**Mitral Valve Dynamics With Different Pacing Sites**

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**Background:** The influence of pacing site on 3-D annular/leaflet dynamics and mitral valve function is incompletely understood.

**Methods:** Eight adult sheep underwent surgical insertion of radiopaque markers on the LV, mitral annulus and mitral leaflets. Hemodynamic and 3-D marker dynamics were studied one week later with biplane 60Hz videofluoroscopy during atrial (pacing site=left atrium, 115 min^-1) and A-V sequential pacing (140ms interval) with three epicardial ventricular pacing sites: apical RV, RVOT and anterolateral LV wall.

**Results:** Compared with atrial pacing: 1.) LV-AV-pacing delayed valve closure (time from ED to minimum distance between opposing leaflet edge markers) at leaflet center and anterior (ACOM) and posterior commissures (PCOM); 2.) Leaflet angle (angle between leaflet center edge marker and annular plane) at ED was significantly greater with LV-AV-pacing; 3.) Regurgitant fraction (LVEDV – LV volume at leaflet closure) / SV was increased with LV-AV-pacing.

**Conclusions:** AV-sequential pacing with the antero-lateral LV epicardium as pacing site produced more widely open leaflets at ED and delayed mitral valve closure resulting in pacing-induced mitral regurgitation. Such changes in the mitral valvular apparatus have potential clinical implications since the LV has become a popular pacing site with the advent of transcoronary venous leads.

<table>
<thead>
<tr>
<th>Control: atrial pacing</th>
<th>RVsequential-AV-sequential pacing</th>
<th>RVOT-AV-sequential pacing</th>
<th>LV-AV-sequential pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve closure @ ACOM (ms)</td>
<td>27.1 ± 9.4</td>
<td>43.8 ± 8.9</td>
<td>37.6 ± 6.1</td>
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<tr>
<td>Valve closure @ leaflet center (ms)</td>
<td>20.9 ± 10.3</td>
<td>35.5 ± 8.0</td>
<td>35.5 ± 6.6</td>
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<tr>
<td>Valve closure @ PCOM (ms)</td>
<td>16.7 ± 10.0</td>
<td>23.0 ± 3.1</td>
<td>25.1 ± 7.1</td>
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<tr>
<td>Anterior leaflet angle (°) @ ED</td>
<td>31.9 ± 1.8</td>
<td>39.4 ± 2.0</td>
<td>36.6 ± 2.1</td>
</tr>
<tr>
<td>Posterior leaflet angle (°) @ ED</td>
<td>55.5 ± 3.9</td>
<td>61.6 ± 4.1 *</td>
<td>58.8 ± 3.8</td>
</tr>
<tr>
<td>Regurgitant fraction (% SV)</td>
<td>5.5 ± 2.8</td>
<td>7.0 ± 1.7</td>
<td>9.8 ± 2.4</td>
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</tbody>
</table>

*p<0.05 vs. atrial pacing RM ANOVA, Dunnnett’s post hoc test

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**Cardiac Contractility Modulation by Nonexcitatory Electrical Currents for Treating Systolic Heart Failure Early Multicenter Experience**

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**Background:** Cardiac contractility modulation (CCM) by means of non-excitatory currents delivered during action potential plateau, has been shown to acutely enhance systolic function in humans with HF.

**Objective:** To report on our early multicenter experience of chronic safety and functionality of this novel form of electrical therapy.

**Methods:** Thirteen patients with drug-resistant HF (NYHA class III) were consecutively implanted with a device (OPTIMIZER ITM) delivering CCM biphasic square-wave pulses (20µs, 7 to 17V, 300ms after local activation) through two right ventricular leads screwed-in the right aspect of the interventricular septum. CCM signals were delivered 3 hours daily over 8 weeks (3hr phase) and 7 hours daily over the next 16 weeks (7hr phase). Safety and feasibility of this novel therapy were regarded as primary endpoints. Preliminary clinical efficacy was assessed at baseline, and at the end of each phase.

**Results:** At the end of follow-up all patients were alive, without heart transplantation or left ventricular assist device Serial 24-h Holter analysis revealed no major arrhythmias in any patients. No device failed for reason other than end of battery life. During the 3hr phase EF improved from 22.7±7% to 28.7±7% (P=0.01), 6-MWT from 454±103m to 498±112m (P=0.06), LVEF increased with LV-AV-pacing.

