# Improvement in Endocardial Border Delineation Using Tissue Harmonic Imaging

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Background and Methods: *For years, tissue has been assumed to be a linear medium in diagnostic ultrasound applications; thus, no backscattered signals in the second harmonic band are expected in harmonic imaging without the injection of a contrast agent. However, it has been shown that a useful tissue image is formed even without a contrast agent. The aim of this study was to evaluate whether this tissue harmonic image provided improved visualization of endocardial borders. Fifty-six adult patients with various heart diseases were investigated using conventional two-dimensional echocardiography and tissue harmonic imaging. In 30 of these patients, the left ventricular endocardial borders were well defined in the standard parasternal and apical views using conventional two-dimensional echocardiography. In the remaining 26 patients, delineation of endocardial borders was not possible in at least two segments. The equipment used was an ATL HDI-3000 diagnostic system equipped with harmonic imaging.* Results: *In all 56 patients, the myocardium and valves could be imaged with tissue harmonic imaging. Harmonic recordings were sharper and contained fewer clutter artifacts than conventional recordings. Most striking was the enhancement of left ventricular endocardial borders. In the 26 patients with incomplete delineation of left ventricular endocardial borders, wall motion could be evaluated in 290 of 312 (93%) segments with tissue harmonic imaging compared with only 168 of 312 (54%) segments with conventional echocardiography ($P < 0.001$).* Conclusions: *Tissue harmonic imaging improves image quality and can be used to enhance the definition of left ventricular endocardial borders. These findings can be explained by the nonlinear propagation of ultrasound within the tissue, which results in distortion of the transmitted signal and, thus, harmonic generation. (ECHOCARDIOGRAPHY, Volume 15, July 1998)*

*tissue harmonic imaging, left ventricular endocardial border delineation, clutter, artifacts*

Correct delineation of endocardial borders is the prerequisite for confident assessment of left ventricular function. Despite tremendous technical advancement in echocardiographic instrumentation, there remains a substantial number of patients who cannot be adequately imaged with conventional two-dimensional echocardiography. Contrast echocardiography may be an alternative procedure in some of these patients, especially when used in conjunction with harmonic imaging.[1] Harmonic imaging, the method in which an image is formed from the second harmonic component of the backscattered signal, originally was invented to use the nonlinear properties of contrast microbubbles.[2] Contrast microbubbles resonate when exposed to diagnostic ultrasound. Resonant microbubbles scatter not only ultrasound at the sonification frequency but

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also harmonic frequencies, which are multiples of the transmit frequency.[3] The spectrum of the backscattered ultrasound received by the transducer from the microbubbles consists of both the fundamental frequency and the harmonic frequencies. If in the receive phase only the second harmonic frequency is processed, signals from microbubbles would be selectively displayed, and those from tissue and blood would be suppressed.[3]

If tissue is assumed to be a linear medium, no image would be formed if harmonic imaging is used in patients without the injection of contrast. However, we were surprised to find good-quality images from valvular and myocardial structures during noncontrast harmonic imaging when the receiver gain was increased and optimized.[4] The current study was performed to evaluate this effect in consecutive patients and to assess its potential in the clinical setting.

## Methods

### *Study Patients*

The study population consisted of 56 consecutive patients (mean age, 53 years; age range, 23–76 years; 42 men and 14 women) who were referred for an echocardiographic investigation before left heart catheterization. The indication was suspected ischemic heart disease or valvular heart disease.

### *Ultrasound Image Acquisition and Analysis*

Standard parasternal and apical views of the left ventricle were recorded with a diagnostic ultrasound system equipped with harmonic imaging (HDI-3000, ATL, Bothell, WA, USA). The output power was set to the highest possible level (mechanical index = 1.5) when available. Fundamental images were obtained at 2.7-MHz frequency and harmonic images at 1.67 MHz and 3.33 MHz receive frequency. Gain settings and transducer position were individually optimized in each patient using the fundamental mode. At the end of a standard echocardiographic study using fundamental B-scan, the apical four-chamber view was recorded in the fundamental mode, and the imaging mode was switched to harmonic B-scan, holding the transducer in the same position as in the fundamental B-scan. In this position, the initial recordings were obtained with the same transmit and receive gain as in fundamental imaging. Subsequently, the receiver gain was increased and individually optimized as in fundamental B-scan to optimally visualize myocardial and valvular structures. The same procedure was performed using the apical two-chamber view.

