Ventricular Dyssynchrony at Echo: Detection by Two-Dimensional Tracking and Tissue Doppler Imaging in Candidates to Biventricular Pacing

C Valzania[1], M Bertini[1], S Pedri[2], G Domenichini[1], J Frisoni[1], M Ziacchi[1], M Biffi[1], C Martignani[1], I Diemberger[1], I Corazza[1], G Pedrizzetti[3], G Boriani[1]

[1]Cardiovascular Department, University of Bologna, Bologna, Italy
[2]Product Planning Dept, Esaote Spa, Firenze, Italy
[3]Dept of Civil and Environmental Engineering (DICA), University of Trieste, Trieste, Italy

Abstract

Left ventricular (LV) dyssynchrony is a predictor of response to biventricular (BiV) pacing in patients with heart failure (HF) and LV dysfunction. In this study we compared a novel two-dimensional speckle tracking technique to standard Tissue Doppler Imaging (TDI) with regard to LV dyssynchrony assessment in 10 HF patients candidated to BiV pacing. Substantial correlation was found between the two techniques in measuring LV dyssynchrony (r=0.69; p<0,05). Two-dimensional speckle tracking was able to detect variations in LV dyssynchrony induced by simultaneous BiV pacing. This pilot evaluation suggests that two-dimensional speckle tracking may be a valuable alternative to standard TDI to assess LV dyssynchrony before implant and during follow up in candidates to BiV pacing.

1. Introduction

Biventricular (BiV) pacing is a firmly established additive treatment for patients with severe drug-refractory heart failure (HF) and ventricular dyssynchrony [1]. It is based on left ventricular (LV) stimulation (by a pacemaker or defibrillator), usually performed in synchrony with right ventricular stimulation. LV pacing is obtained by positioning a lead into the coronary sinus, preferably in a postero-lateral vein [1]. Improvement in clinical end-points (symptoms, exercise capacity, quality of life) and echocardiographic end-points (left ventricular size, systolic function, mitral regurgitation) has been reported by large, randomized trials on BiV pacing [1]. Furthermore, BiV pacing has been shown to reduce hospitalizations for HF and mortality [1]. However, to date 20% to 30% of patients do not respond to BiV pacing, and the reasons are still unknown.

LV dyssynchrony has been identified as an important predictor of response to BiV pacing in patients with HF and dilated cardiomyopathy [2]. Therefore, there is now an increasing need for diagnostic modalities able to quantify LV dyssynchrony, in order to improve the selection of candidates to BiV pacing. Tissue Doppler Imaging (TDI) is the most commonly used technique, but it is angle dependent due to the use of Doppler effect [2].

A novel two-dimensional (2D) speckle tracking algorithm in an operator driven automatic approach (XStrain™, Esaote, Italy) has been recently developed and implemented on commercially available ultrasound systems. In this approach, the LV endocardial border is tracked over time, and segmental velocities are displayed as vectors, without any angle dependence, thus allowing a quantification of myocardial synchronicity.

Aim of the study was to compare this tissue tracking technique to standard pulsed TDI with regard to LV dyssynchrony assessment in candidates to BiV pacing. Furthermore, we evaluated the impact of simultaneous BiV pacing on LV dyssynchrony, as assessed by tissue tracking.

2. Methods

2.1. Image analysis: tracking method

XStrain™ relies on a novel patented [3] speckle tracking imaging method which can be used to assess regional and global LV function. With XStrain™, the borders are not "detected", they are rather "tracked", i.e. followed in time, starting from one reliable instantaneous trace manually drawn by the operator over one frame. Similar methods have been used in several different formulations in many research fields. These methods fall in the general category known as *Optical Flow* in advanced image analysis [4,5], and they are commonly referred to as *Speckle Tracking* in echographic imaging [6,7].

As shown in figure 1.1, the LV endocardial border points are manually traced from one side to the other of the mitral annulus. Such border can be defined as a

sequence of N points, identified by their coordinate pairs (xi,yi) with i=1…N. The border tracking proceeds by tracking first a few reference points, depending on the physiological geometry to be followed. The general topology of the border is reproduced on all the images by tracking the motion of these representative points. These are commonly the starting and final points of the border when this is an open one. Typically, in projections like that of figure 1.1, representing a long axis view of the heart, the two reference points are placed at the mitral annulus, as shown in figure 1.2. According to heart physiology, the motion of these points is tracked in the direction orthogonal to the mitral plane, that is defined by the conjunction of these points.

The tracking along a specified direction is performed by using the method of transmural cuts. A line crossing the wall, passing through the point, is drawn; in the case shown in figure 1.2, the appropriate direction is orthogonal to the mitral plane. The pixels taken along the transmural line are placed in columns so that each column corresponds to one frame of the sequence of images. In this way, the evolution along a transmural cut can be represented for all instants at once in a 2D representation, where one axis is the distance along the line, and the other axis is the time. An example of such a representation is shown in figure 1.3. To improve the reproducibility, in the event of poor images with a low signal-to-noise ratio, the space-time representation is built using a line for the transmural cut with a thickness larger than that of a single pixel, and extracting the average value across such thickness.

