Subcutaneous Implantable Cardioverter Defibrillator (S-ICD)

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The Problem:

• 300,000 people die each year in the United States due to sudden cardiac arrest (SCA)
• People who have severe coronary heart disease are at a heightened risk for SCA
• Several studies show that an implantable cardioverter-defibrillator (ICD) can reduce the chance of dying from SCA
A Solution:

• Transvenous implantable cardioverter-defibrillator (T-ICD)
• First human implant in 1980
• Gained FDA approval in 1985
• First were “shock only”
• Now able to provide pacing and have advanced rhythm discrimination
Recognized Mortality Benefit

• Superior to antiarrhythmic therapy  
  AVID STUDY

• Improvement in mortality in patients with CAD and high risk for VT  
  MADIT STUDY

• In patients with a prior myocardial infarction and advanced left ventricular dysfunction, prophylactic implantation of a defibrillator improves survival and should be considered as a recommended therapy.  
  MADIT II STUDY

• Implantation of a simple-shock only ICD decreased mortality by 23%.  
  SCD HeFT STUDY
Problems with T-ICD:

- Infections in the venous system
- 2,201 patients required lead removals between 2000-2011
- Complex and highly invasive operation
- T-ICD’s often unsuccessful in children
- Requires x-ray imaging to ensure the lead is placed correctly
Risks at the time of insertion

- De novo implantation
- Upgrade procedure
- Follow up period time
Delayed risks over the lifetime of the device

• Lead failure
• Lead infection
• Lead extraction
Analysis from Cleveland Clinic evaluated survival in patients who developed a CIED infection and found a 3-fold higher risk of death in those who had an endovascular infection compared to a pocket infection.

- All patients with CIED infections who underwent device and lead removal at the Cleveland Clinic from January 2002 through 2008.
- For patients with CIED infection, 20.3% mortality within the first year:
  - Pocket infection: 12% mortality
  - Endovascular infection: 31% mortality

Kaplan–Meier survival curves over 1 year among TV-ICD patients with pocket infection and endovascular infection following TV-ICD system removal.

A New Alternative:

- The subcutaneous implantable cardioverter-defibrillator (S-ICD) was put into commercial use outside the U.S. in 2009
- The (S-ICD) was approved for observational study by FDA in 2012
Implantation of S-ICD:

• All components implanted just below the skin
• Only requires 3 or 2 small incisions
• Can be an outpatient procedure
Design of S-ICD:

The S-ICD System is comprised of the following four devices:

1. SQ-RX Pulse Generator
   - 80-J biphasic shock
   - Charge time to 80-J < 10 secs
   - 7.3 years longevity
   - 30 seconds post-shock pacing
   - Volume 70 cc, mass 145 gr

2. Q-TRAK Subcutaneous Electrode

3. Q-GUIDE Electrode Insertion Tool (EIT)

4. Q-TECH Programmer
S-ICD Screen Test

A

HEART RATE (25 mm/sec) 2 x RR FROM REFERENCE ARROW

14 cm GUIDE (Note: For screening, ECG electrodes should not extend beyond 14 cm arrows)

B

Peak Zones

INCORRECT PROFILE

CORRECT PROFILE
Ineligibility of S-ICD

- 8-15%
- HCM
- High BMI
- Prolonged QRS duration
- R-T ratio < 3
- TWI in I, II, aVf
A Summary of Different S-ICD Trials

