Has the transvenous ICD lead reached its zenith with new technologies such as S-ICD and leadless pacemaker?

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Disclosures:
Consultant, Clinical Trials, Speaking Fees- BSC, Medtronic, St Jude,
MY CONFLICTS OF INTEREST ARE
Consultant, Clinical Trials, Speaking Fees-
BSC, Medtronic, St Jude
Breakthrough Innovation in Medical Devices

Requires alignment of:

- Unmet clinical needs

- Societal/market readiness
  - Global Megatrends
  - Healthcare trends

- Enabling technology
Introduction

- The ICD was first approved in 1985 as a simple shock box using epicardial patches with few if any programmable parameters.
- It was shown to treat VT/VF effectively and reduce mortality in high risk cohorts.
- Subsequent advances included pacing capabilities, transvenous leads and remote monitoring.
- However, complications associated with these devices are one cause of under utilization.
ICD Systems

The current ICD approach while effective, is not without significant risks

- 11% ICD patients suffer complications during or shortly after implant
- Acute complications add significant costs to the healthcare system (> $7000/pt.)
- Infection rates are rising (one of the most serious complications)
Incidence of Lead Failures in Defibrillation Systems

84/332 = 20%
S-ICD Lead
Structural Differences

- No lumen
  - Greater Tensile Strength
- Less Torque/Stress
- 8cm Parasternal Coil
- Shock vector can ↔ coil (reversible)
S-ICD System Study Design
Prospective, Single-Arm

Enrollment (N=330)
- 33 Sites in the US, NZ, NL, UK

1° Efficacy Endpoint: Acute VF Conversion Rate
- 2 consecutive successes out of 4 attempts
- Lower Bound of 2-sided CI$_{95%}$ > 88%

Optional Sub-Study: VF Conversion Rate at $\geq$150 Days

1° Safety Endpoint: 180-Day System Complication Free Rate
- Lower Bound of 2-sided CI$_{95%}$ > 79%

Semi-Annual Follow-Up Visits Through Study Close

S-ICD System Clinical Investigation
Implant Attempts

- 321 patients underwent implant procedure
  - 95% implanted using only anatomical landmarks (no medical imaging)
- No electrode or pulse generator movement in 99% of implanted patients throughout follow-up period
Primary Effectiveness Endpoints

- **Acute VT/VF Sensitivity**
  - VT/VF Inductions: 809
  - Successful detections: 808 (99.9%)

- **Conversion with 65 J Shocks (2 consecutive times out of 4 attempts)**
  - 100% Successful
Freedom from all Device-, Labeling-, & Procedure-related Complications

180-day Device & Procedure-related Complication-free Rate: 92.1% (88.9% LCL)

180-day Performance Goal (79%)
### Annualized Mortality of ICD Studies

<table>
<thead>
<tr>
<th>Clinical Study</th>
<th>Annualized Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-ICD System IDE Study¹</td>
<td>3.7%</td>
</tr>
<tr>
<td>MADIT²</td>
<td>5.8%</td>
</tr>
<tr>
<td>MADIT II³</td>
<td>6.2%</td>
</tr>
<tr>
<td>AVID⁴</td>
<td>8.2%</td>
</tr>
<tr>
<td>SCD-HeFT⁵</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

¹S-ICD System Clinical Investigation. Study not prospectively designed to evaluate mortality,
²Moss, NEJM 1996
³Goldenburg, Circulation 2010
⁴AVID Investigators, N Engl J Med 1997;337:1576-83
⁵Bardy, NEJM 2005
Incidence and Efficacy of Shocks With the S-ICD: Pooled Long Term Results from the IDE and EFFORTLESS Studies

Michael R. Gold, MD*; Petr Neuzil, MD, PhD, Marcoen Scholten, MD, Pier Lambiase, PhD, FRCP, Margaret Hood, MD, Mayar Rashtian, MD, Bradley Knight, MD, FHRS and Dominic Theuns, PhD

Medical University of South Carolina, Charleston, SC, USA; Na Homolce Hospital, Prague, Czech Republic; Medisch Spectrum Twente, Rotterdam, Netherlands; Heart Hospital, London, United Kingdom; Auckland City Hospital, Cardiology Dept, Auckland, New Zealand; Foothill Cardiology, Pasadena, CA; Northwestern Memorial Hospital, Chicago, IL; Erasmus MC, Rotterdam, Netherlands
Pooled Analysis Cohort

EFFORTLESS
N = 568*

Both Studies
N = 13

IDE
N = 308

Total Pooled
N = 889

Total Implanted
N = 882

Not Implanted
N = 7

Mean FU = 21.7 months

* Includes 314 enrolled prospectively and 254 enrolled retrospectively
## Induced VT/VF Conversion

<table>
<thead>
<tr>
<th>Category</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful Conversion ≤ 65 J</td>
<td>728</td>
<td>94.4</td>
</tr>
<tr>
<td>Successful Conversion ≤ 80 J</td>
<td>760</td>
<td>98.6</td>
</tr>
</tbody>
</table>

* Includes all available conversion tests.