In ten patients, additional recordings in fundamental and harmonic modes were obtained using the HDI 3000 system with a different transducer with a higher transmit frequency of 2.3 MHz and a higher corresponding harmonic frequency of 4.6 MHz. All images were stored on S-VHS videotape using a commercially available videotape recorder as well as on a magneto-optical disk using the storage system of the ultrasound devices.

Two experienced observers, who were blinded to each other's results, evaluated the recordings stored on the magneto-optical disc. Endocardial border delineation was scored in each of 12 segments using a 3-point scoring scale in which 0 indicates no delineation, 1 indicates poor delineation, and 2 indicates excellent delineation. A consensus of these two experienced observers was required to use the segment score for further comparative analysis. Mean endocardial border delineation score was calculated for each segment in both fundamental and harmonic modes. Using the area–length method, left ventricular volumes and ejection fraction were calculated from the stored frames after manual tracing of the endocardial borders by one observer.[5]

Left ventricular volumes and ejection fractions were determined in all patients in whom the endocardial border delineation scores of all segments in the apical four- and two-chamber views were 2. These data were compared with the findings of left ventricular angiography, which was performed within 24 hours of the echocardiographic examination. Paired Student's $t$-tests were performed to compare endocardial border delineation scores, left ventricular volumes, and ejection fractions obtained from fundamental recordings with measurements from harmonic B-scans. The P value, mean difference, and limits of agreement were calculated.

## Results

In 30 of 56 patients, fundamental imaging provided adequate recordings of the two apical views with good delineation of left ventricular endocardial borders. Adequate recordings were images that were classified as having an endocardial border delineation score of 2 by both readers in all segments. The recordings of the remaining 26 patients were judged as suboptimal echocardiograms. With harmonic imaging and optimization of the receiver gain, endocardial borders, myocardial tissue, and valvular structures appeared enhanced and more echo dense compared with use of the fundamental mode (Fig. 1). In addition, spontaneous echo contrast within the left ventricle was found in 51 of 56 patients when the receiver gain was adjusted for best visualization of endocardial borders. All 30 patients with an endocardial border delineation score of 2 on fundamental imaging retained the same score in harmonic imaging. In these patients, left ventricular end-diastolic and end-systolic volumes, as well as ejection fractions, obtained with harmonic imaging were not significantly different from the values measured in the fundamental mode.

In the 26 patients with endocardial border delineation scores of $< 2$ in at least two segments, wall motion could be evaluated in 168 of 312 (54%) segments with conventional echocardiography and in 290 of 312 (93%) segments with tissue harmonic imaging ($P < 0.001$) (Fig. 2). The improvement in left ventricular border delineation was statistically significant in the lateral segments (apical four-chamber view) and the anterior segments (apical two-chamber view) (Figs. 3 and 4). In comparison with fundamental mode, harmonic endocardial border delineation scores were not significantly higher in septal and inferior segments, but the display of these segments was less noisy and more pronounced.

In the ten patients in whom additional imaging was performed with a higher frequency transducer and a correspondingly higher frequency harmonic imaging, harmonic imaging also resulted in a better visual display of cardiac structures than did fundamental imaging. Spatial resolution was improved with higher frequencies (Fig. 5). Both lower and higher frequency transducers resulted in reduction in clutter artifacts in the harmonic mode compared with fundamental imaging.

