Analysis of Transmural Trend of Myocardial Integrated Ultrasound Backscatter for Differentiation of Hypertrophic Cardiomyopathy and Ventricular Hypertrophy Due to Hypertension

JOHJI NAITO, MD, TOHRU MASUYAMA, MD, JUN TANOUCHI, MD, TOSHIAKI MANO, MD, HIROYA KONDO, MD, KAZUHIRO YAMAMOTO, MD, REIKO NAGANO, MD, MASATSUGU HORI, MD, MICHITOSHI INOUE, MD, TAKENOBU KAMADA, MD
Suita, Japan

Objectives. This study was undertaken to differentiate hypertrophic cardiomyopathy from hypertensive hypertrophy using a newly developed M-mode format integrated backscatter imaging system capable of calibrating myocardial integrated backscatter with the power of Doppler signals from the blood.

Background. Myocardial integrated ultrasound backscatter changes in patients with hypertrophic cardiomyopathy; however, it is unknown whether ultrasound myocardial tissue characterization may be useful in differentiating hypertrophic cardiomyopathy from hypertensive hypertrophy.

Methods. Calibrated myocardial integrated backscatter and its transmural gradient were measured in 31 normal subjects, 13 patients with hypertensive hypertrophy and 22 patients with hypertrophic cardiomyopathy. The gradient in integrated backscatter was determined as the ratio of calibrated integrated backscatter in the endocardial half to that in the epicardial half of the myocardium.

In addition to the pathologic ventricular hypertrophy seen in patients with hypertrophic cardiomyopathy, ventricular hypertrophy may develop physiologically in patients with hypertension, as an adaptive process to pressure overload (1,2). Although conventional echocardiography is particularly useful in detecting increased left ventricular mass or abnormal myocardial function, or both, in patients with possible ventricular hypertrophy (3–8), the two entities are most clearly differentiated by detection of the presence of myocardial fiber architecture distortion or extremely increased collagen (9–14). Thus, one of the goals of myocardial tissue characterization is to distinguish pathologic from physiologic hypertrophy. This may become possible because a number of experimental studies have shown that measurements of integrated ultrasonic backscatter are useful in detecting physiologic and pathologic changes in the myocardium (15–24).

Myocardial tissue characterization in human hypertrophied hearts has been attempted by a few groups (25–30). They clearly showed the difference in ultrasonic tissue variables between hypertrophied and normal hearts; however, it has not been documented whether ultrasound tissue backscatter can distinguish between hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension.

In this study, we measured acoustic properties of the myocardium in patients with hypertrophied hearts to clarify whether any integrated backscatter measure may be useful in distinguishing between hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension. Therefore, calibrated myocardial integrated backscatter was measured using a newly developed M-mode format integrated backscatter imaging system capable of calibrating myocardial integrated backscatter with the power of Doppler signals from the blood. We also analyzed the transmural trend of the acoustic properties of the myocardium.

Results. Cyclic variation of integrated backscatter was smaller and calibrated myocardial integrated backscatter higher in patients with hypertrophied hearts than in normal subjects, but there were no significant differences in either integrated backscatter measure between patients with hypertensive hypertrophy and those with hypertrophic cardiomyopathy. Transmural gradient in myocardial integrated backscatter was present only in patients with hypertrophic cardiomyopathy (5.0 ± 1.8 dB [mean ± SD] for the septum; 1.2 ± 1.6 dB for the posterior wall).

Conclusions. Hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension can be differentiated on the basis of quantitative analysis of the transmural gradient in integrated backscatter.

(J Am Coll Cardiol 1994;24:517–24)
Methods

Ultrasound backscatter instrumentation. The integrated backscatter imaging system consisted of a commercially available echocardiograph (ME-130A, Fujitsu Co.) with a 3.5-MHz frequency transducer, analog/digital converter and personal computer system (FMR-80H1L, Fujitsu Co.). Unlike a conventional imaging system, the ultrasound signals were accessed with the integrated backscatter processor to produce a continuous signal that is proportional to the logarithm of integrated backscatter. In this study, myocardial integrated backscatter was calibrated by the backscatter power from the blood. To correct for the attenuation or signal loss resulting from transmission through intervening tissue between the transducer and Doppler sample volume, the logarithmic power of Doppler signals scattering from the blood was subtracted from the logarithmic power at the area of interest in the myocardium. In this study Doppler sample volume was positioned just below the septum in the left ventricular cavity, and the area of interest for tissue characterization was positioned in the septum or posterior wall along the same interrogated beam. Characteristics of the transducer and system were adjusted beforehand using a dextran particle suspension of the known backscatter coefficient so that we could compare the amplitudes of ultrasound backscatter from the areas of interest with different depths.

