Structural Remodeling of Human Myocardial Tissue After Infarction
Quantification With Ultrasonic Backscatter

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Background. Remodeling of myocardial tissue after infarction may culminate in the development of either a well-healed scar or a thin, expanded heart wall segment that predisposes to ventricular aneurysm formation, congestive heart failure, or ventricular tachycardia. The three-dimensional architecture of mature human infarct tissue and the mechanisms that determine it have not been elucidated. We have previously shown that quantitative ultrasonic backscatter can be used to define the transmural organization of human myofibers in the normal ventricular wall by measuring the dependence of backscatter on the angle of insonification, or ultrasonic anisotropy. We propose that measurement of ultrasonic anisotropy of backscatter may permit quantitative characterization of the transmural architecture of tissue from areas of myocardial infarction and facilitate identification of fundamental mechanisms of remodeling of the ventricular wall.

Methods and Results. We measured integrated backscatter in 33 transmural sections from 12 cylindrical biopsy specimens (1.4-cm diameter) sampled from central regions of mature infarction in six explanted fixed human hearts. Tissue samples were insonified in two-degree steps around their entire circumference at successive transmural levels with a 5-MHz broad-band piezoelectric transducer. Backscatter radio frequency data were gated from the center of each specimen, and spectral analysis was performed on the gated radio frequency for the computation of integrated backscatter. Histological morphometric analysis was performed on each specimen for determination of the predominant fiber orientation and the percentage of tissue infarcted at consecutive transmural levels. The average percentage of tissue infarcted for all transmural levels was 49±3% (range, 13–80%). Histological attributes varied from patchy fibrosis to extensive confluent zones of scar tissue. The angle-averaged integrated backscatter for all transmural levels in infarct tissue was approximately 5 dB greater than that previously measured in normal tissue in our laboratory (−48.3±0.5 versus −53.4±0.4 dB, infarct versus normal). Marked anisotropy of backscatter was observed in tissue from areas of infarction and was characterized by a sinusoid-like dependence on the angle of insonification at each transmural level. Insonification perpendicular to infarct fibers yielded values for integrated backscatter 14.8±0.5 dB greater than those for insonification parallel to these fibers. Juxtaposition of the sinusoid-like anisotropy functions from all consecutive transmural levels demonstrated a progressive shift in the orientation of scar tissue elements from epicardial to endocardial levels of 14.6±1.5°/mm of tissue. The transmural shift in fiber orientation per millimeter of tissue from the area of infarction exceeded that previously measured for normal tissue (9.2±0.7°/mm) by 59%. This marked augmentation in angular shift per millimeter of tissue results from a generalized structural rearrangement (or reorientation) of fibers across the entire ventricular wall in the infarct zone that we hypothesize is determined in part by dynamic mechanical forces, imposed by the surrounding functional normal tissue, that tether the “infarcted” tissue.

Conclusions. Myocardial tissue from areas of myocardial infarction manifests substantial anisotropy of ultrasonic scattering that may be useful for quantitative characterization of the alignment and overall three-dimensional anatomic organization of mature infarct scars. (Circulation 1992;85:259–268)
The evolution of changes in global and regional left ventricular shape after myocardial infarction has been referred to as “remodeling.” A process of infarct expansion may begin within the first 24 hours after infarction and produce early cardiac dilatation. Tissue remodeling culminates in the development of healthy scar tissue or in the formation of ventricular aneurysms that predispose to the development of congestive heart failure and ventricular tachycardia. Empiric treatments intended to improve the outcome of remodeling, such as afterload reduction or maintenance of patency in an infarct-related artery, have demonstrated promise for limitation of morbidity and mortality after infarction. However, factors that govern the deposition and maturation of collagenous scar tissue have not been sufficiently well defined to allow determination of how such therapeutic strategies might facilitate better infarct healing. Furthermore, conventional diagnostic techniques such as two-dimensional echocardiography or ventriculography do not permit identification of ineffective remodeling at a sufficiently early stage to enable therapeutic intervention based on objective assessment of tissue architecture.