## Discussion

Difficult-to-image patients include individuals who have thick chest walls, emphysema, or narrow intercostal spaces or who have had previous surgery (coronary bypass surgery, breast implants, and so on). Many of these technically difficult patients undergo echocardiographic

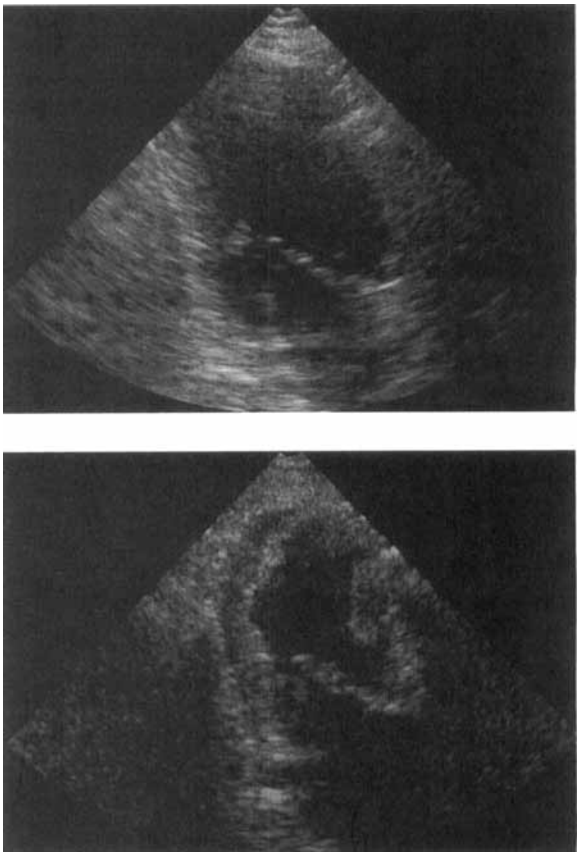

**Figure 1.** *Corresponding frames of an apical two-chamber view obtained with fundamental (top) and harmonic (bottom) imaging. The lateral wall is not delineated using fundamental mode due to "noise." With harmonic imaging, the lateral wall endocardium is fully displayed.*

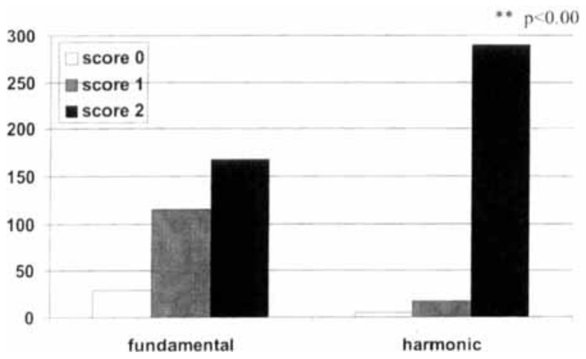


**Figure 2.** *Left ventricular endocardial border delineation showing a comparison of fundamental and harmonic modes. The total numbers of segments with different endocardial border delineation scores are shown.*

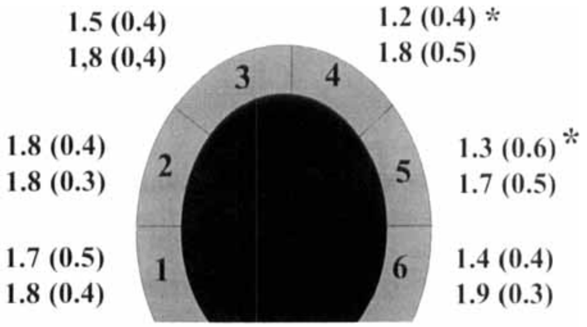


**Figure 4.** *Apical two-chamber view. Left ventricular endocardial border delineation scores are shown in the same manner as in Fig. 3. An improvement of endocardial border delineation values was found in segments 4 and 5.*

evaluation because of suspected ischemic heart disease. Left ventricular wall motion analysis by two-dimensional echocardiography is a key step in the noninvasive diagnostic workup of these patients.[6] Thus, an improvement in imaging techniques would be expected to have a significant impact on clinical decision making in the management of these patients. The results of our preliminary study suggest that harmonic imaging without contrast is a significant advance toward more confident evaluation of patients with suboptimal echocardiograms with fundamental imaging. Our data clearly demonstrate the superiority of harmonic imaging without contrast over funda-