Subjects. Thirty-eight patients with hypertrophied hearts were considered for this study. Three were excluded because integrated backscatter images of adequate quality could not be obtained. Therefore, the study group included 35 patients with hypertrophied hearts (29 men, 6 women; mean age 55 years, range 14 to 80 years). The etiology of hypertrophied hearts was considered to be hypertension in 13 patients and hypertrophic cardiomyopathy in 22. The mean age 55 years, range 14 to 80 years). The etiology of hypertrophied hearts was considered to be hypertension in 13 patients and hypertrophic cardiomyopathy in 22.

Table 1. Echocardiographic and Integrated Backscattering Measurements

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Gender (M/F)</th>
<th>Calibrated IB</th>
<th>PW (dB)</th>
<th>Variation IB</th>
<th>PW (dB)</th>
<th>LVD (mm)</th>
<th>Septal thickness (mm)</th>
<th>FS (%)</th>
<th>% Systolic thickening</th>
<th>Posterior wall thickness (mm)</th>
<th>FS (%)</th>
<th>M = male; PW = posterior wall; Variation IB = magnitude of cardiac cyclic variation of integrated backscatter</th>
</tr>
</thead>
<tbody>
<tr>
<td>46 ± 13</td>
<td>26/F</td>
<td>42 ± 4.2</td>
<td>7.7 ± 1</td>
<td>47 ± 4</td>
<td>9.7 ± 2</td>
<td>47 ± 2</td>
<td>Corected IB</td>
<td>45 ± 7</td>
<td>49 ± 7</td>
<td>22 ± 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>31 ± 3</td>
<td>31/F</td>
<td>31.1 ± 5.3</td>
<td>7.7 ± 1</td>
<td>47 ± 4</td>
<td>9.7 ± 2</td>
<td>47 ± 2</td>
<td>FS (%)</td>
<td>45 ± 7</td>
<td>49 ± 7</td>
<td>22 ± 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38 ± 4</td>
<td>38/F</td>
<td>38.8 ± 2.8</td>
<td>4.7 ± 1</td>
<td>27 ± 7</td>
<td>27 ± 7</td>
<td>27 ± 7</td>
<td>FS (%)</td>
<td>26 ± 7</td>
<td>27 ± 7</td>
<td>26 ± 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 ± 5</td>
<td>40/F</td>
<td>43 ± 10</td>
<td>4.8 ± 0.5</td>
<td>43 ± 10</td>
<td>4.8 ± 0.5</td>
<td>43 ± 10</td>
<td>FS (%)</td>
<td>41 ± 12</td>
<td>41 ± 12</td>
<td>22 ± 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 ± 1</td>
<td>9/M</td>
<td>15 ± 2</td>
<td>9 ± 1</td>
<td>15 ± 2</td>
<td>9 ± 1</td>
<td>15 ± 2</td>
<td>FS (%)</td>
<td>19 ± 4.4</td>
<td>19 ± 4.4</td>
<td>19 ± 4.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 ± 2</td>
<td>13/M</td>
<td>20 ± 4</td>
<td>13 ± 2</td>
<td>20 ± 4</td>
<td>13 ± 2</td>
<td>20 ± 4</td>
<td>FS (%)</td>
<td>22 ± 4</td>
<td>22 ± 4</td>
<td>22 ± 4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data analysis. The integrated backscatter study was performed without any knowledge of patient characteristics by monitoring the two-dimensional echocardiographic image with an interrogated beam and Doppler sample volume in the right half of the display and an M-mode echocardiogram in the left half. The Doppler spectrum was monitored only by sound, not on the display. Once the toggle switch was turned to the "on" position, radiofrequency signals were converted to digital ones, and data longer than 5 s were stored in the memory. The integrated backscatter images were then reconstructed by the personal computer system using the stored data. On the monitor, the area of interest for backscatter measurements was traced midway between the endocardial and epicardial borders in the septum and posterior wall. We tried to exclude the thick bright lines of the endocardium and intramyocardial specular bright echoes from the area of interest. The depth of this area was 5 mm; the trace of the center of it is indicated by a bright line.

