# Real-Time Three-Dimensional Echocardiography as a Novel Approach to Quantify Left Ventricular Dyssynchrony: A Comparison Study with Phase Analysis of Gated Myocardial Perfusion Single Photon Emission Computed Tomography

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*Background:* Different imaging modalities have been explored for assessment of left ventricular (LV) dyssynchrony. Gated myocardial perfusion single photon emission computed tomography (GMPS) with phase analysis is a reliable technique to quantify LV dyssynchrony and predict response to cardiac resynchronization therapy.

*Objective:* Real-time 3-dimensional echocardiography (RT3DE) is a novel imaging technique that provides a LV systolic dyssynchrony index, based on regional volumetric changes as a function of time and calculated as the SD of time to minimum systolic volume of 16 standard myocardial segments expressed in percentage of cardiac cycle. The aim of this study was to compare LV dyssynchrony evaluated with GMPS with LV dyssynchrony assessed with RT3DE.

*Methods:* The study population consisted of 40 patients with heart failure who underwent both GMPS and RT3DE.

*Results:* Good correlations between LV dyssynchrony assessed with RT3DE and GMPS were demonstrated ($r = 0.76$ for histogram bandwidth, $r = 0.80$ for phase SD, $P < .0001$). Patients with substantial LV dyssynchrony on GMPS (defined as ≥135 degrees for histogram bandwidth and ≥43 degrees for phase SD) had significantly higher LV systolic dyssynchrony index than patients without substantial LV dyssynchrony.

*Conclusions:* The good correlations between LV dyssynchrony assessed with GMPS and with RT3DE provide further support for the use of RT3DE for reliable assessment of LV dyssynchrony.

*Keywords:* Three-dimensional echocardiography, Left ventricular dyssynchrony, Heart failure, Left ventricular function, SPECT

Patients with heart failure, depressed left ventricular (LV) function, and wide QRS complex may benefit from cardiac resynchronization therapy (CRT). Previous studies have shown that the presence of LV dyssynchrony is important for the response to CRT.[1] Different imaging modalities have been explored for assessment of LV dyssynchrony, including echocardiography,[2,3] magnetic resonance imaging (MRI),[4] and gated myocardial perfusion single photon emission computed tomography (GMPS) with phase analysis.[5,6] A 3-dimensional (3D) technique may be preferred because these techniques provide information on LV dyssynchrony in the entire LV. In addition, reliable information on LV ejection fraction (LVEF) can simul-

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Disclosure: J. J. Bax has research grants from GE Healthcare and BMS Medical Imaging. E. V. Garcia receives royalties from the sale of the Emory Cardiac Toolbox. The terms of this arrangement have been reviewed and approved by Emory University in accordance with its conflict-of-interest practice. G. B. Bleeker is financially supported by The Netherlands Heart Foundation, grant No. 2002B109. N. Ajmone Marsan is financially supported by the Research Fellowship of the European Society of Cardiology.

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0894-7317/$34.00



doi:10.1016/j.echo.2007.12.006

taneously be obtained. Recently, a novel echocardiographic technique has emerged for the assessment of LV dyssynchrony: real-time 3D echocardiography (RT3DE).[7] This technique allows accurate quantification of LV volumes and LVEF[8-10] and functional assessment of 16 LV segments. In addition, a LV systolic dyssynchrony index (SDI), based on analysis of regional volumetric changes, can be derived from RT3DE to quantify the severity of LV dyssynchrony.[7]

Initial results with RT3DE for assessment of LV dyssynchrony are promising but further validation is needed. In the current study, assessment of LV dyssynchrony by RT3DE was compared with GMPS using phase analysis. Phase analysis is a count-based method that extracts the phase from the regional LV count changes during the cardiac cycle. Phase information is related to the onset of mechanical contraction in the 3D myocardial wall and, therefore, provides information on the synchrony of the contraction of the LV.[11-13] This approach provides important information on the presence of LV dyssynchrony in patients with heart failure and can predict response to CRT.[5,6]

The aim of the current study was to investigate how LV dyssynchrony as evaluated with phase analysis with GMPS relates with LV dyssynchrony as assessed with RT3DE. Assessment of LVEF with both techniques was also compared.

## METHODS

### Patients and Study Protocol

The study population consisted of 40 consecutive patients with drug-refractory heart failure, who were referred to our heart failure outpatient clinic for evaluation of therapeutic options (eg, medical therapy, surgery, CRT).