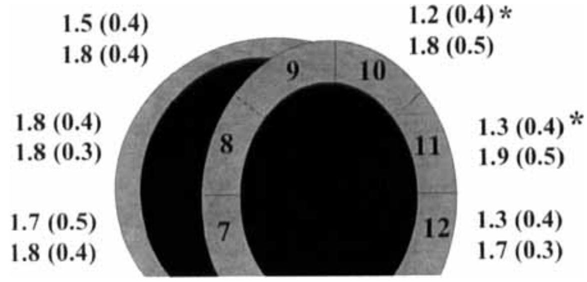


**Figure 3.** *Apical four-chamber view. Left ventricular endocardial border delineation scores (mean values and standard deviation). (Top) Results of fundamental imaging. (Bottom) Results of harmonic imaging. An improvement in endocardial border delineation values was found in segments 10 and 11.*

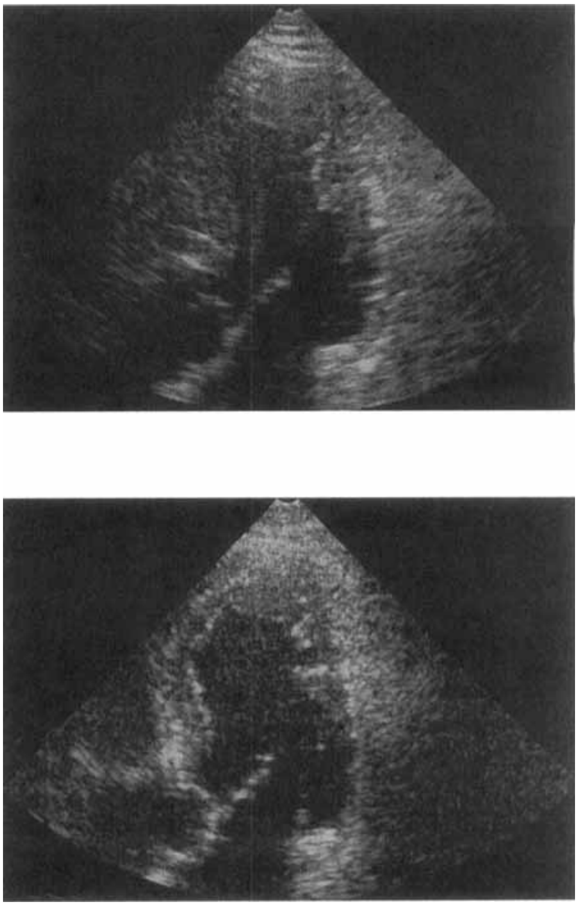

**Figure 5.** *Corresponding frames of a five-chamber view obtained with a 2.3/4.6-MHz transducer. Left ventricular endocardial borders are obscured on the fundamental image (top) but are well defined on the harmonic recording (bottom).*