To calibrate myocardial integrated backscatter, we determined the power of Doppler signals sampled in the left ventricular cavity as follows. The depth of the sample volume was 7 mm. In the Doppler power spectrum displayed on the computer screen, we selected by hand the intervals when signals were considered adequate for calculating Doppler power. The Doppler power averaged over the selected intervals was used for calibrating myocardial integrated backscatter. It is noteworthy that strong signals considered to have originated from the structure movement are eliminated automatically by the computer program. In addition, the power of Doppler signals does not vary instan-
taneously. Thus, one may use the averaged Doppler power for calibrating myocardial integrated backscatter even at different instances if the ultrasound beam direction is constant.

After placing the area of interest for backscatter measurements in the M-mode integrated backscatter images and selecting time intervals with adequate Doppler signals in the Doppler image, the computer screen shows curves of myocardial integrated backscatter calibrated by the power of the Doppler signals. From these curves, we consistently measured two variables in all subjects. The magnitude of cyclic variation in integrated backscatter was determined as the difference between minimal and maximal peaks. The value of myocardial integrated backscatter at maximal peak was defined as the calibrated myocardial integrated backscatter at end-diastole. Averaged values over at least 3 beats were provided for quantitative analysis. Both variables are essentially independent of the transmitted ultrasound power and attenuation by the chest wall and therefore may be compared among subjects.

In addition to the averaged value of myocardial integrated backscatter in the area of interest, our system provides the values of myocardial integrated backscatter of the upper and lower halves in the area of interest. This function was used to assess the transmural trend in the measures of myocardial integrated backscatter (gradient integrated backscatter) in 21 normal subjects and in all patients with hypertrophied hearts.

Reproducibility. Interobserver and intraobserver variabilities of the measurements of the integrated backscatter variables were studied. Integrated backscatter measures were determined on screen, and variability was therefore assessed as follows. M-mode integrated backscatter images were obtained in 12 subjects by one observer. Two observers independently analyzed the integrated backscatter images to determine their variables. These were compared for determination of interobserver variability. Intraobserver variability was determined by one observer repeating the analysis process a second time in these 12 subjects for comparison with the first measurements. Mean (±SD) absolute differences of the magnitude of cyclic variation of integrated backscatter between observations were 0.7 ± 0.4 dB (interobserver) and 0.6 ± 0.4 dB (intraobserver) for the septum and 0.8 ± 0.3 dB (interobserver) and 0.5 ± 0.4 dB (intraobserver) for the posterior wall. Mean absolute differences of the calibrated integrated backscatter at end-diastole between observations were 0.8 ± 0.4 dB (interobserver) and 0.6 ± 0.3 dB (intraobserver) for the septum and 0.7 ± 0.4 dB (interobserver) and 0.5 ± 0.4 dB (intraobserver) for the posterior wall. Absolute differences of the regional calibrated integrated backscatter at end-diastole between observations were 0.7 ± 0.4 dB (interobserver) and 0.6 ± 0.3 dB (intraobserver) for the septum and 0.7 ± 0.5 dB (interobserver) and 0.5 ± 0.4 dB (intraobserver) for the posterior wall.

Statistical analysis. Data are presented as mean value ± SD. Intergroup differences were tested for significance using analysis of variance, with subgroup analysis by the Scheffé F test. Relations between two variables were studied using a simple linear regression analysis.

Results

Integrated backscatter measures in normal subjects and patients with hypertrophied hearts. The magnitude of cyclic variation in integrated backscatter was significantly smaller and calibrated myocardial integrated backscatter significantly greater in patients with hypertrophied hearts than in normal subjects. There was no difference in either measure between patients with ventricular hypertrophy due to hypertension and the patient with hypertrophic cardiomyopathy. Measurements of the magnitude of cardiac cyclic variation of integrated backscatter and calibrated myocardial integrated backscatter are shown by thin (left) and thick (right) white arrows, respectively, in the upper left panel.