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Bardy et al. (10)</th>
<th>Olde Nordkamp et al. (12)</th>
<th>Kobe et al. (15)</th>
<th>Jarman et al. (13)</th>
<th>Aydin et al. (16)</th>
<th>Dabiri Abkenari et al. (11)</th>
<th>Weiss et al. (14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>55</td>
<td>118</td>
<td>69</td>
<td>111</td>
<td>40</td>
<td>31</td>
<td>330 (321 attempted)</td>
</tr>
<tr>
<td>Patient follow-up, mean ± SD</td>
<td>10 ± 1 months</td>
<td>18 ± 7 months</td>
<td>217 ± 138 days</td>
<td>12.7 ± 7.1 months</td>
<td>229 days</td>
<td>-</td>
<td>330 days</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Successful termination: induced VF</td>
<td>52 (98%)</td>
<td>-</td>
<td>64 (95.5%)</td>
<td>111 (100%)</td>
<td>39 (97.5%)</td>
<td>31 (100%)</td>
<td>304 (304%)</td>
</tr>
<tr>
<td>Successful termination: spontaneous</td>
<td>3 (100%)</td>
<td>8 (100%)</td>
<td>3 (100%)</td>
<td>13 (100%)</td>
<td>4 (100%)</td>
<td>4 (100%)</td>
<td>20 (21)</td>
</tr>
<tr>
<td>VT/VF (patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications: Infection</td>
<td>2 (3.6%)</td>
<td>7 (5.9%)</td>
<td>1 (1.4%)</td>
<td>11 (9.9%)</td>
<td>-</td>
<td>-</td>
<td>18 (5.6%)</td>
</tr>
<tr>
<td>Lead migration/dislodgement</td>
<td>6 (10.9%)</td>
<td>3 (2.5%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2 (6.5%)</td>
<td></td>
</tr>
<tr>
<td>Rate of inappropriate shocks</td>
<td>5 (9%)</td>
<td>15 (13%)</td>
<td>5 (7.2%)</td>
<td>17 (15%)</td>
<td>2 (5%)</td>
<td>5 (16.1%)</td>
<td>41 (13.1%)</td>
</tr>
</tbody>
</table>
Head-to-head comparison of arrhythmia discrimination performance of subcutaneous and transvenous ICD arrhythmia detection algorithms: the START study.

- Comparison between S-ICD and multiple transvenous pulse in the classification of various arrhythmias.
- All devices accurately and appropriately detected VF.
- S-ISD showed best specificity in discriminating SVT including AF.

Appropriate ventricular arrhythmia detection is excellent for all ICD systems evaluated; however, specificity of supraventricular arrhythmia discrimination by the S-ICD system is better than discrimination by 2 of 3 TV systems.
Primary Results From **START** Comparing Transvenous and Subcutaneous Discrimination of Induced Supraventricular Arrhythmias

Specificity Results for Transvenous* and S-ICD Systems

<table>
<thead>
<tr>
<th></th>
<th>Single Chamber</th>
<th>Dual Chamber</th>
<th>S-ICD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriately</td>
<td>115</td>
<td>100</td>
<td>49</td>
</tr>
<tr>
<td>withheld therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inappropriate shock</td>
<td>35</td>
<td>47</td>
<td>1</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>77</td>
<td>68</td>
<td>98</td>
</tr>
</tbody>
</table>
S-ICD 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 follow-up 22 months

* Includes 314 enrolled prospectively and 254 enrolled retrospectively
43% of implanted patients primary prevention with EF ≤35

Pooled Study Implanted Patients (N=882)

