Two-dimensional ultrasonic tissue characterization: backscatter power, endocardial wall motion, and their phase relationship for normal, ischemic, and infarcted myocardium

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ABSTRACT To understand the possible differences in reflected ultrasonic energy from normal, ischemic, and infarcted myocardium, we studied 20 open-chest dogs with a commercially available two-dimensional ultrasonic scanner. Echocardiographic radiofrequency images of anterior myocardium were obtained serially during complete coronary occlusion for 2 hr (n = 15) or 5 hr (n = 10), or after temporary coronary clamping for 15 min with release for 1 hr (n = 5). We investigated two variables: the cyclic backscatter power and the phase difference among endocardial wall motion (EWM), cyclic backscatter power (BSP), and left ventricular pressure (LVP). The cyclic BSP decreased from a control (nonischemic) level of 5.1 ± 0.8 to 2.3 ± 0.7 dB during ischemia (up to 30 min after coronary ligation). The phase difference between the EWM and BSP progressed from a control (nonischemic) value of 38 ± 20 to 115 ± 23 degrees during ischemia. For the infarction period (2 to 5 hr after coronary ligation), the cyclic BSP progressively returned toward baseline control levels to 4.0 ± 1.2 dB, but the phase had increased further to 170 ± 28 degrees. The reperfusion study showed a similar decrease in cyclic BSP and an increase in phase after arterial clamping and both returned to near-normal nonischemic values upon arterial release. Simultaneous LVP recordings were performed to assess the phase contribution of endocardial dyskinesia to the total phase difference measurement. At 5 hr the dyskinesia had contributed 46% to the total phase difference, while the backscatter power contributed 54%. However, the EWM contribution occurred immediately while BSP contribution changed progressively during the 5 hr study period. Because cyclic BSP returns to near-normal nonischemic values, it becomes difficult to distinguish 5-hr-old infarcts from normal tissue based on this variable alone. On the other hand, the phase difference remains significantly different during ischemia and early infarction compared with normal values. Thus, a combination of cyclic BSP and phase difference between EWM and BSP may provide a noninvasive tool for discriminating among normal, ischemic, and infarcted myocardium. Circulation 76, No. 4, 850–859, 1987.

DETECTION and characterization of acute myocardial ischemia by ultrasonic means would provide a clinically valuable and cost-effective tool in diagnostic cardiology. Many investigators have observed qualitative regional wall motion abnormalities by echocardiography during acute myocardial ischemia.1–4 Over the last 7 years much effort has been directed toward quantitative analysis of abnormalities of segmental wall motion5–10 and myocardial thickening11–14 during ischemia. There have, however, been several problems. The major shortcoming has been the lack of consistent visualization of the endocardial border throughout the ventricle. This is especially apparent at the lateral edges, where multiple echocardiographic dropout precludes true epicardial definition. Schnittger et al.5 established the fact that different reference systems yield different sensitivities for classifying motion abnormalities and that different echocardiographic views require readjustment of the reference system to compensate for cardiac motion within the thorax. Weyman et al.15 further stated that despite the use of the most optimal reference system, simple measurements

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of endocardial excursion at end-diastolic and end-systole may fail to detect important wall motion abnormalities. Blumenthal et al.\textsuperscript{16} showed that wall motion abnormalities may persist long after transient ischemia, even when myocardial blood flow is reestablished and histology is normal. All in all, quantitative wall motion analysis for defining the presence and severity of myocardial ischemia has been only partially successful.

Over the past few years, a number of investigators\textsuperscript{17–26} have analyzed the reflected sound waves from the myocardium in an effort to characterize the presence of cardiac pathology. It has been shown that the amount of collagen\textsuperscript{17} and fibrosis\textsuperscript{18, 25} within myocardium changes the scattering properties of the tissue. Other investigators have observed intrinsic backscatter changes during myocardial infarction\textsuperscript{19–23} and certain cardiomyopathic states.\textsuperscript{24, 25} A major contribution in the area of myocardial tissue characterization has been achieved by the group at Washington University in St. Louis. Several studies by this group\textsuperscript{26–30} have demonstrated that integrated backscatter power of a single radiofrequency line increases during ischemia. They have also reported a cyclic variation in integrated backscatter for normal myocardium throughout the cardiac cycle and a blunting of the cyclic variation during ischemia. In addition they have reported a phase change between ventricular pressure and backscatter power during ischemia and during passive left ventricular distention.\textsuperscript{31} Our laboratory has also reported a decrease in cyclic backscatter power and a phase shift between backscatter power and endocardial wall motion during ischemia.\textsuperscript{32}