The border tracking is thus performed along the space-time image, starting from a known position at one instant. With reference to figure 1.3, let us call x the horizontal direction and y the vertical direction. Let the columns be annotated xi, i=1…M, where M is the number of columns in the image, i.e. the number of frames in the clip. The tracking is given by determination of a discrete sequence of real numbers yi=y(xi), starting from a known point yk corresponding to the columns xk.

This is a one dimensional tracking problem: the displacement from the known point yk to the point yk+1 is estimated by evaluating the cross-correlation between the entire column at xk with the entire column at xk+1. The cross-correlation function will present a maximum, whose position gives the value of the vertical displacement required to maximize the similarity between the two columns, therefore yk+1 is estimated by adding such a displacement to yk. This procedure is repeated between all pairs of nearby columns and the result is an estimate of the entire border yi , i=1…M.

The cross-correlation is computed using a FFT: a windowing technique (to force a circular periodicity along the space direction) is employed to avoid side effects given by the two ends of the finite size columns. The first estimate yi is further refined iteratively. For this purpose, a subset of the image is extracted by taking a few points above and below the previous estimate yi, and a new image, whose center corresponds to the sequence yi, is generated and used for the correction tracking. This refinement is repeated until no correction is found. To further improve the result, a final snake procedure [8] is performed to follow, in the space-time image, the image brightness level that passes through the fixed point yk. The result of this preliminary tracking procedure is the position, at all instants, of the reference points along the predefined direction.

After tracking the reference points, all the other points of the original border are rescaled in order to get, at each instant, a topologically equivalent border geometry. In the example of figure 1.1, all the points are translated in the direction normal to the mitral plane of a quantity that varies linearly from the apex (assumed to have zero displacement), to the mitral plane. This preliminary rescaling procedure permits to keep the reference points always at the proper position in all the frames, and to rearrange the other points so that the reference maintains the same meaning in all the frames. This step is not performed when no reference point has to be tracked a priori, like in short axis view.

The tracking of each point is then performed with a 2D technique. A square window of 16 pixels on each side of the current position of the point is extracted from all B-mode frames, then the frame by frame displacement (Δxk, Δyk) in the horizontal and vertical directions that minimizes the total brightness pattern convention error

$$\sum_{all-pixels}\left(B_{k+1}-B_{k-1}+\Delta x_k\frac{\partial B_k}{\partial x}+\Delta y_k\frac{\partial B_k}{\partial y}\right)^2$$

is computed by the least squares method, that represents a 2x2 linear system that is solved analytically. This is performed in two steps with predictor-corrector strategy or corrector strategy to improve results reliability.

The tracking stategy is then completed by performing, for each point independently, a sequence of one-dimensional tracking along specified directions using again the method of transmural cuts. A line crossing the wall, passing through the point, and directed normally to the current border is drawn. This operation is made for each instant/frame, because the points are not fixed in time, but they have been displaced at each instant accordingly to the previous tracking steps. As shown in figure 1.4, the appropriate direction is taken at each instant as orthogonal to the rescaled border where the maximum brightness contrast is also found. The pixels taken along each transmural line are placed in columns, each column corresponding to one frame of the sequence of images.