Mechanisms of myocardial tissue remodeling have been examined previously from global and cellular perspectives. Weisman et al recently reported that a physical rearrangement of myofibers results from cell slippage within the first 3 days after infarction in rat and human hearts and accounts for a substantial portion of the acute regional thinning of infarct segments. Other reports have described the organization of mature infarcts in the context of local anatomic pathways associated with intramural electrical reentry in ventricular tachycardia. However, the three-dimensional transmural organization of mature scar tissue after myocardial infarction in humans has not been delineated systematically to our knowledge, and mechanisms that determine the ultimate outcome of remodeling in such scars have not been addressed.

Recently, we reported that the complex intramural organization of normal myocardial fibers in canine and human hearts can be characterized with quantitative ultrasonic backscatter. The specific orientation of myofibers at individual transmural levels can be determined by measuring the dependence of backscatter on the angle of insonification. We have shown that insonification perpendicular to normal human myocardial fibers produces greater backscatter than does insonification parallel to myofibers by at least 14 dB. We have also quantified the physiologic transmural shift in human myofiber orientation that occurs from epicardium to endocardium, which was described previously by Streeter and Hanna. The physical property of highly aligned scattering elements such as myofibers that produces this directional dependence of scattering with respect to the angle of insonification is referred to as “anisotropy.” We propose that the three-dimensional transmural organization of myocardial scar tissue represents an important determinant of the mechanical properties of mature infarcts that can be characterized with quantitative ultrasound. We and others have shown that the physical composition of tissue from areas of infarction renders it more echogenic than normal tissue in both experimental and clinical settings. Measurements of ultrasonic backscatter reflect not only the amount of collagen present in scar tissue but also its specific tertiary organization.

We have previously used ultrasonic tissue characterization to differentiate normal myocardial tissue from cardiomyopathic, infarcted, and stunned tissue in experimental animals and patients.

The present study was designed to quantify the local architecture of human tissue from areas of mature myocardial infarction in which remodeling had occurred. Accordingly, we measured the ultrasonic anisotropy of backscatter in biopsy specimens from explanted fixed human hearts with mature infarcts to determine the predominant orientation of scar tissue fibers at selected transmural levels. Acquisition of these data represents an important preliminary step toward the development of a clinical imaging method useful for quantitative characterization of tissue remodeling early after infarction based on elucidation of intramural organization of scar tissue elements.

Methods

Pathological Specimens

Twelve pathological specimens of fixed human heart tissue were obtained from explanted formalin-fixed native hearts of six patients who underwent cardiac allograft transplantation for end-stage ischemic heart disease at our institution within the past 5 years. Central regions of mature transmural infarction were identified easily by gross inspection and confirmed later by histological analysis (see below). No specimens were taken from myocardial regions known to be associated with acute or recent infarction. A No. 10 cork borer (1.4-cm diameter) was used to remove transmural cylindrical plugs of tissue with long axes orthogonal to the epicardial surface. The orientation of each plug with respect to the ventricular apex was marked before excision. The tissue plugs were mounted flush on the end of 2-cm-long cylindrical styrofoam holders of equal diameter by
gluing the endocardial surface to the styrofoam with cyanoacrylate (Figure 1).

**Acquisition of Ultrasonic Data**

Tissue plugs were interrogated with ultrasound after immersion in a water bath at room temperature (~20°C). A 5-MHz focused piezoelectric transducer (1/2-in. diameter, 2-in. focal length; model V309, Panametrics) was used to insonify tissue samples. The tissue-styrofoam assembly was suspended from a rotating stage and oriented so that the ultrasound beam interrogated tissue parallel to the epicardial surface (Figure 1). The focal zone of the transducer was positioned at the front wall surface of each cylindrical tissue specimen. Ultrasonic radio frequency pulses were launched from the transducer with a Metrotek pulser (model 215) and traveled through the water before interacting with the tissue. Backscattered radio frequency was amplified with a Metrotek receiver (model 106), and a segment of the radio frequency trace corresponding to the central portion of the tissue sample (14-μsec round trip, or ~10.8 mm of tissue) was gated out with a Metrotek stepless gate (model 701) and passed to a Hewlett Packard spectrum analyzer (model 8557A). The power spectral density data for each gated segment of radio frequency was stored off-line under the control of a MacIntosh II computer outfitted with an IEEE-488 general-purpose interface bus (GPIB-NB, National Instruments). Each power spectrum comprised 481 frequency bins in the range of 0–10 MHz.