Thus far all approaches for detecting the presence of ischemia, from a tissue characterization standpoint, have used either a single M mode line for analysis or have used specific times in the cardiac cycle for two-dimensional analysis. To date there is only one abstract\textsuperscript{33} reporting two-dimensional radiofrequency analysis throughout the cardiac cycle for normal myocardium. Logically, the next approach would be an analysis of two-dimensional radiofrequency data throughout the entire cardiac cycle for normal, ischemic, and infarcted tissue. Consequently, we investigated the backscatter cyclic power variation throughout the cardiac cycle at multiple time intervals up to 5 hr after coronary occlusion. We also combined wall motion analysis with the cyclic backscatter variation to determine how this phase relationship was affected by ischemia. The effect of reperfusion after temporary coronary occlusion on these two variables, cyclic backscatter power and phase, were also investigated. Simultaneous left ventricular pressure recordings were obtained throughout the study period in five animals for proper phase referencing. Our prediction was that as a relative measure this combined approach would be promising because it requires no external or internal calibration. A secondary objective was to determine the effects of reperfusion on these variables.

Methods

Data acquisition. Two-dimensional echocardiograms were obtained with use of a commercially available ultrasonic scanner (Hewlett-Packard 77020A) in open-chest dogs. A 5 MHz phased-array right-angle transducer (bandwidth 1800 KHz), held in place by the pericardium, was placed beneath the heart of each dog to obtain anterior myocardial radiofrequency samples. This is schematically represented in figure 1, A. Myocardial regions of interest were positioned within the focal zone (5 to 7 cm) of the transducer. Images were oriented so that the regions of interest were crossed nearly perpendicularly by the sound waves and were deemed acceptable if clear blood/myocardial interfaces were visualized throughout the cardiac cycle. Modifications to the HP ultrasound scanner were made such that communication with an HP 1000 (A700) computer was possible. A high-speed data link between scanner and computer allowed acquisition of 16.7 MHz sampled two-dimensional radiofrequency data in real time (33 msec intervals). The software allows the user to define a region of interest or subsector on the sector scanner itself. The highlighted region in figure 1, B, demonstrates an example of a typical subsector of myocardium chosen for acquisition. Blood and epicardium were included in these regions to provide references during off-line analysis. Myocardial test samples were acquired before each study to ensure that myocardial radiofrequency levels were not saturated. The time-gain control (TGC) level was adjusted equally throughout the sector field, so that each depth would have constant gain emphasis. After the initial adjustment, the TGC remained fixed throughout the study period. Sixty continuous subsectors (regions of interest) were obtained over four to five successive cardiac cycles for normal, ischemic, and infarcted myocardium. In five studies the simultaneous electrocardiogram and left ventricular pressure recordings were digitized and transferred along with the regions of interest. A detailed description of our analysis system and calibration and definition of the systematic error is discussed elsewhere.\textsuperscript{34}

Data analysis. Processor software enabled each of the radiofrequency-acquired regions of interest to be transformed (rectified and filtered) and redisplayed in video format on the sector scanner. Figure 1, C shows one of 60 frames read from disk memory and displayed on the scanner. This provided a means for frame-by-frame review of the acquired data for several cardiac cycles. Additional software allowed each frame to be edited so that epicardial and endocardial specular interfaces could be eliminated from the analysis window. This permitted analysis of midmyocardial regions. From each analysis window, consisting of approximately 15 to 20 lines and 100 to 300 points per line (roughly 2 cm × 1 cm), the 8 bit radiofrequency data were combined and a resultant probability distribution was obtained. Because the mean or direct-current level of the radiofrequency data is very nearly zero, the variance (alternating current level) derived from the probability distribution is representative of the total average backscatter power. For each of 60 midmyocardial regions the average power was calculated from the probability distribution and recorded as a function of time. Cyclic backscatter power was calculated by a search through the 60 backscatter power values and determination of the local maximum and local minimum for each cycle. Since
each sample was 33 msec apart from the next and the average heart rates were 115 to 135 beats/min, this yielded three to four minimum values and three to four maximum values. The average maximum and minimum values were calculated and their ratio was expressed in decibels. Endocardial wall motion was derived by the computer from regions of interest by threshold detection of the blood/endocardial border. Along each radial line within each region of interest the radial distance from the top of the region to the blood/endocardial edge was recorded and averaged for all lines. This operation was performed for all frames and the result was recorded as a function of time.

