Measurements of the Cyclic Variation of Myocardial Backscatter From Two-Dimensional Echocardiographic Images as an Approach for Characterizing Diabetic Cardiomyopathy

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In this technical brief, we discuss the implementation of an echocardiography-based tissue characterization technique on a commercially available imaging system that can be used to assess the intrinsic properties of the heart in a clinical setting. This approach may be useful for characterizing alterations of myocardial properties in patients with a variety of pathologic conditions, including type 2 diabetes.

Studies have demonstrated the intimate relationship between measured ultrasonic parameters (attenuation, backscatter, speed of sound) and the inherent properties of myocardial tissue. Both the nature of the intrinsic material properties (e.g., the types and concentrations of proteins present that result in specific intracellular and extracellular viscoelastic properties) as well as the geometric properties (structural morphology) of the myocardium combine to produce the observed ultrasonic parameters. For example, several studies have been published illustrating the relationship between the measured ultrasonic attenuation and backscatter properties and collagen content in myocardial tissue. Results demonstrate that an increase in both the measured ultrasonic attenuation and backscatter correlate well with increased collagen concentration determined biochemically or histologically.

Background

One of the most successful approaches to ultrasonic tissue characterization has been the measurement of the systematic variation of backscattered ultrasonic energy from the myocardium over the heart cycle (i.e., the cyclic variation of myocardial backscatter). Measurements of the cyclic variation were first reported by our laboratory in 1983 and have been successfully applied to characterize a growing number of cardiac pathologies, including diabetes mellitus. To date, there have been more than 200 cyclic variation studies reported in the published literature. The relative success of cyclic variation-based methods is due, in part, to the self-reference nature of these measurements. That is, the quantification of the cyclic variation of backscatter from the myocardium over the heart cycle does not require the acquisition or estimation of separate reference backscatter measurements as would be required for “absolute” measurements of myocardial tissue properties. This self-reference approach enables cyclic variation to be a very robust approach for characterizing myocardial tissue and relatively easy to implement clinically.

A majority of previously published cyclic variation studies have utilized an integrated backscatter imaging mode to estimate the level of backscattered ultrasonic energy from the myocardium. However, with the relatively large frequency bandwidths commonly utilized by current echocardiographic imaging systems, reliable measurements can be obtained from analyses of conventional grayscale echocardiographic images when the imaging system is configured in an appropriate manner. The objective of this technical brief is to describe how to acquire and analyze cyclic variation data using a commercially available echocardiographic imaging system with a special emphasis on acquiring and analyzing data from diabetic patients.

Methods

Echocardiographic Imaging System Configuration and Grayscale Image Calibration. The initial step in obtaining measurements of the cyclic variation of myocardial backscatter is to configure the echocardiographic imaging system to provide grayscale images that can be subsequently analyzed to provide quantitative estimates of the level of backscattered energy. This can be accomplished by configuring the post-processing controls on the imaging system to provide a (nearly) linear relationship between the measured backscattered ultrasound intensity (expressed in decibels) and grayscale value (i.e., a linear compression curve). The relationship between changes in measured grayscale values and changes in backscatter values expressed in decibels can be determined using the following grayscale image calibration procedure. A series of images of a tissue-mimicking phantom (or a sponge immersed in water) are obtained as the (overall) receiver gain is changed in known decibel increments (e.g., 2 dB) over the entire available gain range for a specific post-processing and dynamic range setting. Subsequent analyses of these images using available image...
analysis software packages (e.g., NIH ImageJ, National Institutes of Health, Bethesda, MD) provides the relationship between the change in mean grayscale level for a region of interest placed in the phantom image and the known change in backscatter signal strength (i.e., the change in overall gain setting) expressed in decibels. Furthermore, this permits the identification and characterization of the useful dynamic range (the linear backscatter to grayscale range) of the imaging system for a specific configuration. Figure 1 illustrates the relationship between backscatter level and mean grayscale value for one specific configuration of a commercially available imaging system. The conversion factor relating a change in grayscale value to the equivalent change in decibels is found by determining the slope of the best-fit line in the “linear range” region.

**Echocardiographic Image Acquisition.**

With the echocardiographic imaging system configured in a manner to provide a linear relationship between the measured backscattered ultrasound intensity and grayscale value, images of the standard echocardiographic views\(^22\) of a subject can be obtained. The overall receive gain and time gain compensation controls should be adjusted to provide relatively strong backscatter (unsaturated, midlevel grayscale values) from the mid-myocardial regions. Digital cine loops of approximately four or five heart cycles with a frame rate of at least 30 frames/sec should be acquired and saved in a standard 8-bit image format (e.g., DICOM format). Because it is difficult to know the mean grayscale level of the mid-myocardium before subsequent analyses, it is often useful to acquire several sets of image data with different values of overall system gain. Although the cyclic variation has been characterized for several myocardial regions in all of the standard echocardiographic views,\(^23,24\) the parasternal long-axis view is often used. This view provides images with the insonifying ultrasonic field perpendicular to the predominant myocardial fiber orientation and, hence, reduces the confounding effects of tissue anisotropy on measurements.

**Generation of Cyclic Variation Data.**

To illustrate the generation and analyses of cyclic variation data from a patient, we highlight measurements obtained from a white 37-year-old man with type 2 diabetes mellitus. Figure 2 shows the placement...
of a region of interest in the posterior wall of the parasternal long-axis view for one of the image frames acquired using a GE Vivid 7 imaging system (General Electric Medical Systems, Waukesha, WI) and analyzed using NIH ImageJ software. Cyclic variation data were generated by placing a region of interest in the mid-myocardium and adjusting its position in every image frame over the heart cycle such that approximately the same myocardial region was analyzed in each frame. A data curve representing the mean grayscale value within the region of interest as a function of frame number (time) was produced and the changes in mean grayscale values over the heart cycle were converted to changes in decibel values using the calibration measurements described above. Figure 3 illustrates the measured cyclic variation data over four heart cycles. These data are presented as a zero-mean curve.

Characterization of the Cyclic Variation of Backscatter. We advocate characterizing the measured cyclic variation data in terms of its magnitude and normalized time delay. We define the magnitude of cyclic variation as the difference in backscatter between the average peak and average nadir values. The corresponding normalized time delay of cyclic variation is expressed in terms of a dimensionless ratio, obtained by dividing the time interval from end-diastole to the nadir of the mean backscatter trace by the systolic interval. The systolic and diastolic intervals are identified from analyses of the echocardiographic images. Figure 4 illustrates the characterization of cyclic variation data in terms of its magnitude and normalized time delay. In practice, an automated algorithm is often employed to determine the magnitude and time delay values.

Summary

This approach for obtaining and characterizing cyclic variation measurements based on analyses of grayscale echocardiographic images may represent a valuable tool for assessing the state of the myocardium in diabetic patients. Several published studies have demonstrated a significant decrease in the measured magnitude of cyclic variation for type 1 diabetic patients when compared with control subjects. Inclusion of the delay parameter further enhances the discriminating power of cyclic variation measurements. These published studies demonstrate altered cyclic variation characteristics in asymptomatic type 1 diabetic patients without overt coronary heart disease or systolic dysfunction and, hence, suggest that cyclic variation measurements may represent a useful approach for obtaining an early marker of a diabetic cardiomyopathy.

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REFERENCES


Figure 3. Measured cyclic variation data over four heart cycles. These data are presented as a zero-mean curve.

Figure 4. Characterization of the measured cyclic variation data in terms of its magnitude and normalized time delay.