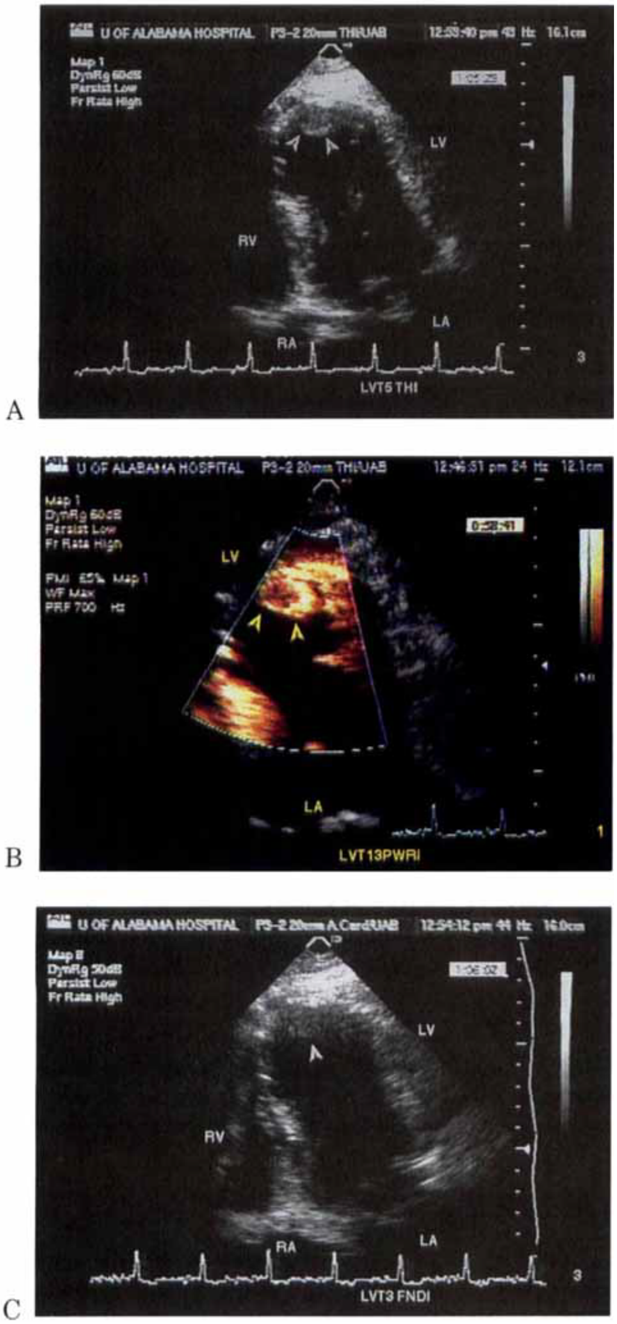


**Figure 6.** *Apical four-chamber view. The clot (arrowheads) in the left ventricular apex is much better visualized using tissue harmonic imaging (A) and power imaging (B) compared with fundamental imaging (C). LA = left atrium; RA = right atrium; RV = right ventricle.*

mental echocardiography in the delineation of endocardial borders. Use of this technology

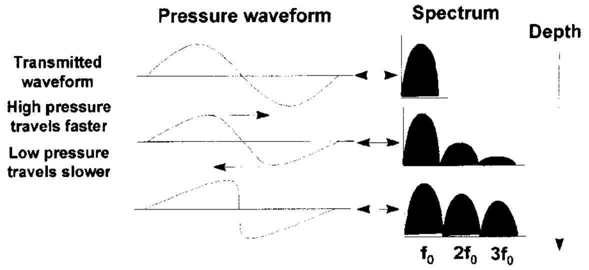


**Figure 7.** *Demonstration of the development of harmonic frequencies due to nonlinear acoustic propagation through tissue.*

should reduce the number of patients with ill-defined endocardial borders and result in a more accurate assessment of left ventricular function.[7] Our preliminary experience suggests that tissue harmonic imaging also may result in superior visualization of intracardiac lesions such as clots (Fig. 6).

Harmonic imaging originally was developed for contrast agents to use the nonlinear nature of contrast microbubbles. Although it has been well known for many years that propagation through tissue does create some harmonic energy, it has been assumed that the increased attenuation that occurs at the higher frequencies would attenuate the harmonics as quickly as they were produced. Thus, in the early days of harmonic contrast imaging, it was believed that the residual harmonic tissue image was due to incomplete rejection of the transmitted fundamental image. However, it was observed that the tissue harmonic image has some significantly improved characteristics that could not be explained by this description of this phenomenon. This effect is especially pronounced in technically difficult patients.[4,7]

Recent data suggest that the harmonic image is due to nonlinear propagation in tissue.[8] The velocity of sound propagation depends on the density of the insonified material.[9] During the compression phase, the tissue becomes denser, and hence the ultrasound waves travel faster through the tissue than during the rarefaction phase; the compression phase tends to overtake the rarefaction phase (Fig. 7). This results in a distortion of the ultrasound waveform, which further develops with propagation distance.[10-12] (Fig. 8). Due to these effects, the tissue tends to