The phase measurements for cyclic backscatter power, endocardial wall motion, and left ventricular pressure were determined by computing the fast-Fourier transform (FFT) of each waveform. The FFT yields a series of peaks (harmonics) in the frequency domain representing the periodic nature of the waveform in the time domain. The first harmonic (fundamental frequency) of the FFT yields a complex number with an associated magnitude and phase that represents the most dominant sinusoidal component in the time-varying waveform.35 Because each waveform for each study started at exactly the same point in time, the absolute phase calculation for each waveform allowed the calculation of the relative phase separation among the backscatter power, endocardial motion, and ventricular pressure. Figure 2 illustrates the approximate phase relationship among these waveforms during the cardiac cycle.

The cyclic backscatter power and phase measurements from each animal were averaged for the 2 hr studies (n=15), the 5 hr studies (n=10), and the reperfusion studies (n=5). The results are reported as the mean ± SD. Data were combined in the ischemic group (up to 30 min) and the infarcted group (2 to 5 hr) and an unpaired t test used to test the null hypothesis.

Animal preparation. Twenty mongrel dogs of either sex weighing 25 to 45 kg were anesthetized with intravenous sodium pentobarbital (0.5 mg/kg), supplemented as needed during the experiment. Ventilation was assisted by room air, cuffed endotracheal tube, and a Harvard ventilator, set to provide a minute volume of 300 cc/kg. A long 18-gauge polyethylene catheter was inserted in the right femoral artery for pressure monitoring with a Hewlett-Packard (1280C) transducer and Hewlett-Packard (4578A) recorder. Limb electrocardiographic leads provided direct input into the ultrasonic scanner. A single catheter was placed in a peripheral vein for intravenous hydration with a solution of 5% dextrose in water that was adjusted to maintain a systemic systolic blood pressure of 120 mm Hg and a heart rate of approximately 120 beats/min, and for infusion of antiarrhythm-
mic drugs. With the animal in the right lateral decubitus position, a left posterolateral thoracotomy was performed with the incision over the apical cardiac impulse. The heart was supported and positioned by manipulation of a pericardial sling that was opened caudally. An 18-gauge catheter was inserted into the left atrial appendage and passed into the left atrium and across the mitral valve for intraventricular pressure measurements. A counterincision in an appropriate inferolateral intercostal space allowed for insertion of the right-angle transducer in such a position within the pericardium that the image of the anterior left ventricular wall positioned orthogonally in the focal zone of the transducer and minimal external manipulation was required for repeated data acquisition. After baseline radiofrequency data were recorded and before the induction of ischemia, lidocaine (10 mg/kg) was given intravenously; supplemental doses were given as needed to control ventricular ectopy. Ventricular ectopy refractory to lidocaine was treated with procainamide (1 to 2 mg/kg).

For the complete occlusion studies, a heavy silk suture was used to ligate the left anterior descending coronary artery (LAD) just distal to the first diagonal branch. Running locked sutures of 3-0 polyglycolic acid were placed along the LAD and significant diagonal and circumflex collaterals to inhibit epicardial reperfusion of the ischemic zone.

For the reperfusion study, a tie that had been placed about the LAD just distal to the first diagonal branch was lifted and an atraumatic vascular clamp was placed to occlude flow. The clamp was released 15 min after placement and care was taken to ensure that full patency was restored.