Tissue plugs were interrogated from multiple angles at multiple transmural levels (Figure 1). At each selected transmural level, the plugs were rotated around their centers in two-degree angular increments while the transducer remained fixed. These circumferential scans were initiated at the fiducial point previously marked to orient the plug to the ventricular apex. Figure 2 illustrates typical backscattered radio frequency A-lines for insonification perpendicular to the predominant fiber axis. Bottom panel: Relatively less backscatter from tissue insonified parallel to fiber axis as determined by histological analysis.
demonstrated previously that this scanning protocol produces reproducible measurements of integrated backscatter at all angles. After all transmural levels had been interrogated for a single plug, the plug was submitted for histological analysis.

**Analysis of Ultrasonic Data**

The analysis of backscatter is based on a convolution model that equates convolutions of ultrasonic properties in the time domain with products in the frequency domain. The power spectrum of a signal scattered from a material that produces both scattering and attenuation can be written as:

\[ |E(f)|^2 = |P(f)|^2|A(f)|^2|S(f)|^2 \]

where \( |P(f)|^2 \) is the power spectrum of an interrogating ultrasonic signal, \( |A(f)|^2 \) is a parameter that represents attenuation that occurs along the path to and within the gated volume, and \( |S(f)|^2 \) is the intrinsic backscatter transfer function of the material. The transducer power spectrum, \( |P(f)|^2 \), is deconvolved by replacing the scattering material with a reflector of known properties (i.e., a polished, flat steel plate) positioned at the focal point of the transducer. By normalizing the spectrum measured from a scattering material to the spectrum from the “perfect” reflector and expressing the result on a logarithmic scale, we obtain the frequency-dependent “apparent” (not compensated for attenuation) backscatter transfer function \( |B(f)|^2 \) in units of decibels below the backscatter from a reflector from 10\( \log_{10} |B(f)|^2 = 10 \log_{10} \left( \frac{|E_{meas}(f)|^2}{|E_{ref}(f)|^2} \right) \). To generate a single relative index of backscatter efficiency, we calculate the frequency-averaged or integrated backscatter over the useful bandwidth of the transducer (typically, 3–7 MHz). Ultrasonic measurements of apparent backscatter are analogous to measurements that can be made in a clinical setting with a real-time two-dimensional integrated backscatter imager developed in our laboratory.

Integrated backscatter was computed for 180 independent angles in two-degree steps for each consecutive transmural level. Plots of integrated backscatter typically revealed a sinusoid-like dependence on the angle of insonification that comprised two peaks and two troughs for the amplitude of integrated backscatter per 360° (see “Results”). The peak and trough values for integrated backscatter amplitude were measured from the plots, and their averages were used to determine the magnitude of anisotropy as the peak-to-trough excursion.

A previously described cross-correlation method was used to determine the shift in orientation of scar tissue fiber from one transmural section to the next. The maximum correlation between two sinusoid-like integrated backscatter functions from adjacent transmural levels represents the best fit between the two functions after shifting one function through an angle that corresponds to the transmural shift in the orientation of scar tissue fibers. This relative shift of angular position on consecutive scans was compensated for the thickness of tissue between each scan (1.5 mm) to yield an estimate for the angular shift in orientation of scar tissue fibers per millimeter of tissue.

