CRT in Heart Failure: New Frontiers

Davos, Feb 2013

D Gras, MD, Nantes, France
CRT in Heart Failure: New Frontiers

- **Background**
- Dual-Site LV Pacing during CRT
- Quadripolar LV Pacing approach
- LV Endocardial Pacing: LVEP
- Vagal Nerve stimulation in HF
CRT-D - Units per million inhabitants

Units / Million Population

<table>
<thead>
<tr>
<th>Year</th>
<th>Austria</th>
<th>Belgium &amp; Lux</th>
<th>Czech Republic</th>
<th>Denmark</th>
<th>Finland</th>
<th>France</th>
<th>Germany</th>
<th>Greece</th>
<th>Ireland</th>
<th>Italy</th>
<th>Netherlands</th>
<th>Norway</th>
<th>Portugal</th>
<th>Spain</th>
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Source population data: OECD
Units - Eucomed based on reports from major manufacturers
* Europe represents total of listed countries (N/A countries excluded)
Left Ventricular Lead Position and Clinical Outcome in the Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy (MADIT-CRT) Trial

Jagmeet P. Singh, MD, DPhil*; Helmut U. Klein, MD*; David T. Huang, MD; Sven Reek, MD; Malte Kuniss, MD; Aurelio Quesada, MD; Alon Barsheshet, MD; David Cannom, MD; Ilan Goldenberg, MD; Scott McNitt, MS; James P. Daubert, MD; Wojciech Zareba, MD; Arthur J. Moss, MD
The Target Study

All Cause Mortality following CRT in the TARGET and Control Groups

Combined Endpoint of Death and Heart Failure Related Hospitalisation between the TARGET and Control Groups

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<th>No. At Risk</th>
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<th>CONTROL</th>
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log rank p=0.30

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<th>No. At Risk</th>
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<th>CONTROL</th>
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log rank p=0.03
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<th>Care HF Implantation</th>
<th>Treatment Group (n=404 attempts)</th>
<th>Control Group (n=65 attempts)</th>
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<tr>
<td>1</td>
<td>349 (86.3)</td>
<td>58 (89.2)</td>
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<tr>
<td>2</td>
<td>36 (8.9)</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>3</td>
<td>5 (1.2)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>390 (96.4)</td>
<td>60 (92.3)</td>
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</table>
LV Lead Events frequency as percentage of total events over 12 months (164/1647 pts)

- Elevated Pacing Thresholds: 15 events reported
- Loss of Capture: 16 events reported
- Phrenic Nerve Stimulation:
  - 91 PNS events reported in total
  - 52 events reported at scheduled visits
  - 39 events reported at unscheduled visits
- Lead Displacement: 61 events reported
CRT in Heart Failure: New Frontiers

- Background
- **Dual-Site LV Pacing during CRT**
- Quadripolar LV Pacing approach
- LV Endocardial Pacing: LVEP
- Vagal Nerve stimulation in HF
A randomized comparison of triple versus dual site ventricular stimulation in patients with congestive heart failure

Christophe Leclercq¹, MD, PhD, Fredrik Gadler², MD, PhD, Wolfgang Kranig³, MD, Sue Ellery⁴, MD, Daniel Gras⁵, MD, Arnaud Lazarus⁶, MD, Jacques Clémenty⁷, MD, Eric Boulogne⁸, MSc, Jean-Claude Daubert¹, MD, for the Triple Resynchronization In Paced Heart Failure Patients (TRIP-HF) study group
Interest of Multisite LV Pacing

Baseline

Postero-lateral LV pacing

Tri-LV pacing

HR 10, P Bordachar
Atrial based, Dual Site LV, RV Pacing

Clinical Trials

Addition of a Second LV Pacing Site in CRT Nonresponders Rationale and Design of the Multicenter Randomized V³ Trial

PIERRE BORDACHAR, MD,¹ CHRISTINE ALONSO, MD,² FREDERIC ANSELME, MD,³ SERGE BOVEDA, MD,⁴ PASCAL DEFAYE, MD,⁵ STEPHANE GARRIGUE, MD,⁶ DANIEL GRAS, MD,⁷ DIDIER KLUG, MD,⁸ OLIVIER PIOT, MD,⁹ NICOLAS SADOUL, MD,¹⁰ AND CHRISTOPHE LECLERCQ, MD¹¹
Atrial based, Dual Site LV, RV Pacing
(ongoing V3 Trial)
Interest of Additional LV Lead during CRT
Non-Traditional CRT: Novel Implant Techniques
Atrial based, Dual Site LV, RV P