<table>
<thead>
<tr>
<th>Demographic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.3 ± 16.9</td>
</tr>
<tr>
<td>Male (n, %)</td>
<td>636 (72.5)</td>
</tr>
<tr>
<td>Ischemic</td>
<td>330 (37.8%)</td>
</tr>
<tr>
<td>Genetic</td>
<td>58 (6.7%)</td>
</tr>
<tr>
<td>Idiopathic VF</td>
<td>40 (4.6%)</td>
</tr>
<tr>
<td>Channelopathies</td>
<td>90 (10.3%)</td>
</tr>
<tr>
<td>NYHA Classification II-IV</td>
<td>327 (37.5%)</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>143 (16.4%)</td>
</tr>
<tr>
<td>Previous Defibrillator</td>
<td>120 (13.7%)</td>
</tr>
<tr>
<td>Statistic / Category</td>
<td>Pooled IDE and EFFORTLESS Patients</td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Lowest Rate Zone</td>
<td>Mean ± SD: 197.5 ± 19.2 bpm</td>
</tr>
<tr>
<td></td>
<td>Median: 200.0 bpm</td>
</tr>
<tr>
<td>Zones (n, %)</td>
<td></td>
</tr>
<tr>
<td>Dual Zone</td>
<td>689 (80%)</td>
</tr>
<tr>
<td>Single Zone</td>
<td>170 (20%)</td>
</tr>
<tr>
<td>Vector (n, %)</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>452 (53%)</td>
</tr>
<tr>
<td>Secondary</td>
<td>313 (37%)</td>
</tr>
<tr>
<td>Alternate</td>
<td>94 (11%)</td>
</tr>
</tbody>
</table>
S-ICD Pooled Results
Mortality Compared to TV-ICD Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Mortality (At 2 years)</th>
<th>Average Age</th>
<th>1° Prevention</th>
<th>Ischemic</th>
<th>NYHA</th>
<th>LVEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-ICD Pooled</td>
<td>3.2%</td>
<td>50</td>
<td>70%</td>
<td>38%</td>
<td>37.5% class II-IV</td>
<td>39%</td>
</tr>
<tr>
<td>MADIT RIT¹</td>
<td>5-7%</td>
<td>63</td>
<td>100%</td>
<td>53%</td>
<td>98% class II or III</td>
<td>26%</td>
</tr>
<tr>
<td>High rate and Delayed Therapy Arms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIMPLE²</td>
<td>11%</td>
<td>64</td>
<td>70%</td>
<td></td>
<td>63% class II or III</td>
<td>32%</td>
</tr>
</tbody>
</table>

The S-ICD Pooled analysis was not designed or powered to assess mortality and care should be taken as the population in this analysis was more heterogeneous than the patient population in TV-ICD studies.

2. Healy JS et al. *Heart Rhythm* 2014;LBCT01;LB01-01.
### S-ICD Pooled Results

**S-ICD and TV-ICD Spontaneous Conversion Efficacy**

<table>
<thead>
<tr>
<th>Study Description</th>
<th>First Shock</th>
<th>Final Shock in episode</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-ICD Pooled Data*</td>
<td>90.1%</td>
<td>98.2%</td>
</tr>
<tr>
<td>ALTITUDE First Shock Study(^1)</td>
<td>90.3%</td>
<td>99.8%</td>
</tr>
<tr>
<td>SCD-HeFT(^2)</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td>PainFree Rx II(^2)</td>
<td>87%</td>
<td></td>
</tr>
<tr>
<td>MADIT-CRT(^3)</td>
<td>89.8%</td>
<td></td>
</tr>
<tr>
<td>LESS Study(^4)</td>
<td></td>
<td>97.3%</td>
</tr>
</tbody>
</table>

* S-ICD Pooled Data excluded VT/VT Storm events

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**S-ICD Pooled Data**

100% Clinical conversion to normal sinus rhythm

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**Of two “unconverted” episodes**

- One spontaneously terminated after the 5th shock
- In the other episode, the device prematurely declared the episode ended. A new episode was immediately reinitiated and the VF was successfully terminated with one shock

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Appropriate ICD Shock

An electrogram from a patient with an S-ICD who received a shock for fast ventricular tachycardia (lightening symbol) with restoration of sinus rhythm with premature beats. S-ICD = subcutaneous implantable cardioverter-defibrillator.
**S-ICD Pooled Results: Self-terminating episodes per indication category**

- Self-terminating VT occur >50% of pts
- Shock is often avoided in pts with PPrEF

Boersma et al. HRS abstract 2015
Efficacy of ATP for MVT PainFREE-II

ATP very efficacious in terminating fast MVT up to 250bpm

Overall 72% efficacy

Real-world registries show ~75% of stored ventricular device episode terminated by ATP

(kleeman et al Europace 2015)
How often is ATP really needed?

