and no normal record had a velocity slower than 85 mm./sec.

Following successful mitral commissurotomy, a change in the ultrasound pattern is usually seen. Figure 6A is a preoperative rec-

*The patients in this study who underwent cardiac surgery were operated upon by Dr. Julian Johnson or Dr. Charles K. Kirby.
ord from a patient with tight mitral stenosis. The velocity is 11 mm/sec. At surgery, the orifice of the mitral valve, which would initially admit the tip of the index finger, was increased to a 2 1/2-finger opening. One week after operation (fig. 6B), the nearly flat plateau-like complex is changed to a faster curve with a steeper slope moving from peak 4 at a velocity of 45 mm/sec. Thirty-five of our patients with mitral stenosis were studied before and after valvulotomy. In figure 7, the preoperative velocity and the valve size found at operation are plotted against the postoperative velocity and estimated final valve opening for each patient. The mean preoperative velocity was 16 mm/sec. (range 2 to 35), with a mean postoperative velocity of 36 mm/sec. (range 10 to 70). Although the mitral stenosis pattern was changed toward a more normal appearing complex, postoperatively, as illustrated in figures 6A and 6B, we have not yet obtained a truly normal configuration in any postoperative patient. The most rapid velocity found was 70 mm/sec. as compared with the lowest normal value of 85 mm/sec. Most of the postoperative records were obtained within a month of surgery, but an occasional one was recorded as late as 3 months after operation.

In 12 patients with "pure" mitral regurgitation, the curve had an essentially normal configuration. The velocity of motion during the diastolic descent was normal or even faster than our normal range. Figure 8 is a record from a patient with massive mitral regurgitation due to a dilated annulus. Wave 1 is not seen, since there is atrial fibrillation, but peak 4 is prominent. The descent from this peak is rapid with a measured velocity of 150 mm/sec.

Ultrasound records have also been recorded from 135 patients presenting conditions other than mitral valve disease. Among these were patients with pericarditis, heart block, hypertension, symptomatic coronary artery disease, thyrotoxic heart disease, and various congenital cardiac lesions. None has presented the ultrasound pattern found in mitral stenosis.

Discussion

The ultrasound curve of heart motion can be obtained easily from most individuals, but we have failed to record a satisfactory pattern from about one of every 15 persons studied. The incidence of failures was higher earlier in the series, and has decreased with increased experience in "aiming" the transducer.
haps some further reduction in the number of uninterpretable records can be obtained; however, the poor transmission of ultrasound through lung tissue is a definite limiting factor. Most of the patients from whom we are not able to obtain a satisfactory recording have unusual chest configurations, severe emphysema, or marked displacement of the heart.

In spite of these limitations, recording the ultrasound pattern is a simple, rapid procedure requiring only a few seconds in those cases in which an interpretable record can be obtained. There is no discomfort to the patient with the procedure since the power output of 0.012 watts/cm.² is considerably less than the 1 to 3 watts/cm.² employed to produce safe heat levels with ultrasonic irradiation therapy. Very high intensity ultrasound can damage tissue, but no adverse effects are known to result from ultrasound irradiation of the duration and intensity employed in our studies. Exposure of the human eye for 45 minutes has proved safe with an instrument having an average power output of less than 0.07 watts/cm.². From their extensive review of the literature concerning the biological effects of ultrasound, Edler and co-workers concluded that there was no evidence that damage would result from the ultrasound intensity used in their studies of heart motion. Also, they found no evidence of harm after performing over 2,500 examinations since 1953 with an instrument having an average output of 0.003 to 0.08 watts/cm.². Heart-motion studies on an additional 700 patients have been reported by other investigators with no suggestions of hazard to the patient. Over the more than 10 years of experience with experimental ultrasound scanning around the extremities and trunk, there has been no sign of tissue damage. There are no known delayed effects of ultrasound such as those that may occur long after exposure to ionizing radiation.