• **Goal:**
  - To Improve Ventricular activation & CRT Impact
  - Ongoing V3 Trial

• **Potential Difficulties**
  - Subclavian Vein Occlusion
  - Y Adaptor & Electrical csqces
  - Higher Risks of PNS
  - CS Anatomical Limitations
CRT in Heart Failure: New Frontiers

- Background
- Dual-Site LV Pacing during CRT
- **Quadripolar LV Pacing approach**
- LV Endocardial Pacing: LVEP
- Vagal Nerve stimulation in HF
Single Site vs. MSLV in Healthy Heart
Subselection of Lateral Cardiac Vein during Quadripolar LV Lead Implant
Quadripolar LV Lead in case of LSVC
Non-Traditional CRT: Novel Implant Techniques

Benefits of Quadri vs Bipolar LV Lead

- Management of PN Stimulation
- Pacing Vector offering
  - The Best Hemodynamics
  - The Best Pacing Thresholds
- Lower Need for LV Lead Revision
- Similar Lead Implant procedure
- Simultaneous 4 P Pacing for a better CRT impact to be investigated
CRT in Heart Failure: New Frontiers

- Background
- Dual-Site LV Pacing during CRT
- Quadripolar LV Pacing approach
- **LV Endocardial Pacing: LVEP**
- Vagal Nerve stimulation in HF
Endocardial vs. Epicardial Biventricular Pacing.

Garrigue S., Jais P, et. al. AJC, 2001 88:858–862

Morgan J M , Delgado V Europace 2009;11:v22-v28
Endocardial vs Epicardial CRT provides:

- Better LV Filling and Systolic Performance
- More Homogenous Resynchronization

Van Deursen, Circ Arrhythmia Electrophysiol. 2009;2:580-587

Prinzen et al

Pooled data from 8 LV sites

*=p<0.05 with BL;  †=p<0.05 with EPI-BiV
WISE-CRT: **Wireless Stimulation Endocardially for CRT**

- Works with any PM or ICD
- Simple co-implant
  - Transvenous right side system
  - Wireless left side system

Figure 2. An example of clinically determined acoustic windows in 4 body positions (in red with the patient lying supine; in green with 30° right tilt; in yellow with 30° left tilt; in purple with 30° upright tilt) superimposed on the CT-determined acoustic window (in light blue with the patient lying supine and during end inspiration) on 3D reconstruction CT of the thorax. 3D = three-dimensional; CT = computed tomography.
TEE Evaluation before Transseptal Puncture

Location of Fossa Ovalis

Ongoing Evaluation
LV Endo Pacing in Non CRT Responder

LV Lead placement under TEE guidance

Ongoing Evaluation
LV Lead Position post Implant, No Change in MR
LV Endo Pacing in Non CRT Responder
LV endocardial Pacing during CRT

AP View

LAO View
PNS still happens during LV endo Pacing !!
Echo prior to Transseptal LV Lead implant

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
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<tbody>
<tr>
<td>FE VG (sim.A4C)</td>
<td>19%</td>
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<tr>
<td>Vol. Eject. (simpson A4C)</td>
<td>25 m</td>
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<tr>
<td>2 VGs Long (A4C)</td>
<td>8.5 cm</td>
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<tr>
<td>Vol.VG.tS (sim.4cav)</td>
<td>106 cm</td>
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<tr>
<td>1 VGd Long (4cav)</td>
<td>9.2 cm</td>
</tr>
<tr>
<td>Vol.VG.tD (sim.4cav)</td>
<td>131 cm</td>
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</table>
LV EF Echo Evaluation (Simson)
Permanent LV Endocardial Pacing in Clinical Practice