Transmural trend of integrated backscatter measures. The magnitude of cyclic variation in integrated backscatter did not differ between the right and left ventricular halves of the septum or between the endocardial and epicardial halves of the posterior wall in all normal subjects and all patients with hypertrophy (Fig. 2, Table 2). There was no significant difference in the calibrated myocardial integrated backscatter between the right and left ventricular halves of the septum or between the endocardial and epicardial halves of
Figure 2. Curves of myocardial integrated backscatter (IB) versus time in the left ventricular endocardial half (LV [endo] half) and the right ventricular epicardial half (RV [epi] half) of the septum (upper panels) and in the endocardial half (endo half) and epicardial half (epi half) of the posterior wall (PW) (lower panels) in a patient with hypertensive hypertrophy (a) and in a patient with hypertrophic cardiomyopathy (b). There was no difference in the magnitude of cardiac cyclic variation of integrated backscatter between the right and left ventricular halves or between the endocardial and epicardial halves in both patients. In contrast, calibrated myocardial integrated backscatter was significantly greater in the right ventricular epicardial half than in the left ventricular endocardial half of the septum only in the patient with hypertrophic cardiomyopathy (b).

Table 2. Transmural Trend in Integrated Backscatter Measures

<table>
<thead>
<tr>
<th></th>
<th>Normal Subjects</th>
<th>Hypertensive Heart</th>
<th>Hypertrophic Cardiomyopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 21)</td>
<td>(n = 13)</td>
<td>(n = 22)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>44 ± 10</td>
<td>59 ± 8*</td>
<td>54 ± 17</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>16/7</td>
<td>96/4</td>
<td>29/2</td>
</tr>
<tr>
<td>Calibrated IB (dB)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV-half</td>
<td>42.5 ± 3.8</td>
<td>48.0 ± 2.6*</td>
<td>50.8 ± 4.1*</td>
</tr>
<tr>
<td>LV-half</td>
<td>42.4 ± 3.8</td>
<td>47.8 ± 2.6*</td>
<td>45.7 ± 4.2*</td>
</tr>
<tr>
<td>Epi-half</td>
<td>30.8 ± 5.6</td>
<td>38.8 ± 2.7*</td>
<td>38.6 ± 6.0*</td>
</tr>
<tr>
<td>Endo-half</td>
<td>30.7 ± 5.7</td>
<td>38.7 ± 2.7*</td>
<td>37.4 ± 5.6*</td>
</tr>
<tr>
<td>Variation IB (dB)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV-half</td>
<td>7.7 ± 1.1</td>
<td>4.7 ± 0.6*</td>
<td>5.0 ± 1.1*</td>
</tr>
<tr>
<td>LV-half</td>
<td>7.7 ± 1.1</td>
<td>4.7 ± 0.6*</td>
<td>5.0 ± 1.1*</td>
</tr>
<tr>
<td>Epi-half</td>
<td>7.9 ± 1.2</td>
<td>4.8 ± 0.5*</td>
<td>5.1 ± 1.0*</td>
</tr>
<tr>
<td>Endo-half</td>
<td>7.9 ± 1.1</td>
<td>4.9 ± 0.5*</td>
<td>5.2 ± 1.0*</td>
</tr>
<tr>
<td>Gradient IB (dB)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septum</td>
<td>0.1 ± 0.2</td>
<td>0.2 ± 0.3</td>
<td>5.0 ± 1.8*§</td>
</tr>
<tr>
<td>PW</td>
<td>0.1 ± 0.2</td>
<td>0.1 ± 0.3</td>
<td>1.2 ± 1.6*</td>
</tr>
</tbody>
</table>

* p < 0.01 versus normal subjects. † p < 0.01 versus left ventricular half in septum or endocardial half in posterior wall. ‡ p < 0.05 versus normal subjects. § p < 0.01 versus hypertensive hearts. † † p < 0.05 versus hypertensive hearts. Data presented are mean values ± SD. Endo-half = endocardial half in posterior wall (PW); Epi-half = epicardial half in posterior wall; Gradient IB = transmural gradient in integrated backscatter. LV-half = left ventricular half in septum; RV-half = right ventricular half in septum; other abbreviations as in Table 1.