**Histology**

Each plug was divided into consecutive 1.5–2.5-mm-thick segments parallel to the epicardial surface so that the segments roughly corresponded to the transmural levels scanned by ultrasound. The apical orientation of the plug was marked to provide a reference for accurate alignment of the ultrasound scans with the histological sections. It was not always possible to slice segments thin enough to correspond exactly to each scan level, but enough sections were acquired from each plug to permit assessment of the shift in orientation of scar fiber from epicardium to endocardium. Each segment was embedded in paraffin, and two sections (10-μm thick) from each segment were stained with hematoxylin and eosin and with Masson trichrome stains.

The orientation of scar tissue fibers in sections stained with Masson trichrome were estimated by methods previously reported. Briefly, the histological sections were magnified, printed on photographic paper, and digitized with an Epson flatbed scanner. The scanned images were then analyzed with the use of image-processing software available from the National Institutes of Health (IMAGE 1.29; author, Wayne Rasband). The predominant orientation of scar tissue elements was readily apparent in the majority of tissue samples by gross inspection and by light microscopy (Figure 3, left and right). Scar tissue was usually oriented along the axis of the remaining normal myofibers in each section. Even for sections with confluent regions of scar tissue mostly devoid of normal myofibers (e.g., Figure 3, right), light microscopy revealed that collagen fibers retained the orientation of the remaining viable myocytes in the section. The wavy collagen fibrils in confluent scar tissue also manifest a definite orientation along the myofiber axis in the majority of cases. For each sequential section, the orientation of scar tissue fibers relative to the apical fiducial mark was computed, and the overall difference in angular orientation between consecutive sections was recorded. The average change in the angle of orientation between sections was compensated for the thickness of each section to yield the average transmural shift in fiber angle per millimeter of tissue.

The percentage of tissue infarcted in each section was computed by photographing the sections stained with Masson’s trichrome and printing, on photographic paper, filtered enlargements that were then digitized with an Epson flatbed scanner at 72 dots per inch. Computer-assisted planimetry of the areas occupied by infarcted and normal tissue components was accomplished with the IMAGE 1.29 program by application of a gray-scale threshold function to separate normal from abnormal tissue elements according to their differential staining and contrast features. The results of the thresholding analyses
were checked qualitatively against the actual tissue histology by microscopic inspection of each slide.

Statistical Analysis

The measurements of transmural shifts of scar fiber orientation (°/mm of tissue) were compared for histological and ultrasonic methods of analysis. Nonpaired Student’s t tests (two-tailed) were used to determine the significance of differences, and statistical significance was attributed at the level of \( p < 0.05 \). SEM values are reported in the text and figures.

Results

Ultrasonic Interrogation of Human Myocardial Tissue From Areas of Infarction

Thirty-three transmural sections of tissue from infarct zones were scanned and analyzed. Figure 2 illustrates typical backscattered radio frequency A-lines for insonification perpendicular and parallel to the predominant orientation of scar tissue fibers in one transmural section. Visual inspection of the raw radio frequency data revealed a greater magnitude of scattering for insonification perpendicular compared with that parallel to fibers for each transmural section. The average integrated backscatter for all angles of interrogation and for all transmural levels was \(-48.3 \pm 0.5\) dB.

Figure 4 illustrates the dependence of integrated backscatter on the angle of insonification in one tissue plug at one transmural level. The magnitude of backscatter manifested a sinusoid-like dependence on angle of insonification with a period of approximately 180°. The average peak-to-trough difference, or magnitude of anisotropy, for integrated backscatter for all transmural sections from all human biopsy specimens was 14.8±0.5 dB.

Figure 5 illustrates the dependence of integrated backscatter on the angle of insonification for three transmural levels (epicardial, midmyocardial, and endocardial) from one tissue sample. The specimens from areas of infarction were significantly thinner than normal ventricular wall tissue and permitted an average of 1.9±0.3 independent determinations of the shift of fiber angle for consecutive transmural levels per tissue plug. One plug could be studied with ultrasound only at a single transmural level. Nevertheless, in all cases, the positions of the peaks and nadirs of the integrated backscatter functions shifted

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**FIGURE 3.** Histological sections at selected transmural levels from two cylindrical plugs of myocardial infarct tissue. Sections (diameter, 1.4 cm) are cut parallel to epicardial surface. Orientation of fibers relative to an apical fiducial mark is determined for comparison with ultrasonic measurements (see text for description). Left panel: Tissue with more diffuse fibrosis. Right panel: Tissue with confluent regions of scar.