Patients (N = 771)*
**Incidence of Appropriate Shocks at 2 years**

KM Estimate at 720 Days: 7.9%
UBCI$_{95\%}$: 10.8%

<table>
<thead>
<tr>
<th>Post Op Days</th>
<th>0</th>
<th>60</th>
<th>120</th>
<th>180</th>
<th>240</th>
<th>300</th>
<th>360</th>
<th>420</th>
<th>480</th>
<th>540</th>
<th>600</th>
<th>660</th>
<th>720</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts w/Episodes (Cum)</td>
<td>0</td>
<td>13</td>
<td>25</td>
<td>28</td>
<td>35</td>
<td>40</td>
<td>43</td>
<td>46</td>
<td>48</td>
<td>52</td>
<td>53</td>
<td>55</td>
<td>57</td>
</tr>
<tr>
<td>No at Risk</td>
<td>882</td>
<td>837</td>
<td>798</td>
<td>755</td>
<td>738</td>
<td>704</td>
<td>664</td>
<td>625</td>
<td>586</td>
<td>535</td>
<td>453</td>
<td>378</td>
<td>303</td>
</tr>
<tr>
<td>K-M Estimate (%)</td>
<td>0.0</td>
<td>1.5</td>
<td>2.9</td>
<td>3.3</td>
<td>4.2</td>
<td>4.9</td>
<td>5.3</td>
<td>5.7</td>
<td>6.0</td>
<td>6.7</td>
<td>6.9</td>
<td>7.3</td>
<td>7.9</td>
</tr>
<tr>
<td>95% LBCI (%)</td>
<td>0.0</td>
<td>2.3</td>
<td>4.1</td>
<td>4.6</td>
<td>5.6</td>
<td>6.4</td>
<td>6.9</td>
<td>7.5</td>
<td>7.9</td>
<td>8.7</td>
<td>9.1</td>
<td>9.9</td>
<td>10.8</td>
</tr>
</tbody>
</table>
## Conversion of Spontaneous VT/VF

<table>
<thead>
<tr>
<th>Rhythm</th>
<th>Episodes N (Pts)</th>
<th>1st Shock Conversion (%)</th>
<th>≥ 1 Shock Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVT</td>
<td>60 (40)</td>
<td>55 (91.7)</td>
<td>60 (100.0)</td>
</tr>
<tr>
<td>PVT/VF</td>
<td>51 (32)</td>
<td>45 (88.2)</td>
<td>49 (96.1)</td>
</tr>
<tr>
<td>All</td>
<td>111 (59)</td>
<td>100 (90.1)</td>
<td>109* (98.2)</td>
</tr>
</tbody>
</table>

*Of two unconverted episodes, one terminated after the 5th shock but beyond the time frame of EGM recording. In the other episode, the device prematurely declared the episode ended after 2 shocks due to undersensing. A new episode was immediately reinitiated and the VF was successfully terminated with one additional shock.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Storms</th>
<th>Device Episodes</th>
<th>VT/VF STORMS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Final Storm Conversion (%)</td>
</tr>
<tr>
<td>7</td>
<td>12</td>
<td>88</td>
<td>S-ICD Shock: 10 (83.3%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>External Shock: 1 (8.3%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No Conversion: 1 (8.3%)</td>
</tr>
</tbody>
</table>
Incidence of Inappropriate Shocks at 2 years