The transmural trend of the calibrated myocardial integrated backscatter was quantified by calculating the difference in decibels between subendocardial and subepicardial regions. Subtracting the logarithmic decibel domain is equivalent to taking a ratio in the linear domain; therefore our variables express the ratio of calibrated myocardial integrated backscatter in the left ventricular (endo) half to that in the right ventricular (epi) half for the septum, and the ratio of calibrated myocardial integrated backscatter in the endocardial half to that in the epicardial half for the posterior wall. The transmural gradient in integrated backscatter was significantly greater in patients with hypertrophic cardiomyopathy than in normal subjects and in patients with ventricular hypertrophy due to hypertension in both the septum and posterior wall (Fig. 3).

Transmural gradient in integrated backscatter and echocardiographic variables. The transmural gradient in integrated backscatter was compared with ventricular wall thickness (Fig. 4). It is again noteworthy that the transmural gradient in integrated backscatter was not observed in normal subjects and in patients with ventricular hypertrophy due to hypertension. Most patients with hypertrophic car-
Figure 3. Comparison of transmural gradient in integrated backscatter (IB) among normal subjects, patients with ventricular hypertrophy due to hypertension (HT) and patients with hypertrophic cardiomyopathy (HCM) in the septum (left) and posterior wall (PW) (right). Transmural integrated backscatter gradient was significantly greater in patients with hypertrophic cardiomyopathy than in normal subjects and patients with ventricular hypertrophy due to hypertension, but there was no significant difference in this measure between normal subjects and patients with ventricular hypertrophy due to hypertension in both the septum and the posterior wall.

Figure 4. Relation between wall thickness and transmural gradient in integrated backscatter in the septum and posterior wall. Abbreviations as in Figure 3. See text for explanation.

Discussion

Several experimental studies (15–22) support the idea that both the absolute integrated backscatter and the magnitude of the cardiac cycle-dependent variation of integrated backscatter reflect the acoustic properties of the myocardium, because absolute integrated backscatter increases in myocardial fibrosis (15–17) and the magnitude of the cardiac cycle-dependent variation of integrated backscatter has been demonstrated to decrease with myocardial ischemia and infarction (19–22). Such changes in integrated backscatter measures were observed in patients with hypertrophied hearts; however, there was no difference in either measure between ventricular hypertrophy due to hypertension and hypertrophic cardiomyopathy. Thus, we failed to distinguish between ventricular hypertrophy due to hypertension and hypertrophic cardiomyopathy by using these integrated backscatter measures. In contrast, myocardial integrated backscatter was greater in the right ventricular half than in the left ventricular half in the septum only in patients with hypertrophic cardiomyopathy, and the measure of the transmural trend of integrated backscatter was useful in distinguishing between ventricular hypertrophy due to hypertension and hypertrophic cardiomyopathy.

Ventricular hypertrophy due to hypertension. This study showed that calibrated myocardial integrated backscatter increased significantly in patients with ventricular hypertrophy due to hypertension. Tanaka et al. (14) indicated that the percent area of fibrosis in the left ventricular wall was greater in hypertensive heart disease than in normal hearts. Myocardial fibrosis increases absolute integrated backscatter in both in vitro and in vivo experiments (15–17,32), and thus the possible structural changes of an increase in fibrosis of the myocardium may account for the increase in calibrated integrated backscatter in our patients with ventricular hypertrophy due to hypertension.

Cyclic variation in integrated backscatter was significantly smaller in patients with ventricular hypertrophy due to hypertension than in normal subjects. This finding is consistent with our previous finding (28). The mechanism for this phenomenon is still unknown, but reduced regional myocardial contractile function may be the most likely explanation because the dependence of the magnitude of cardiac cyclic variation of integrated backscatter on contractile performance has been documented in experimental studies (33–36). Furthermore, regional myocardial contractile function assessed with percent systolic wall thickening was depressed in our patients with ventricular hypertrophy due to hypertension.