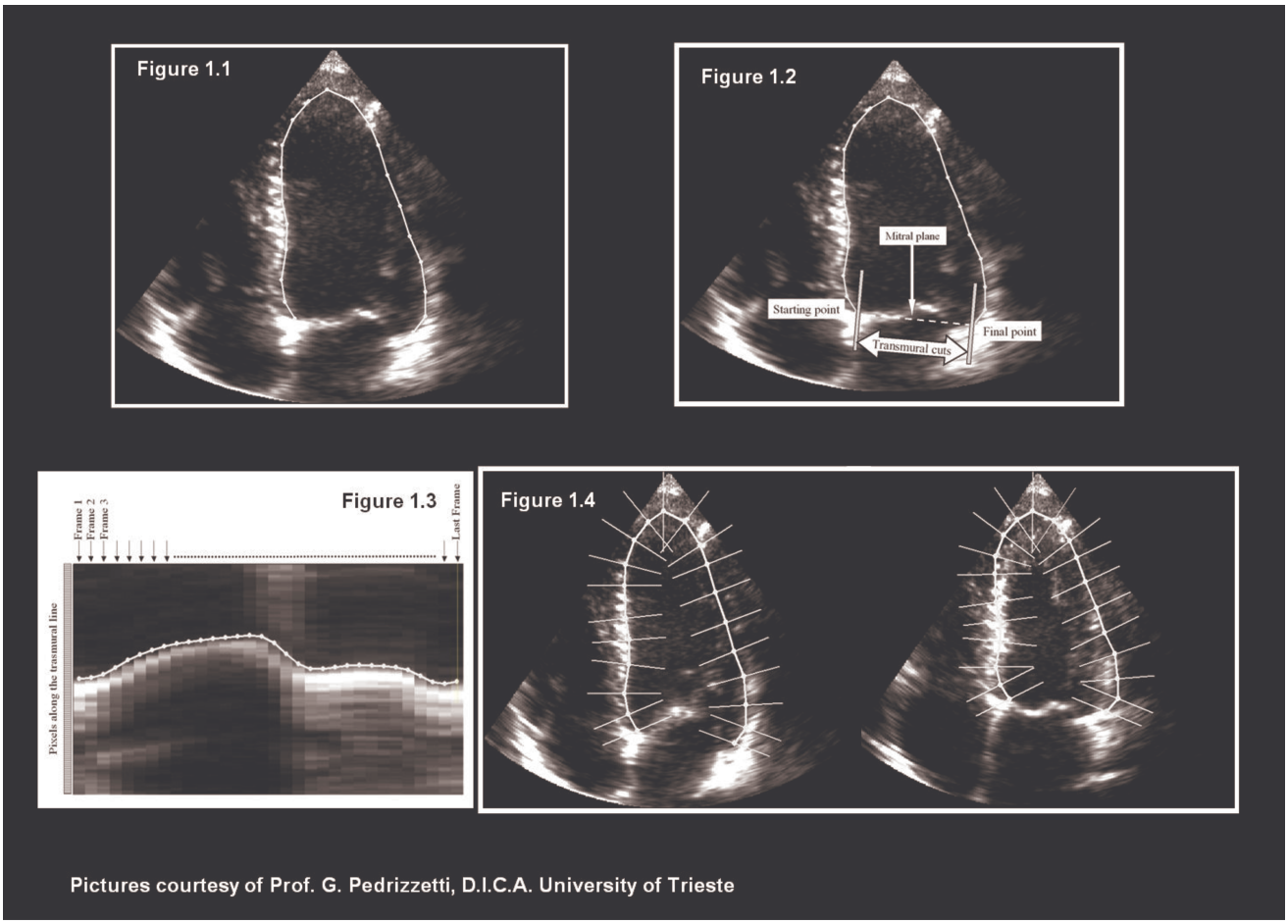

Fig. 1.1: Echographic image of the left ventricle, in a long axis view, with traced endocardial border.
Fig. 1.2: Echographic image with highlighted the position of the transmural cuts, passing from the edge points and normal to the transmitral plane.
Fig. 1.3: Space-time representation (space is along a transmural cut of the echographic images, and time evolution is represented for each frame.
Fig. 1.4: Echographic image of the left ventricle in diastole (left) and systole (right), showing the instantaneous transmural cuts on each of the points.

In this way the evolution along a transmural cut can be represented for all instants at once in a 2D space-time representation analogous to that shown in figure 1.3. The border tracking is then performed along the space-time image using the same technique described above. The same one-dimensional tracking is finally performed along the orthogonal direction to span again a 2D space. At this stage, all the original points have been tracked in time, and we have a new border tracked over all frames.
In all tracking steps, a spatial coherence in the tracked border is ensured by applying a 3-points median filter and a 3-points Gaussian filter for the displacement computed at neighboring points. The entire process makes use of the time periodicity to ensure a cyclic result and avoid the drift effects. The border velocity is then computed by a 5-points time differentiation of the positions found.

2.2. Image analysis: quantification

Once the border is tracked, one-dimensional strain and strain rate are evaluated along the border. Following the approach introduced in TDI [9], the strain is defined as the instantaneous local border lengthening or shortening St(t)=(L(t)-L0)/L0 with respect to one arbitrary instant t0, when L(t0)=L0, commonly taken at the end of diastole (ECG R-wave). The percent value of strain is 100xSt. Strain rate is defined as the rate of lengthening/shortening: $SR(t)=L^{-1}(t)\ dL/dt$. The mathematical relationship between St (t) and SR (t) is:

$$SR(t) = (St+1)^{-1}\frac{dSt}{dt}, \quad St(t) = \exp\int_0^t SR(t')dt' - 1. \tag{1}$$

In the present application the strain rate is computed from the velocity by the general formula:

$$\frac{1}{L(t)}\frac{dL}{dt} = \frac{dV_s}{ds} + \frac{V_n}{R}; \tag{2}$$

where the subscripts s and n indicate the velocity vector components along and normal to the border, respectively;