<table>
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<th>Avantages</th>
<th>Disavantages</th>
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<tr>
<td>Easier access to LV Ventricle</td>
<td>Transeptal Approach</td>
</tr>
<tr>
<td>Better Hemodynamics</td>
<td>Embolic risk</td>
</tr>
<tr>
<td>Faster Depolarization</td>
<td>X Ray exposure</td>
</tr>
<tr>
<td>Faster Vent activation</td>
<td>Anticoagulation</td>
</tr>
<tr>
<td>Low risk of PNS</td>
<td>Mitral Regurgitation</td>
</tr>
<tr>
<td>Better short &amp; long term PT</td>
<td>Lead Extraction ??</td>
</tr>
</tbody>
</table>
CRT in Heart Failure: New Frontiers

• Background
• Dual-Site LV Pacing during CRT
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• LV Endocardial Pacing: LVEP
• Vagal Nerve stimulation in HF
Spinal Cord Stimulation (SCS): SCS generator implant in abdomen or paraspinous region with a lead placed in dorsal epidural space between T1-T4.

Vagal Nerve Stimulation (VNS): VN stimulator placed in right subpectoral region with a lead placed in cervical vagus region.

Baroreflex Stimulation (BRS): Baroreflex stimulation generator placed in right subpectoral region with bilateral stimulation leads tunneled to the carotid baroreceptor region.

Vagal stimulation for the treatment of heart failure: a translational success story

Peter J Schwartz
Heart failure as an autonomic nervous system dysfunction

Takuya Kishi (MD, PhD)
Vagal stimulation therapy achieved a 73% reduction in a relative risk ratio of death.

Adapted from Li M, Circulation 2004; 109: 120 -124
VNS in HF Canine High Rate Pacing Model

Adapted from Zhang Y, Circ Heart Fail 2009; 2:692-699
### VNS in HF Canine High Rate Pacing Model

<table>
<thead>
<tr>
<th></th>
<th>Baseline Control</th>
<th>Baseline VNS</th>
<th>4-wk Pacing Control</th>
<th>4-wk Pacing VNS</th>
<th>8-wk Pacing Control</th>
<th>8-wk Pacing VNS</th>
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<td>RR, ms</td>
<td>510.7±77.0</td>
<td>514.5±61.5</td>
<td>394.8±36.7</td>
<td>428.8±55.7</td>
<td>407.1±47.2</td>
<td>451.0±76.1</td>
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<td>SDNN, ms</td>
<td>84.2±21.7</td>
<td>86.6±21.8</td>
<td>23.2±5.9</td>
<td>36.6±5.1*</td>
<td>28.7±8.0</td>
<td>42.2±7.4*</td>
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<td>RMSSD, ms</td>
<td>68.9±10.6</td>
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<td>31.0±6.1*</td>
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<td>LF, norm</td>
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<td>LF/HF</td>
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<td>2.23±1.46</td>
<td>1.22±0.75</td>
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Adapted from Zhang Y, Circ Heart Fail 2009; 2:692-699
Chronic vagus nerve stimulation: a new and promising therapeutic approach for chronic heart failure

Gaetano M. De Ferrari, Harry J.G.M. Crijns, Martin Borrgrefe, Goran Milasinovic, Jan Smid, Markus Zabel, Antonello Gavazzi, Antonio Sanzo, Robert Dennert, Juergen Kuschyk, Srdjan Raspopovic, Helmut Klein, Karl Swedberg, and Peter J. Schwartz, for the CardioFit Multicenter Trial Investigators
NECTAR-HF Study: Protocol Overview

- **Study Design**
  - Single-blind, placebo controlled, randomized 2:1(therapy/control)
  - Multicentre (European sites)
  - Control patients crossed over to therapy at 6M follow-up & followed for safety through 18 months

- **Sample Size**
  - 250 pts screened for eligibility
  - 96 pts implanted with the system

- **Patient Population:**
  - NYHA class III HF pts
  - Ejection fraction of ≤35%
  - Not CRT candidate, QRS ≤ 130 ms
CRT in Heart Failure: New Frontiers

Summary

• Increasing Consideration for CRT
• Dual-Site LV Pacing during CRT: The V3 Trial
• Quadripolar LV Pacing approach: MPP Study
• LV Endocardial Pacing: The AlSync Study
• Vagal Nerve stimulation in HF: Nectar Trial …