Hypertrophic cardiomyopathy. In this study, calibrated integrated backscatter increased significantly, and the magnitude of cyclic variation in integrated backscatter decreased significantly, in patients with hypertrophic cardiomyopathy compared with normal subjects. This finding is consistent with our previous findings and those of Lattanzi et al. (28–30). The changes in integrated backscatter measures
were not different from those observed in patients with ventricular hypertrophy due to hypertension, and the mechanism may also be the same (i.e., myocardial fibrosis and regional myocardial contractile function). Although myocardial fibrosis is usually more severe in hypertrophic cardiomyopathy than in ventricular hypertrophy due to hypertension, the changes in the integrated backscatter measures were not different between these subsets. This finding suggests the possible effects of myocardial cell disorganization on these integrated backscatter measures in patients with hypertrophic cardiomyopathy. Although both integrated backscatter measures failed to distinguish between hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension in the present study, we still believe that both integrated backscatter measures are useful to assess ventricular hypertrophy, partially because Lattanzi and colleagues showed that myocardial integrated backscatter was normal in subjects (elite athletes) with physiologic ventricular hypertrophy caused by intense physical training (30).

Transmural trend in acoustic properties of the myocardium. The distinction between hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension was possible only with the measurements of transmural trend of integrated backscatter in our patients with hypertrophy. Transmural gradient in integrated backscatter was observed only in patients with hypertrophic cardiomyopathy. Fujisawa et al. (37) conducted histologic studies on autopsied human hearts to show that myocardial fiber disarray in patients with hypertrophic cardiomyopathy was present mostly in the middle third of the septum and in the middle and outer thirds of the posterior wall. If myocardial fiber disarray worked to increase integrated backscatter, the observed transmural gradient of integrated backscatter might be explained as the effect of the transmural nonhomogeneity of myocardial fiber disarray. The transmural gradient of integrated backscatter measure was obviously larger and more frequent in the septum than in the posterior wall in patients with hypertrophic cardiomyopathy. This finding may be also explained by the effect of the transmural nonhomogeneity of myocardial fiber disarray because this disarray is more extensive in the septum than in the posterior wall (37–39).

The transmural gradient in integrated backscatter did not correlate with wall thickness in patients with hypertrophic cardiomyopathy either in the septum or posterior wall. Further, the transmural gradient in integrated backscatter was not observed even in patients with advanced hypertrophy due to hypertension. These findings are in contrast to the previous finding that the magnitude of variation of integrated backscatter decreases as wall thickness increases in patients with pressure overload hypertrophy, hypertrophic cardiomyopathy and cardiac transplants (28, 40). Thus, assessment of the transmural gradient in integrated backscatter is likely to expand the use of myocardial ultrasound tissue characterization in patients with hypertrophied hearts.

The abnormal acoustic properties of the myocardium may be an expression of the intrinsic myopathic process. Thus, our findings support the hypothesis that the intrinsic myopathic process involves the myocardium in a transmurally nonhomogeneous fashion, even in nonhypertrophied segments of the wall. This hypothesis is consistent with the previous findings that histologic abnormalities are observed even in segments of the wall with normal or minimally hypertrophied thickness (38, 41–43).

Integrated backscatter in the septum versus posterior wall. The present study showed the significant regional differences in calibrated myocardial integrated backscatter between the septum and posterior wall in patients with hypertrophied hearts and in normal subjects. This finding is comparable with those obtained by other investigators (29, 44, 45). It may be explained by the techniques used in the determination of integrated backscatter measures and thus was observed in all subjects. Alternatively, regional differences in muscle fiber orientation may account for regional differences in acoustic properties (44). Regional myocardial contractile function appears to be a less significant contributor to the calibrated myocardial integrated backscatter than to the magnitude of cyclic variation in integrated backscatter (28) because this measure is unaffected by an alteration of cardiac function in dogs (unpublished observations). To exclude the possible effects of the regionality of myocardial integrated backscatter measures on the results of this study, the septum and posterior wall were analyzed separately.