**Acute infarct studies.** We studied 15 dogs for 2 hr after LAD and collateral coronary ligation. In addition we allowed 10 of the dogs to continue in an ischemic state for a total of 5 hr. Sixty frames of normal anterior myocardium were acquired for baseline control data. Special care was taken to ensure that the nonischemic muscle sample was from the zone of coronary distribution that would become ischemic. Data samples were taken at 15, 30, 60, 90, and 120 min after LAD/collar ligation for all 15 animals and at 180, 240, and 300 min for the remaining 10 dogs. A transmural myocardial needle biopsy was obtained from the zone of infarction after the 5 hr study.

**Reperfusion studies.** Five dogs were studied during 15 min of temporary LAD occlusion followed by 60 min of reperfusion. Radiofrequency samples (60 frames) of the anterior wall were taken before ischemia and at 1, 5, 10, and 15 min of LAD clamping. Immediately after the 15 min ischemic sample, the artery was released and 60 frames of reperfusion data were taken at 5, 10, 20, 30, and 60 min and stored on disk. A transmural myocardial biopsy sample was obtained from the reperfusion zone on completion of the study.

**Electron microscopy.** Biopsy samples were obtained with a 17-gauge transmyocardial needle. The tissue samples were placed immediately in 4% glutaraldehyde buffered with 0.05M Na cacodylate, postfixed in 2% osmium tetroxide buffered with 0.1M Na cacodylate, dehydrated in graded acetones, and imbedded in Epon 812. The studies were assessed by one of us (D. H. J.) and were reviewed by an independent electron microscopist (C. P. D.).

**Results**

**Acute infarct studies.** Figure 3, A, shows the cyclic power variation (y axis) for 5 hr after coronary occlusion (x axis). At 30 min, the cyclic variation was 2.4 ± 0.5 dB, compared with 5.1 ± 0.8 dB for normal. As time progressed beyond 90 min the cyclic backscatter power increased so that by 5 hr after occlusion the cyclic variation was very near the normal baseline value. We have defined ischemia (reversible) as the

**FIGURE 2.** Schema of the phase relationship in the time domain between backscatter power (BSP), endocardial wall motion (EWM), and left ventricular pressure (LVP) for normal myocardium. The phase between EWM and LVP is labeled as ϕ_E, and the phase between BSP and LVP as ϕ_B.

**FIGURE 3.** A, Summary of cyclic backscatter power in decibels on the y axis for control (nonischemic) myocardium (t = 0), ischemic myocardium (t = 15 to 30 min), and infarcted myocardium (t = 120 to 300 min) on the x axis. B, Summary of phase difference between cyclic backscatter power and endocardial wall motion in degrees on the y axis for control, and on the x axis for ischemic and infarcted myocardium.
lack of blood supply to myocardium for up to 30 min\(^6, 7\) and infarction (irreversible) as the lack of blood supply for greater than 2 hr. Combining the results shown in figure 3, A, the average cyclic power for ischemia was \(2.3 \pm 0.7\) dB and the average cyclic power for infarction was \(4.0 \pm 1.2\) dB. It is noteworthy that there is significant overlap in the standard deviations for the normal and infarcted groups (\(p < .065\)), whereas the standard deviations do not overlap for the normal versus ischemic group (\(p < .001\)). This implies that cyclic backscatter power measurements can differentiate ischemic muscle from normal muscle but are less useful in distinguishing infarcted myocardium from normal myocardium. Figure 3, B, demonstrates the phase difference between endocardial wall motion and cyclic backscatter variation (y axis) for several time intervals after coronary ligation (x axis). The phase difference progressively increased from a normal value of about 40 degrees until about 3 hr after ligation, at which time it stabilized at around 160 degrees. The phase difference during the ischemic period was \(115 \pm 23\) degrees, which has a significance level when compared with normal (38 \(\pm 20\) degrees) of \(p < .001\). During the infarcted period it further increased to \(170 \pm 28\) degrees, which has a significance level when compared to the ischemic period of \(p < .001\). Clearly, unlike the cyclic power variation variable, a tendency to return to normal baseline is not apparent during this study interval.