**FIGURE 4.** Plot of apparent integrated backscatter versus angle of insonification for human myocardial infarction. Typical backscatter function manifests two peaks and two nadirs that reflect perpendicular and parallel insonification of highly aligned fibers at this transmural level.
progressively from epicardial to endocardial layers in a counterclockwise direction (Figure 5). This counterclockwise direction was defined by comparing the orientation of scar fibers with the position of the apically oriented fiducial mark on the tissue plugs. Epicardial scar fibers coursed more obliquely toward the apex, midmyocardial fibers maintained a circumferential orientation, and endocardial fibers coursed more obliquely toward the base. The average angular shift in the positions of the peaks and nadirs for consecutive transmural layers for tissues from areas of infarction was 14.6±1.5°/mm for all samples.

Comparison of Ultrasound With Histology

Twenty-nine transmural sections were prepared for histological analysis. Segments from areas of myocardial infarction analyzed by light microscopy exhibited distortion of normal fiber architecture ranging from increased interstitial collagen to widespread deposition of scar tissue (Figure 3, left and right). The majority of sections contained some normal myofibers that were interdigitated with scar tissue elements. Occasionally, large confluent areas of fibrosis predominated in a section and completely replaced normal myofibers. The average percentage of tissue infarcted for all transmural sections examined was 49±3% and ranged from 13% to 80%.

Figure 6 compares results of ultrasonic and histological analyses of scar tissue fiber orientation. The peaks and nadirs of integrated backscatter were aligned closely with perpendicular and parallel fiber orientation, respectively, as judged by histological analysis. Histological analysis revealed a progressive counterclockwise transmural shift in scar fiber orientation of 12.0±1.1°/mm of tissue from epicardium to endocardium. Ultrasonic and histological analyses did not differ significantly with respect to the computed transmural shift of scar fiber orientation. The concordance between ultrasonic and histological methods for determination of the transmural shift of scar fiber direction attests to the accuracy of ultrasonic charac-

Comparison of Infarct With Normal Myocardium

We recently reported measurements of ultrasonic anisotropy for normal human myocardial tissue. Figure 7 compares several anisotropic properties of normal human myocardial tissue reported previously with those reported in the present study for human myocardial tissue that has undergone infarction. Figure 7A shows that the magnitude of anisotropy (i.e., the peak-to-nadir difference of integrated backscatter for perpendicular versus parallel fiber insonification) does not differ significantly in infarcted and normal tissue.
tissue (14.8±0.5 versus 14.5±0.6 dB for infarcted and normal, respectively; p=NS). Figure 7B shows that the average transmural shift of fiber orientation was significantly greater for infarct than for normal tissue (14.6±1.5 versus 9.2±0.7°/mm of tissue, respectively; p<0.05). Figure 7C demonstrates that the angle-averaged integrated backscatter also was greater for infarcted than for normal tissue (~48.3±0.5 versus ~53.4±0.4 dB, respectively; p<0.05).

Discussion

Our data indicate that mature scar tissue in human hearts after myocardial infarction makes up a highly ordered arrangement of fibers with a predominant orientation that depends on transmural location. To our knowledge, these data represent the first report of a progressive counterclockwise transmural shift in the orientation of aligned scar tissue elements in human myocardium. The transmural organization of scar tissue fibers was delineated accurately by measurement of the dependence of ultrasonic backscatter on the angle of insonification, or ultrasonic anisotropy. Epicardial scar fibers courses more obliquely toward the apex, midmyocardial fibers maintained a circumferential orientation, and endocardial fibers courses more obliquely toward the base. The similarity of ultrasonic and histological measurements of scar fiber orientation illustrates the potential usefulness of ultrasonic tissue characterization for quantification of the three-dimensional structure of tissue from areas of myocardial infarction.