**MADIT-RIT**

- Same incidence of appropriate shocks despite large reductions in unnecessary ATP
- Similar rate of VT/VF shocks in S-ICD, MADIT-RIT, PainFREE SST

- Low incidence of ATP by programming longer delay or higher rate
- Unknown how many ATP therapies were successful in avoiding shocks

**1 Year Rate of Appropriate Therapy**

- **S-ICD**: 5% ATP, 4% Shock
- **Control**: 15% ATP, 4% Shock
- **High rate**: 5% ATP, 4% Shock
- **Delay**: 3% ATP, 7% Shock
- **PainFree SST (VR)**: 4% ATP, 3% Shock

1 year Kaplan Meier incidence shown for S-ICD and PainFREE SST
1 year rate for MADIT-RIT annualized at an average follow-up of 1.4 years

What is the potential need for ATP? incidence rate of recurrent MVT in SCD-HeFT

Total annualized incidence rate (percentage of patients) of recurrent MVT in SCD-HeFT was less than 2%.

Over the course of the 45.5 months of follow up only 7% of all patients had more than a single episode of fast monomorphic VT > 188 bpm, of which it is not know how many episodes would have been self-terminable by using delayed MADIT-RIT programming settings.

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n)</td>
<td>811</td>
</tr>
<tr>
<td>Patients receiving one or more shocks for VT/VF (n)</td>
<td>182</td>
</tr>
<tr>
<td>Patients with at least one episode of MVT &gt; 188 bpm (n)</td>
<td>121</td>
</tr>
<tr>
<td>Patients with recurrent episodes of MVT &gt; 188 bpm (n)</td>
<td>57</td>
</tr>
</tbody>
</table>

(7%) may be candidates for ATP.
The rate of therapy for VT/VF was similar across quartiles of enrollment in the studies (3.5% - 3.0%)

The most recently implanted quartile of patients had a trend toward a lower rate of inappropriate shocks at 6 months (Q1:6.9%, Q4: 4.5%)

There was a major increase in use of dual zone programming from 51% to 95%
Inappropriate Shocks & Underlying mechanisms

The incidence rate of inappropriate shocks (IAS) with S-ICD is similar or lower than observed in non-controlled programming TV-ICD studies, but underlying reasons are different:

- Main reason for IAS with S-ICD is cardiac signal oversensing, whereas AF/SVT & ST are responsible for most of the IAS with TV-ICD’s
- Adoption of dual zone index-programming resulted in less IAS for AF/SVT & ST in Effortless compared to IDE
- Pooled analysis showed only 3 SVT discrimination errors in conditional shock zone, at least one due to a clipped signal

Figure 2 Inappropriate shocks expressed as % patients with ICD.
Comparison of inappropriate ICD therapies reported from six ICD clinical trials and the S-ICD IDE study.

Jeanne E. Poole, and Michael R. Gold Circ Arrhythm Electrophysiol. 2013;6:1236-1245
S-ICD Pooled Results
Inappropriate Shock by Programming

Significantly Lower Rate of Inappropriate Shocks with Dual Zone Programming
**S-ICD Pooled Results**

### Complications

#### Acute Major Complications (% of patients)

<table>
<thead>
<tr>
<th></th>
<th>S-ICD Pooled Data</th>
<th>TV-ICD NCDR Analysis (Peterson et al, JAMA 2013)</th>
<th>TV-ICD Meta-analysis (van Rees et al. JACC 2011)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2%</td>
<td>3 - 5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Hematoma, Lead or Device Mal-position or Displacement, Pneumothorax)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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S-ICD Pooled Results

Complications and Infection with Device Removal by Enrollment Order

Six month incidence of complications

- Incidence of Type I-III Complication (p = 0.05)
- Infection Requiring Device Removal (p = 0.08)
S-ICD Pooled Results
Device Extraction for Pacing

- Extractions for pacing occurred in 0.4% of patients

<table>
<thead>
<tr>
<th>Reason</th>
<th>Number (Percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Pacing Indication</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>ATP</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>CRT Indication</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Ventricular overdrive pacing</td>
<td>1 (0.1%)</td>
</tr>
</tbody>
</table>
PRAETORIAN TRIAL