We were concerned that the phase difference between backscatter power and endocardial motion might, to a large degree, represent the segmental wall dyskinesis that occurred during ischemia. If so, the phase difference would simply be an indirect measurement of wall motion abnormalities. To test this hypothesis we acquired simultaneous left ventricular pressure and radiofrequency data from five dogs studied for 5 hr after coronary occlusion. This allowed comparison of the absolute phase change of backscatter power and endocardial wall motion with respect to left ventricular pressure (figure 4, A). For normal myocardium the phase between backscatter power and left ventricular pressure was \(109 \pm 19\) degrees and the phase difference between endocardial wall motion and left ventricular pressure was \(70 \pm 12\) degrees. During ischemia the phase difference between endocardial motion and ventricular pressure markedly decreased to \(18 \pm 19\) degrees as a reflection of segmental dyskinesis, while the phase difference between backscatter power and ventricular pressure remained nearly unchanged at \(119 \pm 18\) degrees. However, for the infarcted group the phase difference between endocardial motion and ventricular pressure remained approximately the same at \(14 \pm 12\) degrees, while there was a marked increase in the phase difference between backscatter power and ventricular pressure to \(177 \pm 25\) degrees. Figure 4, B, summarizes the contribution of each component (relative to ventricular pressure) to the total phase difference observed between backscatter power and endocardial wall motion for ischemia and infarction. During ischemia the contribution was mainly (84%) due to segmental dyskinesis. However, during infarction the contribution by backscatter power dominated (92%). The overall contribution to phase difference from normal to infarction was 54% and 46% from backscatter power and endocardial motion, respectively. Figure 5 is a schematic representation of the phase shift between
cyclic backscatter power and endocardial wall motion as referenced to left ventricular pressure during infarction. A comparison of this figure with figure 2 shows that the phase difference between endocardial motion and left ventricular pressure decreased (becoming more in phase) as opposed to the phase difference between backscatter power and ventricular pressure, which increased (becoming more out of phase) during infarction.

Reperfusion studies. Figure 6, A, illustrates the cyclic backscatter power values (y axis) for the arterial clamp and release periods (x axis). The cyclic power decreased from normal levels over the 15 min of LAD clamping to 3.1 ± 0.6 dB and then rapidly returned to near-normal cyclic variation of 4.7 ± 0.8 dB after arterial release. Figure 6, B, demonstrates the phase difference between endocardial motion and cyclic backscatter power (y axis) during the clamp period and after coronary release (x axis). As the tissue became more ischemic there was a progressive phase difference that increased to 111 ± 18 degrees, as compared with the normal 47 ± 15 degrees, until the clamp was released. Thereafter the phase difference slowly returned to a near-normal value of 58 ± 20 degrees. From the results of infarct studies in which left ventricular pressure was recorded (figure 4), it appeared that the phase shift during temporary ischemia in these reperfusion studies was mainly due to segmental dyskinesis.

Electron microscopy. All infarct studies showed irreversible changes in epicardium, midmyocardium, and endocardium at 2 and 5 hr after ligation, according to the criteria of Jennings et al. The changes consisted of fragmentation of mitochondrial membranes and sarcoplasmic reticulum, sarcolemma membrane disruption, nuclear margination, N bands, and coarse intra-
cellular electron-dense deposits. The only observed difference between the 2 and 5 hr biopsy samples was the increased presence of edema in the 5 hr studies. Reperfusion studies showed none of these irreversible changes. Only minimal swelling of the mitochondria and sarcolemma was noted, with scattered evidence of mild cellular edema present in biopsy samples taken 1 to 2 hr after release of the clamp on the LAD.

Discussion

In this study we have demonstrated the following in open-chest dogs subjected to coronary artery occlusion. (1) The amplitude of cardiac cycle-dependent variation in ultrasonic backscatter power of myocardium initially decreases and then gradually rises almost to the preischemic value over 5 hr of ischemia. (2) The cyclic variations in endocardial wall motion and backscatter power are nearly in phase for nonischemic tissue
and become almost fully out of phase after 5 hr of ischemia. (3) This phase shift is largely attributable to a decrease in the phase difference between endocardial and ventricular motion in early ischemia and to an increased phase difference between backscatter power and ventricular pressure in late ischemia. (4) Reperfusion after a 15 min coronary occlusion effected a return of the phase between backscatter power and endocardial motion and the cyclic variation in backscatter power to baseline values.