The alignment of infarct scar tissue fibers at selected transmural levels (Figure 7A) parallels the highly organized structure of normal ventricular wall fibers in many respects. Our data suggest that the deposition of these fibers is influenced to some extent by the orientation of previously normal myofibers at each transmural level. This arrangement is undoubtedly determined by the load imposed on the remodeled infarct zone by the active contraction of surrounding normal myofibers. It is known that the alignment of scar tissues in healing surgical wounds manifests a dependence on imposed stress vectors.38 In the case of tissue remodeling after myocardial infarction, passive stretching of tissue within the necrotic zone would result from the tethering of maturing scar tissue fibers to active contractile fibers at the borders of the infarct. Thus, the principal direction of force applied to scar tissue fibers should be determined to a large extent by stress vectors generated by the contraction of highly oriented myofibers at and around the border of infarction.

We observed a 59% greater transmural shift of fiber orientation per millimeter of tissue for infarcted than for normal tissue (14.6° versus 9.2°, Figure 7B), which also is compatible with the hypothesis that forces attributable to mechanical tethering at the lateral borders of the infarct determine the principal axes of scar tissue fibers at each transmural level. Streeter et al20,39 demonstrated that the orientation of myofibers shifts through an angle of approximately 120° from epicardium to endocardium. Midmyocardial fibers assume a predominantly circumferential orientation, epicardial fibers course obliquely toward the apex, and endocardial fibers course obliquely toward the base. We observed that segments from areas of infarction were substantially thinner than the surrounding normal tissue segments. In the present study, we were able to perform an average of 1.9±0.3 independent determinations of fiber angle shift per plug for infarct samples compared with 3.1±0.2 determinations per plug for the thicker normal tissue samples studied previously.18 Thus, the tissues from studied infarct zones were approximately 61% of the thickness of the normal tissues. Based on these estimates of the relative thicknesses of infarcted and normal tissue plugs and the fiber shifts per millimeter of tissue, the total transmural fiber shift for infarcted and normal tissue appears equal (~100°, assuming a wall thickness for normal ventricle of 1.1 cm).

The total transmural shift of infarct scar fibers, which appears to be equal to that for normal myofibers, must occur within the comparatively limited thickness of the remodeled infarct zone. The increased fiber shift per millimeter of tissue in infarct regions compensates for the decreased thickness of the infarct zone so that the total transmural fiber shift approximates that observed within normal tissue segments. This finding implies that structural elements at all transmural levels within the infarct zone reorient themselves to conform to the lateral mechanical forces imposed by the contraction of surrounding normal myocytes. That is, the lateral stress vectors that govern the rearrangement of infarct fibers across the wall enforce the same total transmural fiber shift found in normal segments.

Although lateral stress vectors appear to exert a primary influence on the reorientation of fibers within any transmural plane, it is possible that additional shear stresses operating at the border of the infarct could induce a component of fiber reorientation orthogonal to or across transmural planes. Whittaker et al40 recently used polarized light microscopy to demonstrate the presence of structural anisotropy in scar tissue after induction of myocardial infarction in dogs. They reported well-aligned infarct fibers in central infarct zones but found marked fiber disarray in the border zones of healed infarcts in dogs.

The tissue plugs that we studied were samples taken from central regions of human infarcts and all manifest a high degree of alignment at each transmural level studied. If one considers the possible effect of fiber disarray on our measurements, it is unlikely that any significant extent of fiber disarray or orthogonal reorientation was present in our samples because the magnitudes of anisotropy for normal and infarct hearts were equal (14.5 versus 14.8 dB). If significant fiber disarray were present, the magnitude of anisotropy would be reduced. Any significant orthogonal fiber reorientation would also reduce anisotropy because fibers would always remain some-
what perpendicular to the interrogating ultrasound beam, which would restrict the full range of insonification through perpendicular-to-parallel orientations. The finding of equal anisotropy for infarcted and normal tissues further supports the hypothesis that the principal stress vectors that govern realignment of infarct tissues lie within transmural planes. Thus, lateral “in-plane” stress vectors may govern the reorientation of fibers to a much greater extent than do orthogonal shear stresses for these central infarct segments.