R is the local radius of curvature. This formula is an exact expression for a generic plane curve subjected to a 2D velocity. The strain is then computed by integration from the strain rate as by the definition (1). It's worthy to underline that these estimations take into account the knowledge of 2D velocity vector and tissue curvature. For this reason, this technique allows the analysis of regions of the heart (apex and short-axis projections) that cannot be properly processed with the TDI method.
LV volume is computed by the modified Simpson method (single plane) using 64 equi-spaced disks from the mitral plane to the apex. Velocities, strain, and strain rate are computed over the standard cardiac segmentation [10]. Segmental values are obtained by averaging the values on all the interpolated points that fall into the specified segment. Segmental velocities are employed to compute the time to peak (i.e. the time between the R-wave and peak systolic velocity), which is frequently used in clinical practice to assess LV synchronicity [2].

2.3. Patient selection and study protocol

Ten HF patients (7 men, 67±6 yrs; ejection fraction 26±3%), consecutively referred for BiV pacing to our Cardiology Department, were recruited for this study. For each patient, LV dyssynchrony was assessed by 2D speckle tracking (XStrain™, McLab 30 CV, Esaote) and pulsed TDI (Sonos 5500, Philips) before implantation of a device for BiV pacing. After implant, LV dyssynchrony was evaluated by speckle tracking during simultaneous BiV stimulation. Both echocardiographic methods were applied by placing a sample volume in the basal portions of the septum and LV lateral wall. At each point, the time from the QRS onset to the peak systolic velocity was measured, and the septal-to-lateral delay in peak systolic velocities was calculated as a marker of LV dyssynchrony. Data were expressed as mean ± standard deviation. Comparisons were performed using Student´s *t* test, and relations between variables were assessed using Pearson correlation coefficient. The study protocol was approved by the local Ethics Committee and all patients provided written informed consent for participation.

3. Results

Baseline septal-to-lateral wall delay was 54±36 ms and 63±35 ms, according to tissue tracking and TDI, respectively (p=0.31). A substantial correlation was found between septal-to-lateral wall delay measured by the two techniques (r=0.69; p<0.05). Simultaneous BiV pacing resulted in a significant reduction in LV dyssynchrony as measured by tissue tracking (from 54±36 to 14±7 ms, p=0.01).

4. Discussion and conclusions

In this study we analyzed LV dyssynchrony in candidates to BiV pacing by using a novel speckle-tracking imaging method, based on a quantification of the changes in pixel brightness from one frame to another. Of note, with this technique the segmental velocity is displayed as vector, therefore not presenting any angle dependence, differently from TDI.

Substantial correlation was found between 2D speckle tracking and standard TDI in LV dyssynchrony assessment. Furthermore, tissue tracking was able to detect variations in LV dyssynchrony induced by BiV pacing, thus suggesting the potential of this technique in monitoring the effects of BiV pacing during follow up.

Further studies on wider study populations are required to expand the results of this pilot evaluation, and to investigate the clinical applications of 2D tissue tracking in the management of patients treated with BiV pacing.

References

[1] McAlister FA, Ezekowitz J, Hooton N, et al. Cardiac resynchronization therapy for patients with left ventricular systolic dysfunction. JAMA 2007;297:2502-14.

[2] Gorcsan J, Abraham T, Agler DA, et al. Echocardiography for cardiac resynchroniation therapy: recommendations for performance and reporting. J Am Soc Echocardiogr 2008;21:191-213.

[3] European Patent No. EP1520517 "Method for estimating tissue velocity vectors and tissue deformation from ultrasonic diagnostic imaging data".

[4] Singh A. Optic Flow Computation: A Unified Perspective. Piscataway, NJ: IEEE Comput. Soc. Press, 1992.

[5] Barron JL, Fleet DJ, Beauchemin S. Performance of optical flow techniques. International Journal of Computer Vision 1994;12:43-77.

[6] Bohs LN, Geiman BJ, Anderson ME, et al. Speckle tracking for multi-dimensional flow estimation. Ultrasonics 2000;38:369-75.

[7] Malpica N, Santos A, Zuluaga MA, et al. Tracking of Regions-of-Interest in myocardial contrast echocardiography. Ultrasound in Med. & Biol. 2004;30:303-9.

[8] Blake A., Yuille A. *Active Vision* MIT press, 1992.

[9] D'hooge J, Heimdal A, Jamal F, et al. Regional Strain and Strain Rate Measurements by Cardiac Ultrasound: Principles, Implementation and Limitations. Eur J Echocardiography 2000;1:154-70.

[10] Lang RM, Bierig M, Devereux RB, et al. Recommendations for Chamber Quantification. J Am Soc Echocardiogr 2005;18:1440-63.

Address for correspondence

Cinzia Valzania
Cardiovascular Department, University of Bologna
Via Massarenti 9; 40138 Bologna,Italy
cinzia.valzania2@studio.unibo.it