We have reported recently, also using two-dimensional analysis of radiofrequency signals, a 4.5 dB cyclic variation in backscatter power within the cardiac cycle in normal canine myocardium. We found that the backscatter power peaked during diastole and decreased during systole. Wickline et al. have postulated that the time-varying change in backscattered energy during the cardiac cycle results from a changing acoustic impedance that in turn is caused by variation in tissue elastic modulus during sarcomere shortening. This hypothesis predicts a decrease in backscatter power during systole as sarcomere shortening and series elastic element stretching occur and the elastic modulus increases. Recent canine studies using M mode and real-time two-dimensional radiofrequency signals have confirmed this prediction.

Myocardial ischemia alters the amplitude of the cyclic variation in myocardial backscatter power. Barzilai et al. have shown that 30 min after coronary artery occlusion there is considerable blunting of the diastolic-to-systolic variation in integrated backscatter. We have made similar observations using a two-dimensional approach (figure 3, A). Our study further demonstrated a progressive return to cyclic backscatter variation by 5 hr after coronary occlusion so that a distinction between infarcted tissue and normal tissue may not be possible on this basis alone. Wickline et al. demonstrated that 1 hr after the onset of ischemia the cyclic backscatter power was significantly blunted, but with only a residual 1 to 2 dB cyclic variation remaining. Our residual cyclic variation was somewhat higher (2 to 2.5 dB) at 30 min after occlusion. In contrast to our results, Barzilai et al. reported that the cyclic variation remained blunted (1.0 ± 1.1 dB) after 4 hr of ischemia. The reason for this discrepancy is unclear. Differences in experimental instrumentation, nature of the infarct, and analytic approach may have led to the different results.

Mimbs et al. have shown that integrated backscatter increases with the wet/dry ratio of myocardial tissue. This finding suggests that backscatter power should increase in the presence of interstitial and intracellular edema. The observed increase in cyclic backscatter power between 2 and 5 hr after ligation in our studies may have been caused by progressive edema. The results of electron microscopy show increasing intracellular and interstitial edema between 2 and 5 hr after infarction. Delayed edema formation of variable degree depending on the individual dog’s microvasculature may in part also explain the large standard deviation in cyclic power seen in the 2 to 5 hr period during ischemia. Wickline et al. have found that the maximum negative rate of change in integrated backscatter changes in parallel with global contractile function in normal myocardium. This finding suggests that there is a close relationship between myocardial wall stress and backscatter power. During ischemia, as the ischemic segment thins, bulges, and becomes dyskinetic, the law of Laplace predicts that the wall stress should increase in the compromised segment. This increase in wall stress could produce a decrease in cyclic backscatter power variation early in the ischemic process. As time progresses, edema swells the infarcted segment, which may increase its effective thickness and thus decrease wall stress. This could also help explain the progressive increase in the cyclic power by 5 hr after the onset of ischemia.

Another relative measurement that may be useful in differentiating among normal, ischemic, and infarcted myocardium is the phase of the time-varying backscatter power waveform. In our present study, the phase difference between endocardial motion and backscatter power not only provided a measure for distinguishing between normal and ischemic muscle, but also seemed useful in distinguishing between ischemic and infarcted tissue. Unlike the cyclic power measurements, the phase difference did not return to normal baseline values by 5 hr after coronary occlusion. Our data indicate that the increase in phase difference between endocardial motion and backscatter power is primarily (84%) due to wall dyskinesis in the first 30 min of ischemia. That is, the phase relationship of endocardial motion to left ventricular pressure decreases, becoming nearly in phase. Thereafter the phase relationship of the backscatter power to left ventricular pressure increases, becoming nearly out of phase. This change appears to be the major contributor (92%) to the phase difference between the backscatter power and endocardial motion during infarction. This result seems to imply that even though the wall motion becomes dyskinetic immediately there is an ongoing process for at least 3 hr after coronary ligation that alters the backscatter characteristics such that a phase lag is introduced with respect to ventricular pressure.
Wickline et al.\textsuperscript{38} found that during ischemia a 90 degree phase shift between integrated backscatter and ventricular pressure was observed. This phenomenon is simulated by a left ventricular passive distention experiment performed by this same group.\textsuperscript{31} In this experiment they demonstrated a phase shift between integrated backscatter and left ventricular pressure of 124 ± 11 degrees for normal contracting myocardium. In our experiment we found a similar phase relationship between the backscatter power and left ventricular pressure of 109 ± 19 degrees for normal contracting myocardium. Furthermore, in their experiment the phase between left ventricular pressure and backscatter power was measured for both normal physiologic contraction and passive left ventricular distention. Backscatter power decreased during systole for physiologic contraction, but increased during passive distention. This translates into a significant phase increase between the two conditions. An infarcted myocardial segment may behave in a manner analogous to the passively distended ventricle. As a segment of myocardium becomes transmurally infarcted, it cannot generate intrinsic tension, resulting in paradoxical thinning during ventricular systole. Our data show that during ventricular systole, the backscatter power increases as the ischemic myocardium thins (i.e., sarcomeres are passively stretched). By comparison, normal myocardium during ventricular systole exhibits a decrease in backscatter power, but the tissue is thickening (i.e., sarcomeres are actively shortening). We found a similar phase increase from 109 ± 19 degrees between ventricular pressure and backscatter power for normal myocardial active contraction to 177 ± 25 degrees for infarcted myocardial passive contraction (figure 4, A). The mechanism of the continuing change in backscatter power phase in early infarction remains unexplained.