Figure 7C indicates that infarct tissue is significantly more echogenic on average than is normal tissue. These data corroborate previous results from our laboratory and others that demonstrate a quantitative relation between the concentration of collagen in myocardial scar tissue and the magnitude of backscatter. We also have shown previously that the maturation of collagenous scar tissue influences the magnitude of backscatter. Whittaker et al also recently examined the progressive maturation of collagen after infarction by measuring the “retardation” of polarized light, which provides an index of the extent of “anisotropic molecular organization.” Over a 6-week interval, values for retardation in scar tissue increased progressively as the infarct matured. These data parallel our previous observations of a quantitative relation between the maturity of scar tissue and the magnitude of backscatter. Thus, the structural complexity associated with cross-linking of collagen fibers in mature infarcts represents another primary physical determinant of the interaction of ultrasound with remodeled myocardial tissue.

Whittaker et al observed a transmural shift in the orientation of canine scar tissue fibers that is qualitatively similar to the shift for human scar tissue fibers observed in the present study. They reported that the orientation of scar tissue fibers shifts by approximately 27° from “subepicardial” to “subendocardial” levels. Unfortunately, quantitative comparison with our results is not possible because Whittaker et al did not express their data in terms of an angular shift per millimeter of tissue. A virtue of the present ultrasonic technique that permits robust quantitative measurements of fiber orientation is the ability to measure backscatter over long path lengths of tissue (approximately 10 mm), yielding a measure of the average alignment of fibers across an entire transmural level. Nevertheless, these two studies demonstrated similar transmural shifts in the orientation of scar tissue fibers with the use of different techniques and provided complementary insights into the anatomy and pathophysiology of tissue remodeling of human myocardium after infarction.

Other studies have examined mechanisms of remodeling after infarction, including early reports in which infarct extension was distinguished from expansion. More recent reports have focused on global ventricular dilatation and its possible limitation by reduction of afterload and preload or by mainten-
of backscatter.\textsuperscript{30–35} Although the actual source (or sources) of this cyclic variation has not been completely defined, anisotropy may play a role. Because infarct tissue does not “contract” to any appreciable extent during cardiac systole, we would not expect much fiber rotation and therefore no appreciable change in the magnitude of scattering from an infarct zone over the heart cycle. This is what we demonstrated by clinical measurements of backscatter: Infarct zones typically demonstrate less than 1-dB alteration in scattering intensity from systole to diastole, whereas normal zones demonstrate approximately 5 dB of cyclic variation of backscatter.\textsuperscript{30,32,33,35}

Because we measured anisotropy in samples of infarcted tissue from the hearts of patients who underwent cardiac transplantation for end-stage ischemic heart disease, it is not clear whether our observations apply to hearts that manifest more effective remodeling. Our data reflect the structural composition of tissues from areas of mature infarction that are characterized by substantial anatomic heterogeneity. Patchy infarct was not differentiated from well-healed confluent scar tissue or from aneurysm in the present study, yet all samples clearly demonstrated ultrasonic anisotropy for backscatter.

The demonstration of ultrasonic anisotropy of backscatter in human myocardium for both normal tissue and that from the area of mature infarction illustrates the potential usefulness of ultrasonic tissue characterization for detection of intramural structural detail not apparent by other imaging modalities. We and others\textsuperscript{18,47} have shown recently that ultrasonic tissue characterization is useful for elucidation of intramural fiber orientation in normal subjects. We believe that clinical application of tissue characterization for measurement of ultrasonic anisotropy may provide important information about the mechanisms of structural remodeling of tissue and its effect on ventricular geometry and function.

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