**Single Zone**
- KM Estimate at 720 Days: 19.5%
- UBCI\(_{95}\): 26.6%

**Dual Zone**
- KM Estimate at 720 Days: 10.0%
- UBCI\(_{95}\): 14.2%

<table>
<thead>
<tr>
<th>Post Op Days</th>
<th>0</th>
<th>60</th>
<th>120</th>
<th>180</th>
<th>240</th>
<th>300</th>
<th>360</th>
<th>420</th>
<th>480</th>
<th>540</th>
<th>600</th>
<th>660</th>
<th>720</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dual Zone</strong> No at Risk</td>
<td>688</td>
<td>649</td>
<td>617</td>
<td>576</td>
<td>558</td>
<td>531</td>
<td>494</td>
<td>460</td>
<td>423</td>
<td>378</td>
<td>307</td>
<td>239</td>
<td>180</td>
</tr>
<tr>
<td>K-M Est. (%)</td>
<td>0.0</td>
<td>1.9</td>
<td>3.5</td>
<td>46</td>
<td>6.1</td>
<td>6.9</td>
<td>7.7</td>
<td>8.0</td>
<td>9.1</td>
<td>9.3</td>
<td>9.3</td>
<td>10.0</td>
<td>10.0</td>
</tr>
<tr>
<td><strong>Single Zone</strong> No at Risk</td>
<td>170</td>
<td>158</td>
<td>147</td>
<td>141</td>
<td>137</td>
<td>133</td>
<td>126</td>
<td>123</td>
<td>121</td>
<td>117</td>
<td>111</td>
<td>103</td>
<td>96</td>
</tr>
<tr>
<td>K-M Est. (%)</td>
<td>0.0</td>
<td>5.4</td>
<td>10.8</td>
<td>10.8</td>
<td>12.7</td>
<td>14.0</td>
<td>15.9</td>
<td>17.3</td>
<td>17.3</td>
<td>17.3</td>
<td>18.0</td>
<td>19.5</td>
<td>19.5</td>
</tr>
</tbody>
</table>
1 reported lead failure in US trials when lead inadvertently cut with scapel during implant.

Longest series from Netherlands showed no failures at mean follow-up of 4.5 years.
Pacemaker State-of-the-Art

- **Procedure:**
  - Radiation exposure
  - Surgical pocket + Transvenous leads

- **Device issues – Pocket:**
  - Discomfort
  - Hematomas
  - Infections
  - Cosmetic concerns

- **Leads**
  - Mechanical failures
  - Infections; Extractions
  - Mobility restrictions
  - Challenge in compatibility with MRI
# Incidence of Lead & Pocket Complications

- Over 700,000 people are implanted annually worldwide
  - Nearly 50,000 experience post-implant related problems
- Over 4.4 million people WW currently have pacemaker
  - 65,000 chronic lead related problems annually

## Pacing complication
<table>
<thead>
<tr>
<th></th>
<th>Average of Incremental cost per intervention in 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>$49,652</td>
</tr>
<tr>
<td>Lead revision</td>
<td>$16,285</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>$16,411</td>
</tr>
<tr>
<td>Pocket revision</td>
<td>$12,560</td>
</tr>
</tbody>
</table>

2: MDT, STJ, BSX Product Performance Reports
3: Danish Pacemaker Registry, www.pacemaker.dk
Pacemaker Minutarization

• Percutaneous femoral vein delivery
  - 18F introducer /steerable catheter

• Self-contained device in right ventricle
  - No lead or surgical pocket
  - VVIR w/ Hysteresis
  - Inherently MRI compatible

• Replacement options
  - Catheter-based retrieval
  - Deliver additional leadless pacemakers
  - Revert to conventional pacing lead
LCP Long-Term Outcome: Summary of Pacing/Sensing Parameters
LEADLESS Study
Safety Events

• Early Safety Events:
  • 1 inadvertent placement in LV (across PFO) → promptly removed and device placed in RV
  • 1 Tamponade → Surgery → f/u: Fatal stroke
  • 1 Minor Groin Hematoma → no treatment
  • 1 w/ VT 2 days after implant → LCP removed and ICD placed → ICD shock 2 wks later (same CL)

• Safety Events in follow-up:
  • No device migration / dislodgements
  • No infection
  • No mechanical failures / early battery depletion
  • No pro-arrhythmia
Current Status of Leadless Pacemaker

- **Pacemaker System:**
  - Leadless right ventricular cardiac pacing is feasible
  - Can eliminate the weak link in pacemaker systems: the lead
- Proof of Principle for acute / sub-acute LCP retrieval
- **Potential Limitations:**
  - Single-chamber (RV) pacing only
  - Potential risk for device embolization (not seen in LEADLESS)
  - Large venous sheath (18- 24F):
    - Now increasingly common used for EP procedures
  - How to manage device after battery depletion?
    - Retrieval vs Abandonment
Intravascular leads remain the “weak link” of both pacing and ICD systems.

The S-ICD is approved therapy and effective in patients without pacing requirements. It has been used most commonly in young patients with low risk of monomorphic VT or bradycardia.

Leadless pacing is a new therapy for RV only pacing that will likely be used primarily in AF patients or those with limited access.

Ultimately, multi-chamber leadless pacemakers or pellets will be combined with subcutaneous ICDs to allow for leadless CRT or other systems.