The reperfusion studies were performed to see if these backscatter variables would return to normal levels after a reversible insult. Jennings et al.\textsuperscript{36} demonstrated that a 15 min arterial clamp in dogs does not result in cell death. In our studies backscatter power decreased to a level of 3.1 ± 0.5 dB during the 15 min clamp period. This is a higher level than that for the 15 min period during the acute infarct study (i.e., 2.2 ± 0.7 dB). The exact reason for this is unclear, but one explanation relate to the collateral circulation. In the infarct study, but not in the reperfusion study, the epicardial collateral circulation was interrupted. Hence, the half-life of myocardial viability may be longer in the reperfusion study. The phase between backscatter power and endocardial motion reached a phase shift of 111 ± 18 degrees during the clamp period, which is consistent with the 15 min phase results from the acute infarct studies and probably represents wall dyskinesis. The phase returned to near-normal values by 1 hr after release of the arterial occlusion. Since we observed a return in the cyclic power 2 to 5 hr after arterial ligation, these reperfusion studies acted, in a sense, as a control to make certain that a systemic bias did not exist in our acquisition and analysis procedure. The fact that these variables returned swiftly to normal values during reperfusion increased our confidence in the findings from the 5 hr study.

The clinical usefulness of the use of backscatter variables for detecting ischemia in man has not yet been established. The chest wall not only has nonlinear effects on ultrasonic backscatter, but also limits the angle from which the heart muscle can be viewed. Thus, a variable must be free of any angle dependence with respect to the region of interest and free from attenuation effects. An absolute measurement such as mean backscatter power, which has been used by several investigators,\textsuperscript{22, 23, 28, 29} has certain reference difficulties that potentially limit its clinical usefulness. On the other hand, relative measurements such as the cyclic backscatter power and the phase relationship may be useful in the clinical environment. The cyclic variation did not detect the presence of early ischemia, but by 5 hr variation was approximately the same as in the nonischemic muscle. However, at 5 hr the electron microscopic results showed clear transmural infarct. Thus, from this study, cyclic power alone was unable to distinguish infarcted myocardium from normal myocardium.

Our study does, however, show that the phase difference remains distinctly different 5 hr after coronary ligation. The phase difference is calculated by a frequency analysis technique that depends only on the periodic nature of the waveform and does not need correction for angulation differences or the effects of overlying structures. Because it depends only on the frequency content of the two signals, not the absolute or relative values of the cyclic variation, the phase may have applicability in the clinical environment. An even more useful calculation in the clinical situation may be a comparison of the cyclic backscatter power to the electrocardiogram. Although certain electrocardiographic changes will occur during ischemia, the electrocardiogram may provide a more secure reference for phase calculations. The FFT of the electrocardiogram will yield a fundamental frequency that can be used for backscatter power referencing.

In conclusion, we have found that these two variables, cyclic backscatter power and the phase differ-
ence between backscatter power and endocardial wall motion, used in combination, may provide a means for recognizing and possibly staging the ischemic process.

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