Role of Real Time Three Dimensional Echocardiography (RT3DE) to Guide Cardiac Resynchronization Therapy

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The invasive nature of cardiac resynchronization therapy (CRT), its high cost, and high rate of non-responsiveness (Bax et al., 2004), reaching up to 40–50% when reversed LV remodeling is an end point (Auricchio et al. 2002) have made achieving more optimum CRT response in properly selected candidates a crucial issue.

Conventional parameters influencing response to CRT such as QRS duration and EF% are now well established. However, other factors such as presence of LV scar, accurate and individual determination of mechanical dyssynchrony, and choice of optimum position of resynchronization leads (RL), are still unresolved issues.
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1. Patient Selection Before CRT
   - Assessment of LV function & Dyssynchrony
   - Determination of the most delayed segment
   - Assessment of scar tissue

2. Positioning of LV Lead During CRT Implantation
   - Left Lateral Wall vs. The most delayed segment vs Multisite LV pacing

3. Assessment after CRT
   - Assessment of LV function & resynchronization

I- Patient Assessment Before CRT
Real time three dimensional echocardiography (RT3DE) provides a powerful tool for qualitative and quantitative assessments of the LV. *(Kapetanakis et al., 2005)*.

### 1- RT3DE Assessment of LV Function

LV EF%, EDV and ESV are determined offline with the aid of semiautomatic contour tracing software. Using a 17 segment model, time/volume curves are obtained where time to minimal systolic volumes (Tmsv) are calculated in each of the 16 segments (excluding the apex).
2- RT3DE Assessment of LV Dyssynchrony

A systolic dyssynchrony index (SDI) derived from the regional volumes has been validated as a method of quantifying global LV mechanical delay (Kapetanakis et al., 2005) as it allows comparison between patients with different heart rates.

Systolic Dyssynchrony Index (SDI)

The SDI is automatically obtained by the software. It is defined as the standard deviation of tmsv of the 16 segments corrected for R–R duration and displayed as a percentage (tmsv-16 SD %).
Validation of SDI as a method of quantifying global LV mechanical delay

A mean SDI for normal subjects is 3.5±1.8% while it is 5.4±0.8%, 10.0±2%, and 15.6±1% for mild, moderate, and severe systolic dysfunction respectively. Kapetanakis et al., 2010 identified a cutoff of 10.4% to have the highest accuracy for predicting improvement following CRT.

Other dyssynchrony parameters:

The standard deviation (SD), the maximal difference (Diff), and percentage of cardiac cycle of each of Tmsv among 16, 12 and 6 LV segments can also be automatically obtained from the RT3DE dataset.
3- Identification of the most delayed segments:

a- Parametric imaging

Parametric imaging is applied to identify areas of latest mechanical activation and to identify myocardial velocity and excursion at different segments.

3- Identification of the most delayed segments:

b- Time-volume curves

Asynchronous pattern of contractility is found in dilated cardiomyopathy (DCM) where Tmsv of each segment is dispersed remarkably from other segments.
4- Assessment of scar tissue

Patients with prior myocardial infarcts represent about 50% of patients with a poor CRT response (Diaz 2005). Pacing in the scar border zone attenuated adverse ventricular remodeling (Shuros et al. 2007). Patients with better myocardial viability recorded better response with a significant improvement after the first week of CRT (Pugliese et al 2012).

4- Assessment of scar tissue

Using Parametric Imaging Excursion Map

Allows a bull’s eye representation of wall excursion whereby dark areas represent reduced excursion (mostly scar tissue), bright blue areas exhibit the largest systolic radial excursion, while the red areas represent dyskinesia.
5- Dual site vs single site LV pacing

In order to increase the efficacy of this therapy, various techniques of pacing are being investigated. Dual-site pacing of LV has been proposed as an attractive option of resynchronization. Several mechanisms can justify the use of this type of CRT.
Mechanisms justifying the use of dual site LV Pacing:

1- Using the coronary sinus (CS) to stimulate LV wall in more than one point can stimulate a larger area of the LV wall simultaneously providing better resynchronization.

2- Functional lines of block:

Patients with LBBB have a specific “U-shaped” activation sequence turning around the apex and inferior LV wall generated by a functional line of block, anterior in 50% of cases and lateral in 33%, oriented from LV base to apex.

3- More probability to stimulate non scar-tissue in ischemic cardiomyopathy:

4- Delayed activation of anterior wall in conventional biventricular pacing:

In conventional biventricular pacing, contraction of the anterior wall begins after the activation waveform reaches from the lateral pacing site. The conduction time from the lateral pacing site to the anterior wall increases proportionally as the distance between the 2 sites increases.

(Yoshida et al., 2008)
We performed a small prospective study in our cardiology department, the first in Egypt, assessing the safety and long term efficacy of dual site (DS) vs. single site (SS) LV stimulation in traditional CRT candidates having no scar at anterior and lateral LV walls.

Patients:

Out of 13 traditional CRT candidates, 10 HF patients were prospectively included in the study starting from February 2010 till April 2011. All patients fulfilled the following inclusion criteria:

- Advanced HF (NYHA class III or IV).
- Intrinsic sinus rhythm.
- EF \leq 35\% defined by modified Simpson´s method.
- QRS \geq 120\, ms in LBBB pattern.
**Exclusion Criteria:**

- age < 18 years.
- valvular heart disease.
- reduced life expectancy.
- ischemic episode during last 6 months.
- Previously implanted pacemakers.
- Hemodynamic instability requiring inotropic support.
- Presence of scar tissue at the anterior or lateral LV walls documented by dobutamine stress-echocardiography.