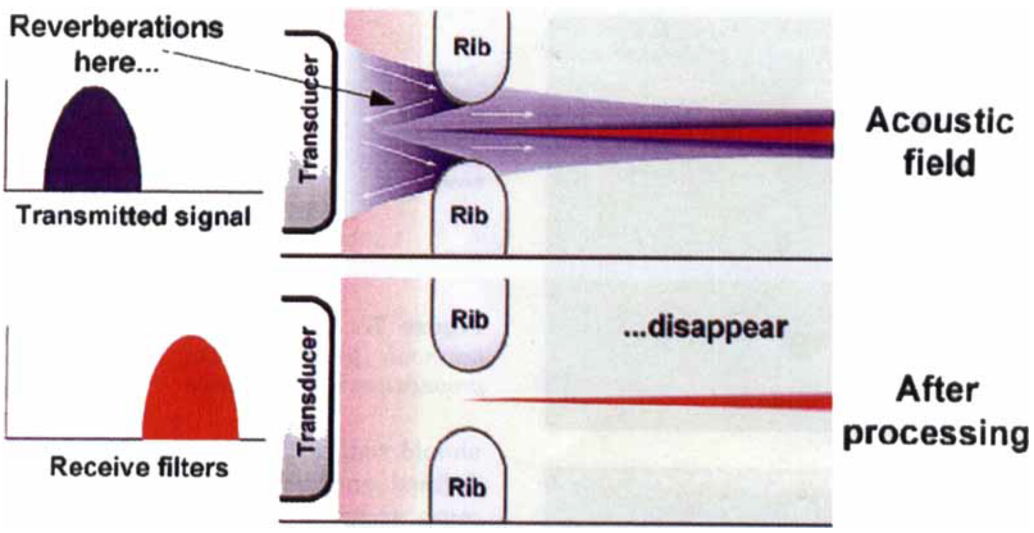


**Figure 8.** *Soundfield in conventional echocardiography (top) and tissue harmonic imaging (bottom). Reverberation artifacts within the nearfield (e.g., ribs) appear as clutter artifacts in deeper areas. These artifacts contain only fundamental frequencies (blue). The harmonic components of the soundfield must be a certain distance from the transducer to develop (red). If only harmonic components are processed, no reverberation artifacts are displayed.*

"generate" harmonics, shifting energy from the fundamental to the harmonic bands.

In technically difficult patients, there often is a diffuse haze caused by distortion of the transmitted beam by shallow surface layers or reverberations between the skin surface and ribs. Because the transmitted beam has not yet had a chance to build up significant harmonic energy, these distortions and reverberations are nearly entirely made up of ultrasound energy at the fundamental frequency. After the beam penetrates these shallow layers, it becomes more focused and begins to create the harmonic energy. However, once it has penetrated these layers, it is less affected by the more uniform tissue below these aberrating layers, and the harmonic beam retains its beam profile and focusing characteristics. When the returned signal is filtered at the harmonic, rejecting the fundamental, the clutter and haze are removed, leaving a much sharper image (Fig. 8). Another proposed reason for the diminished artifact and clutter with harmonic imaging is the reduction in the side lobe level in the second harmonic beam. It has been shown that harmonic imaging reduces side lobe level and main lobe width, leading to improved focusing characteristics.[10,12] Although these effects are well established, it remains under investigation whether they are the primary cause of the effects that have been described in this study.

Nonlinear effects in sound beam propagation are increased at higher ultrasound amplitudes. In this preliminary study, we did not systematically study the effects of transmitted amplitude on harmonic imaging; however, the best results were obtained at high power levels, suggesting that the nonlinear effects of sound propagation are increased at higher emission power levels.

### *Limitations of the Study*

The sequence of recordings in our study was not random because harmonic mode always followed the fundamental recordings. Therefore, some bias cannot be excluded because the investigator always knew which imaging technique was active. In addition, in both imaging modes, the gain settings were not standardized. They were subjectively optimized by the examiner to obtain the best definition of endocardial borders. Also, the observers visually assessed the endocardial border definition score; this also is very subjective.

### *Conclusions*

In conclusion, our preliminary study demonstrates the superiority of tissue harmonic imaging over fundamental B-scan imaging in the delineation of left ventricular endocardial borders in patients with suboptimal echocardiograms. Harmonic imaging resulted in enhancement and superior definition of endocardial borders and a decrease in noise and clutter artifacts.

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