• 1\textsuperscript{st} multicenter, randomized trial to directly compare S vs T-ICDs
• 700 pts enrolled
• Non inferiority study
• Composite primary end-points: inappropriate shocks and device-related complications
• Secondary end-points: shock efficacy and mortality
• What is the ATP role?
S-ICD vs T-ICD

**Advantages**
Extra-vascular

**Disadvantages**
No pacing capability
No advanced diagnostics
Time to defibrillation

**Equivalents**
Pocket infections
Pulse generator complications
Inappropriate shocks

**Unknowns**
Device longevity
Long-term safety profile
S-ICD as a first choice:

- Pediatric or GUCH patients with no venous access
- Acquired stenosis or obstruction of central veins
- Previous endocarditis or device infection
- Patients at very high risk of infection of endovascular leads: dialysis, immunodeficiencies, cancer, need of a chronic indwelling catheter
- Patients candidates to cardiac transplantation.
S-ICD as a reasonable choice:

- Young patients with an active lifestyle and a long life expectancy
- Inherited genetic arrhythmogenic syndromes (Brugada, Long and Short QT, Early Repolarisation)
- Hypertrophic cardiomyopathy
- Prosthetic heart valves (infection risk). Women (“cosmetic” issue).
- Primary prevention patients with ischemic/non ischemic dilated cardiomyopathy
- Secondary prevention patients survivors of out-of-hospital VF
When to avoid the S-ICD:

- Failed pre-implant screening (up to 7% of cases)
- Symptomatic bradycardia requiring permanent pacing
- Previously implanted unipolar pacemaker (sensing/detection pitfalls)
- Systolic heart failure and left bundle branch block indicated for CRT
- Recurrent sustained monomorphic VT treatable with ATP
- Anatomic characteristics: thin patients with poor subcutaneous tissue, “pectus excavatum”.
Selecting devices for SCD prevention TV-ICD or S-ICD?

ICD Indicated Population (non-CRT)

**S-ICD only**
- Access issues
- Recurrent infection

**TV-ICD only**
- Recurrent pace terminable VT
- BY pacing indication
- ECG screen out for S-ICD

**Physician and patient choice**

*The vast middle ground*

**Two primary considerations**

1. Risk to develop TV-lead complications/infections
   - Preserve the vascular until and only if a needed for TV pacing/sensing develops
   - Reduce risk for replacements and re-interventions: 1 device for a lifetime

2. Risk to develop need for cardiac pacing/sensing

**65-75 yrs**

- Older, advanced HF, high arrhythmic burden
- Younger risk for infection
2015 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous defibrillators should be considered as an alternative to transvenous defibrillators in patients with an indication for an ICD when pacing therapy for bradycardia support, cardiac resynchronization or antitachycardia pacing is not needed.</td>
<td>IIa</td>
<td>c</td>
<td>157, 158</td>
</tr>
<tr>
<td>The subcutaneous ICD may be considered as a useful alternative to the transvenous ICD system when venous access is difficult, after the removal of a transvenous ICD for infections or in young patients with a long-term need for ICD therapy.</td>
<td>IIb</td>
<td>c</td>
<td>This panel of experts</td>
</tr>
</tbody>
</table>

ICD = implantable cardioverter defibrillator.

*S-ICD not suitable in...*

1. Patients who need CRT.
2. Patients who require bradycardia pacing*.
3. Patients who suffer from ventricular tachy-arrhythmias that can be easily terminated by ATP.

*Unless this need is confined to the period immediately following delivery of a shock (transcutaneous pacing can be delivered by the device for 30 seconds after the shock).

2015 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of SCD

Two levels of recommendation:

1. Class IIa to stimulate a clinical workflow in which S-ICD is considered for all ICD-indicated patients without an acute pacing requirement: supported by clinical evidence

2. Class IIb to provide additional guidance to the stratification process of patients who could benefit most from the S-ICD: supported by expert opinion
THANK YOU FOR YOUR ATTENTION