**Assessment of synchronicity using 3-D echo before CRT**

![Image of 3-D echo data](image.png)
Implantation Technique:

The right ventricular (RV) apical and right atrial (RA) leads were positioned as usual. Angiography of the CS was performed and target veins were preferably selected as one postero-lateral, and one antero-lateral branch. The 2 LV leads were meant to be implanted with the widest possible separation between the 2 tips.

Device Implantation and Programming:

After implantation of the 2 leads, a Y-Lead adaptor was connected to the LV channel of the pacemaker at one end while the other 2 free ends were connected to the 2 LV leads.
Lead testing

Lead testing was then performed using joined leads and unipolar split cathodal polarity where both lead electrodes serve as cathodes and the pacemaker serves as the common anode (Cooper and Kay, 2008).

Lead testing

Programming the pacing Y-adaptor channel (LV channel) for unipolar stimulation would result in single-site cathodal pacing from the distally placed lead, while programming bipolar stimulation would result in dual-site cathodal-anodal pacing through the 2 LV leads (Padeletti et al., 2008).
Patients were randomly programmed at either SS or DS stimulation mode for 1 month after which echocardiographic and clinical assessment was performed. Then, mode was switched to the alternative program for the next month and the same parameters were re-evaluated.

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2D C-TDI Assessment of Synchronicity

Before CRT

After single site LV pacing

After dual site LV pacing
More optimum cardiac resynchronization therapy in a larger percentage of patients can be achieved using dual-site compared to single-site LV stimulation. Exclusion of scar tissue at possible implantation site of LV leads can also improve CRT response.
II- Guiding LV Lead Positioning During CRT Implantation

Optimal LV lead positioning at the segment of maximal mechanical delay (SMMD) has been proposed to provide the greatest resynchronization and hemodynamic benefit of biventricular pacing (BIVP).  

(Becker et al. 2007).
The single most delayed segment is lateral in about 50% of LBBB patients, and is septal in 12-16 % of cases (Zhang et al., 2011).

Atypical dyssynchronous pattern in which a lateral peak occurs earlier than a septal peak can be observed even in patients with typical LBBB. In these patients, the time difference does not associate with typical mechanical dyssynchrony sequence (Tanaka et al, 2009).

Presently, there has been no clinical study evaluating the role of RT3DE in guiding CRT or its association with cardiac outcomes (Heydari et al., 2012).

We performed a small prospective study in our cardiology department which could be the first study evaluating the role of RT3DE to guide optimum RL position and assess the outcome in CRT patients.
Seventeen HF patients were prospectively included in the study starting from 2008 till 2010. Follow-up ended at June, 2011. All patients fulfilled the following inclusion criteria:
- Advanced HF (NYHA class III or IV) despite optimal medical treatment.
- EF ≤ 35% defined by modified Simpson´s method.
- QRS ≥ 120 ms in LBBB pattern, and SDI ≥ 5 by RT3DE.

**Exclusion Criteria:**
- age < 18 years.
- valvular heart disease.
- reduced life expectancy.
- ischemic episode during last 6 months.
- other pacemaker indication.
- unsuitable echocardiographic window.
Patients were assessed before and after 1, 3, and 6 months of CRT regarding examination of 12-lead surface ECG, clinical evaluation of NYHA functional class score and RT3D echocardiographic evaluation.

**Choice of the resynchronization according to site of SMMD:**

Twelve of the 17 patients had the SMMD at the free LV wall. These patients received conventional BIVP with implantation of the LV lead at the cardiac vein corresponding to the SMMD or nearest possible segment.
Anatomic LV lead position using fluoroscopic orthogonal views guided by RT3DE
BFRVP Implantation Technique:

BFRVP was used in 5 patients who had pre-identified septal SMMD. The atrial lead was connected to the atrial channel of a dual-chamber pacemaker while the 2 ventricular leads were connected to the ventricular channel by a Y-shaped lead adaptor.

Anatomic RV septal lead position using fluoroscopic orthogonal views
Results

RT3DE facilitated positioning of the RL at or nearest to the SMMD in 15 (88%) patients including 10/12 BIVP (4 inferolateral, 5 antrolateral, 1 anterior, while it was technically impossible in 2) and all the 5 BFRVP.

Response to CRT among the study population

Fourteen of 17 patients (82.4%) were initial responders after 1 month of CRT. Twelve patients (70.5%) maintained beneficial CRT response after 6 months compared to 5 non-responders.
Response Rate

- The response rate of the whole study population was 70%.
- The response rate among patients with optimally positioned RL was 80%.
- Notably, 100% of responders had an optimum or near-optimum RL position.

III- Patient Assessment After CRT
A patient with an optimal LV lead position

Parametric imaging and time/volume curve before (right panel), and after (left panel) optimum LV lead positioning of patient No. 5.
A patient with an optimal RV lead position

Parametric imaging and time/volume curve before (right panel), and after (left panel) optimum RV septal positioning of patient No. 7.
SDI Before CRT

SDI After BFRVP

Before CRT

After BFRVP
Until the results of large multicentre studies are available, every effort should be made to implant the RL at the SMMD whenever possible in order to achieve a more optimum CRT response.

RT3DE can be used for individual assessment of LV mechanical dyssynchrony and for optimal RL positioning at the pre-identified SMMD. This can provide more optimum CRT response regardless the method of CRT used.
Thank You