Cyclic variation in integrated backscatter was slightly greater in this study than in most previous ones (46–48). The reason for this could not be clarified but may be related to the system used. We consider this likely because in our system, integrated backscatter was determined using band-limited rather than broad-band frequency ultrasound signals.

Technical limitations. Four technical limitations are noted. First, technically adequate integrated backscatter images were not obtained in 3 of 38 patients. Second, concerns about the accuracy and reproducibility of the evaluation of the magnitude of transmural integrated backscatter variations have been raised by the Iowa group by investigating the reproducibility of measurements for the entire process of data acquisition, including transducer placement and echocardiographic instrument adjustment, as well as longitudinal reproducibility (46). The variance between measurements should be reduced by increasing the number of independent samples of backscatter making up each measurement. Thus, the use of M-mode rather than two-dimensional imaging and the use of a relatively small area of interest were factors that could possibly reduce the reproducibility and reliability of the integrated backscatter measures. In addition, translational and rotational movements of the heart should affect the integrated backscatter measures. Thus, intraobserver and interobserver reproducibility were evaluated in this study. Our data showed that any of our integrated backscatter measures, including regional (endocardial and epicardial) measures, could be obtained as reliably and reproducibly as those in many earlier studies.
(28,44,47,48). Thus, the mean values of the transmural difference (or gradient) in integrated backscatter of 5 dB in patients with hypertrophic cardiomyopathy cannot be explained solely by the error due to possible problems with respect to the accuracy and reproducibility of ultrasound backscatter measurements.

Third, all quantitative analysis was based on the integrated backscatter values determined by hand tracing the area of interest on the integrated backscatter image, and there are problems inherent in the measurements (28,40,47). Thick, bright echo lines of the right or left septal endocardium, intramyocardial septal specular bright echoes or both may have affected the integrated backscatter measures in some patients. The depth of the area of interest was 5 mm in both normal subjects and patients with hypertrophy, and the thick bright lines of septal endocardium prevented us from tracing the midpoint of the septum, particularly in normal subjects with a relatively thin wall. Although this is likely to lead to a reduced signal-to-noise ratio or an increase in the integrated backscatter value not related to changes in the acoustic properties of the myocardium, our current system is capable of eliminating far stronger signals from the computation of integrated backscatter. Thus, the effects of the thick bright lines of septal endocardium and intramyocardial specular bright echoes were minimized in our current system. Finally, ultrasound backscatter is affected by the orientation of myocardial fibers and therefore is view dependent (49,50).

Thus, our transmural as well as regional evaluation of integrated backscatter can be performed only in the limited region of the septum and posterior wall imaged in the parasternal views. Although our methods cannot be used to assess noninvasively the extent of abnormal acoustic properties of the myocardium, the most frequent site of hypertrophy is the septum, and this cannot be considered a serious limitation of the present study.

Clinical implications and conclusions. This study showed clearly that an analysis of the transmural trend of the myocardial integrated backscatter may be useful in distinguishing between hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension. Hypertrophic cardiomyopathy, in most cases, is characterized by asymmetric septal hypertrophy (3–6,51), and thus conventional echocardiography is useful in both the quantification of hypertrophy and the differentiation of this disease from pressure overload hypertrophy. The difference between these two types of hypertrophy in the adult, however, is identified most clearly by histologic analysis, with myocyte disarray observed mostly in the septum in hypertrophic cardiomyopathy and myocardial fibrosis observed in both conditions. Because the transmural trend of myocardial integrated backscatter was observed exclusively in patients with hypertrophic cardiomyopathy, this tissue characterization measure appears to provide a promising noninvasive method for assessing the difference between hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension. Although hypertrophic cardiomyopathy and ventricular hypertrophy due to hypertension may be considered separate entities, their association continues to be a topic of debate (52). The use of myocardial ultrasound tissue characterization may allow practitioners to gain further insight into this issue.

Differentiation of cardiomyopathy from ventricular hypertrophy due to hypertension was accomplished with the use of the endocardial/epicardial ratio of myocardial integrated backscatter. It has been noted that this determination does not need a calibration method because myocardial integrated backscatter in the halves of the wall determined with a relative scale may be used for this calculation. As long as the scale is the same, the endocardial/epicardial ratio is determined properly.

References