**Conclusions:** CCM therapy appears to be safe and feasible. Proarrhythmic effects of pacing-induced protection. By contrast, none of these agents improved functional recovery of the paced hearts.

In conclusion, the optimal shaft length is 14.5 mm for monomorphic fetal pacemaker device deployment at 19-20 weeks. This time of deployment will allow 2-4 weeks for resolution of hydrops prior to achieving viability at 24 weeks. A single device size will support most idiopathic fetuses in the window leading to viability, a larger device being necessary post fetal surgery Support NIH HHS 1R43 HL 67520-01

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**Cardiac Arrhythmias**

**The Monolithic Fetal Pacemaker III: Device Dimensions by Fetal Ultrasonography**

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**Background:** Complete heart block in utero has a high fatality when associated with hydrops fetalis. We have developed a design for closed thorax, closed maternal abdomen over-the-wire placement of a unipolar monolithic pacemaker whose power source and anode reside in amniotic space and whose cathode resides in the left pleural space in direct apposition to the fetal pericardium. Pacing occurs through the pericardium with current passage through the fetal skin.

**Objectives and Methods:** Device prototyping requires measurement of the distance from amniotic space to pleural space along the axis of deployment. 250 Fetal ultrasound studies were reviewed for this measurement as well as for femur length, biparietal diameter, and abdominal circumference to allow estimation of gestational age. This was IRB approved.

**Results:** 80 human fetal studies were adequate for all measurements. Gestational age ranged from 17 to 33 weeks. At 19 weeks the amniotic-to-pleural distance measured 13.9 ± 3.2 mm, at 20 weeks 13.2 ± 2.8 mm and at 21 weeks 15.6 ± 2.2. After this time wide range of dimension precluded identifying an optimal distance.

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**The L-Type Calcium and Sarcolemmal KATP Channels May Contribute to Pacing-Induced Cardioprotection**

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**Background:** Chronic ventricular pacing has been shown to induce post-hypoxic cardioprotection. We hypothesized that L-type Ca++ channel, sarcolemmal (sarcKATP) and mitochondrial KATP (mitoKATP) channels could be involved in this protection.

**Methods:** Hearts of 4-day-old chick embryos were paced in vivo during 12 h using asynchronous and intermittent ventricular stimulation (5 min ON - 10 min OFF) at 110% of the intrinsic rate. Sham operated and paced hearts were then submitted in vitro to normoxia (30min), anoxia (30min) and reoxygenation (60min). L-type Ca++ channel agonist BAY K 8644 (BAY, 1µM) or blocker verapamil (Verap, 10nM), nonspecific KATP channel agonist glibenclamide (Glib, 10µM), mitoKATP channel agonist diazoxide (DIAZO, 100µM) or antagonist 5-hydroxydecanoate (5-HD, 50µM) were used in the sham and paced isolated hearts (n=4). ECG and atrial and ventricular contractions were continuously recorded during experiments. Reoxygenation-induced chronic, drom- and isotropic disturbances, arrhythmias and alterations of electromechanical delay (EMD) in atrium and ventricle were investigated.

Results: Under normoxia, heart rate (170±19 bpm), PR interval (88±21 ms), atrio-ventricular propagation (28±5 ms/0), ventricular shortening velocity (5.7±1 mm/s), atrial EMD (17±2 ms) and ventricular EMD (17±2 ms) (means±SD) were stable and similar in the untreated sham and paced groups. None of the tested agents influenced these baseline parameters, except BAY which increased ventricular EMD by 34% in sham hearts. During reoxygenation, incidence of arrhythmias was lower and ventricular EMD recovered faster in paced hearts than in sham hearts. In sham hearts, BAY (but not Verap) or Glib (but neither 5-HD nor DIAZO) accelerated recovery of ventricular EMD, reproducing the pacing-induced protection. By contrast, none of these agents improved functional recovery of the paced hearts.

Conclusion: Pacing may induce a moderate increase in intracellular Ca++ through subtle activation of L type Ca++ channels and/or inhibition of sarcKATP channels, improving specifically ventricular excitation-contraction coupling during reoxygenation. Supported by the Swiss Cardiology Foundation.