In our series, there is a sharp distinction between the curve obtained from patients with mitral stenosis and that found in the normal subject and those with mitral insufficiency. There was no overlap between the velocities of patients with mitral stenosis and those recorded in other subjects. In fact, no values fell between the 35 mm./sec. top velocity for mitral stenosis and the 85 mm./sec. low velocity for the normal. It would certainly be expected that some patients with less severe degrees of mitral stenosis should fall in the intermediate range; however, the selection of patients for this study would have tended to exclude them. Since the study was undertaken to determine if the technic might have any value in the assessment of mitral valve function, the patients chosen for study were those in whom the surgeon’s estimate of the valve was expected to be available for comparison with the ultrasound pattern. Also, we do not have adequate experience to determine what pattern is to be expected from a stenotic, immobile mitral valve with a fixed opening permitting significant regurgitation.

Many of the persons included in this study had ultrasound recordings repeated on different days with consistently similar curves and calculated velocities. Since there was no appreciable variation in the curves obtained at different times unless surgery was performed, the technic may be an aid in the long-term postoperative evaluation of patients. In particular, it may help determine the mitral valve status of those patients in whom later restenosis of the valve is suspected. The duration of this study is not long enough for us to determine if patients having a successful valvulot-

Figure 8
Ultrasound pattern in a patient with “pure” mitral regurgitation. The velocity is 150 mm./sec.
omy will show further changes toward normal than the velocity increases demonstrated in the early postoperative period (fig. 7). Certainly, none of the postoperative records has become entirely normal although most of the patients have had an excellent postoperative course and a marked decrease in the intensity of the mitral diastolic murmur. Nevertheless, all of these patients have shown some change in the ultrasound pattern toward normal following surgery in contrast to the one patient we have studied before and after an unsuccessful operation. In this patient, in whom an attempted closed mitral commissurotomy could not be accomplished because of a left atrial thrombus, the postoperative records remain identical to the preoperative ones.

Summary
An ultrasound beam directed into a medium of uniform acoustical impedance will travel in a straight line, but a portion of the waves will be reflected at the interface of a medium of different acoustical impedance. A time-distance curve of motion has been obtained from the heart by recording the echoes returned to a send-receive ultrasound transducer applied in the third, fourth, or fifth left interspace. A characteristic curve having two anterior peaks during each cardiac cycle was obtained in the 25 normal patients studied. One peak follows the P wave of the electrocardiogram and is not seen in atrial fibrillation. The other peak of motion toward the anterior chest is followed by rapid regression posteriorly during ventricular diastole. The velocity of the motion was 85 to 160 mm./sec. in normal subjects. In contrast, the records from 90 patients with mitral stenosis demonstrated a distinctive, abnormal pattern having a plateau-type configuration with a velocity of posterior motion of only 2 to 35 mm./sec. The configuration of the curve changed toward normal after successful mitral valvulotomy but none of the 35 patients who were studied before and after surgery has developed a calculated postoperative velocity exceeding 70 mm./sec.

Twelve patients with "pure" mitral regurgitation have had records similar to the normal, with velocities in or above the normal range. None of the 135 other patients studied, representing a variety of conditions, demonstrated a curve of the type found in mitral stenosis.

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References
William Stokes

The other dominating figure in the Dublin School was William Stokes, Graves's pupil and close colleague at the Meath Hospital. His father was a prominent Irish physician, having succeeded Cheyne in the chair of medicine at the College of Surgeons. Young Stokes received his medical education in Edinburgh and then traveled to the leading centers of the Continent for advanced study. An early disciple of Laennec, he presented the first account in the English language of the use of the stethoscope. He is best remembered today for his collaboration in the lucid descriptions of Stokes-Adams syncope and Cheyne-Stokes respiration. Both were recorded in the many English, American, German and French editions of his cardiac classic, Diseases of the Chest and Aorta. Of less dramatic but possibly greater import in the history of medicine was Stokes's insistence on the need for instruction in public health in the medical school. His D.P.H. course in Dublin was the first in the British Isles, and his "Introductory Course on Sanitation" became a standard textbook in the epidemiology of communicable disease.—K. M. Cahill, M.D. The Golden Era of Irish Medicine. The New England J. Med. 266: 545 (March), 1962.
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