In all patients, GMPS was performed to exclude inducible ischemia or viability, and to refer patients to revascularization if indicated.[14,15] In addition, phase analysis was used to evaluate the presence of LV dyssynchrony. All patients also underwent RT3DE for assessment of LV volumes and function, and LV dyssynchrony. Thereafter, LV dyssynchrony measured with RT3DE was compared with LV dyssynchrony measured with phase analysis.

Patients' clinical status was evaluated by assessment of New York Heart Association (NYHA) functional class, exercise capacity (using the 6-minute walk test), and quality-of-life score (using the Minnesota quality-of-life questionnaire).

### GMPS

Resting GMPS with technetium-99m tetrofosmin (500 MBq, injected at rest) was performed using a triple-head single photon emission computed tomography camera system (GCA 9300/HG, Toshiba Corp, Tokyo, Japan) equipped with low-energy high-resolution collimators. A 20% window around the 140-keV energy peak of technetium-99m tetrofosmin was used. A total of 90 projections (step and shoot mode, 35 s/projection, imaging time 23 minutes) was obtained over a 360-degree circular orbit. GMPS acquisition involved 16 frames per cardiac cycle with an average temporal resolution of 45 milliseconds. Data were stored in a 64- × -64 matrix. Data were reconstructed by filtered back projection and then reoriented to yield gated short-axis images. The reconstruction was performed over 360 degrees and took generally 3 to 5 minutes. LVEF was assessed from the gated short-axis images using previously validated and commercially available automated software (quantitative gated single photon emission computed tomography, QGS, Cedars-Sinai Medical Center, Los Angeles, CA).[16]

All studies were then submitted to the Emory Cardiac Toolbox for phase analysis.[11] A phase distribution was extracted from a GMPS study, representing the regional onset of mechanical contraction of the LV. It can be displayed in a polar map or in 3D and used to generate a phase histogram.

Two quantitative indices have been recently validated to assess LV dyssynchrony with phase analysis and to predict response to CRT[5,6]: (1) histogram bandwidth, which includes 95% of the elements of the phase distribution; and (2) phase SD, which is the SD of the phase distribution. In a normal heart LV contraction is homogeneous and phase distribution is nearly uniform with a highly peaked distribution. As the LV mechanical synchrony worsens, histogram bandwidth and phase SD are expected to increase. Based on previous work,[6] we applied a cut-off value of 135 degrees for histogram bandwidth and of 43 degrees for phase SD to define substantial LV dyssynchrony.

### RT3DE

***Acquisition of the 3D data set.*** Patients were imaged in left lateral decubitus position with a commercially available system (iE33, Philips Medical Systems, Bothell, WA) equipped with X3, fully sampled matrix transducer. Apical full-volume data sets were obtained in all patients. The acquisition of all images could be completed in approximately 5 minutes in all patients.

For the evaluation of LV volumes and LVEF, the lowest scan line density was used and gain and compression were adjusted to obtain a good image quality and a clear endocardial border. With dedicated software (Large Volume Size, Vision 2007, Philips Medical Systems) 4 small real-time subvolumes were acquired from alternate cardiac cycles and combined to provide a larger pyramidal volume (up to 103 × 103 degrees) and to ensure a complete capture of the LV. The acquisition was performed during end-expiratory phase of one breath hold and with a relatively stable heart rate to minimize translation artefacts among the 4 subvolumes.

For the evaluation of LV dyssynchrony the frame rate was optimized by reducing the depth and by the acquisition of a full-volume data set of 7 subvolumes with an average temporal resolution of 30 milliseconds.

***Assessment of LV volumes and LVEF.*** RT3DE data sets were stored digitally and quantitative analysis of the 3D data was performed offline using a semiautomated contour tracing algorithm (Q-Lab, Version 5.0, Philips Medical Systems) over a complete heart cycle. The echocardiographic examination and the offline analysis were performed by the same experienced echocardiographer, blinded to the GMPS and clinical data.

After first identifying the apex and mitral annulus on end-diastolic and end-systolic slices, a preconfigured ellipse was fitted to the endocardial border for each frame. The endocardial border definition was optimal in most of patients and, in case of a suboptimal automated contour tracing, manual adjustments were performed (in 12 of 40 patients). A 3D model of the LV was then generated and LV volumes and LVEF fraction were provided (Figure 1). Papillary muscles were included in the LV cavity. The postprocessing of the images required between 2 and 5 minutes.

***Assessment of LV dyssynchrony.*** The LV 3D model was subdivided in 16 pyramidal subvolumes based around a nonfixed central