CLINICAL EVIDENCE
S–ICD VERSUS TV–ICD
META–ANALYSIS OF FIVE STUDIES


JACC: EP. Published online September 28, 2017
1. Meta-analysis of five case-control studies directly comparing S-ICD to TV-ICD.

2. Over 6,400 patients were included in analysis, comparing lead and non-lead complications, infections, and inappropriate shocks.

**Basu-Ray, et al., JACC Electrophysiology, September 2017**
S-ICD vs TV-ICD Meta-Analysis
Study selection process

Identification

Relevant articles identified by keyword search in PubMed and EMBASE and among references
257 citations

Screening

257 abstracts screened

251 references excluded by title or abstract review (excluded case reports, case series, cross-sectional studies, reviews)

Eligibility

6 unique and relevant case-control and retrospective studies identified for full text review

Included

5 studies included in qualitative synthesis

5 studies included in quantitative synthesis (meta-analysis)

## S-ICD vs TV-ICD Meta-Analysis

### Summary of Selected Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Design</th>
<th># of Patients</th>
<th>Patient Population</th>
<th>Study Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Honarbakhsh, et al. (2017)</td>
<td>Retrospective, propensity-matched case-control study</td>
<td>69 S-ICD, 69 TV-ICD</td>
<td>Single tertiary center, St. Bartholomew’s Hospital, London</td>
<td>31±19 (S-ICD) and 32±21 (TV-ICD) months</td>
</tr>
<tr>
<td>Brouwer, et al. (2016)</td>
<td>Retrospective, propensity-matched case-control study</td>
<td>140 S-ICD, 140 TV-ICD</td>
<td>Academic Medical Center and Leiden University Medical Center, Netherlands</td>
<td>Median TV-ICD: 5 yrs S-ICD: 3 yrs</td>
</tr>
<tr>
<td>Friedman, et al. (2016)</td>
<td>Retrospective, case-control, 1:1:1 propensity-matched of S-ICD, single chamber (SC)-ICD, and dual chamber (DC)-ICD</td>
<td>1920 S-ICD, 1920 SC-ICD, 1920 DC-ICD</td>
<td>National Cardiovascular Data Registry (NCDR) ICD Registry</td>
<td>In-hospital outcomes only</td>
</tr>
<tr>
<td>Mithani, et al. (2017)</td>
<td>Retrospective, case-control, matched to dialysis status, gender, and age</td>
<td>91 S-ICD, 91 TV-ICD</td>
<td>Single center, Cooper University Hospital, Camden, NJ</td>
<td>180 days</td>
</tr>
<tr>
<td>Köbe, et al. (2013)</td>
<td>Sex- and age-matched case-control prospective study</td>
<td>69 S-ICD, 69 TV-ICD</td>
<td>University Hospitals of Düsseldorf, Munich, and Münster</td>
<td>217 ± 130 days</td>
</tr>
</tbody>
</table>
S-ICD vs TV-ICD Meta-Analysis
Baseline characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics by Study</th>
<th>N</th>
<th># of Males (%)</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S-ICD</td>
<td>TV-ICD</td>
<td>S-ICD</td>
</tr>
<tr>
<td>Köbe et al.</td>
<td>69</td>
<td>69</td>
<td>50 (72.5)</td>
</tr>
<tr>
<td>Brouwer et al.</td>
<td>140</td>
<td>140</td>
<td>84 (60.0)</td>
</tr>
<tr>
<td>Honarbakhsh et al.</td>
<td>69</td>
<td>69</td>
<td>52 (75.4)</td>
</tr>
<tr>
<td>Friedman et al.</td>
<td>1920</td>
<td>3840</td>
<td>1293 (67.3)</td>
</tr>
<tr>
<td>Mithani et al.</td>
<td>91</td>
<td>91</td>
<td>51 (56)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,289</strong></td>
<td><strong>4,209</strong></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Baseline Characteristics by Study</th>
<th>Ejection Fraction (%)</th>
<th>Indication (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S-ICD</td>
<td>TV-ICD</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Köbe et al.</td>
<td>46.2 ± 15.6</td>
<td>40.6 ± 15.9</td>
</tr>
<tr>
<td>Brouwer et al.</td>
<td>50</td>
<td>49</td>
</tr>
<tr>
<td>Honarbakhsh et al.</td>
<td>57 ± 15</td>
<td>58 ± 13</td>
</tr>
<tr>
<td>Friedman et al.</td>
<td>31.2</td>
<td>31.3</td>
</tr>
<tr>
<td>Mithani et al.</td>
<td>26.8</td>
<td>27.8</td>
</tr>
</tbody>
</table>

N.A.: Not available

Baseline characteristics were not statistically different between the S-ICD and TV-ICD groups.

Baseline characteristics, cont.

<table>
<thead>
<tr>
<th>Baseline Characteristics by Study</th>
<th>Underlying Heart Disease (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardiomyopathy (Ischemic, nonischemic, dilated)</td>
</tr>
<tr>
<td></td>
<td>S-ICD</td>
</tr>
<tr>
<td>Kobe et al.</td>
<td>36</td>
</tr>
<tr>
<td>Brouwer et al.</td>
<td>39</td>
</tr>
<tr>
<td>Honarbakhsh et al.</td>
<td>14</td>
</tr>
<tr>
<td>Friedman et al.</td>
<td>44</td>
</tr>
<tr>
<td>Mithani et al.</td>
<td>62.6</td>
</tr>
</tbody>
</table>

N.A.: Not available

Lead complications were significantly less in S-ICD group compared to TV-ICD group.

No significant differences were found in system/device failure or rate of infection.

S-ICD vs TV-ICD Meta-Analysis
Clinical outcomes: Inappropriate shocks (IAS)¹

- Overall rate of inappropriate shocks did not differ between S-ICD and TV-ICD.
- The rate of IAS due to SVT was significantly higher in TV-ICD than S-ICD.
- The rate of IAS due to T-wave oversensing (TWOS) was significantly higher in S-ICD* than TV-ICD.

* S-ICD devices in these studies were first generation and did not have SMART Pass technology, shown to reduce oversensing by 82%²

Appropriate shocks were similar between S-ICD and TV-ICD in the two studies that were included this analysis, even though the TV-ICD devices offered ATP therapy.


Rate of lead complications was almost 8 times higher in patients with TV-ICD than patients with S-ICD (P=0.0001).

Infection rate with S-ICD was low at 0.35% and similar to TV-ICD with 2 of 5 studies favoring S-ICD.

Inappropriate shocks in TV-ICDs were predominately due to SVT.
Inappropriate shocks in S-ICDs were primarily due to T-wave oversensing.
The overall inappropriate shock rate was not significantly different between the two groups.

S-ICD vs TV-ICD Meta-Analysis
Conclusion

S-ICD reduced lead-related complications but was similar to TV-ICD with regard to non-lead-related complications, including inappropriate shocks and infection.

These results support the concept that S-ICD is a safe and effective alternative to TV-ICD in appropriate patients.

S-ICD vs TV-ICD Meta-Analysis

Summary

- Lead complication rate was almost 8 times higher with TV-ICD compared to S-ICD; however, there was no difference in other complications including infections and inappropriate shocks.

- Overall infection rate with S-ICD was low at 0.35% and similar to TV-ICD, with 2 of 5 studies favoring S-ICD.

- Inappropriate shock rates were similar, occurring in 9.4% of TV-ICD patients vs 8.3% in S-ICD patients.
  - Patients with a TV-ICD were close to 10 times more likely to experience an inappropriate shock for SVT.
  - While patients with an S-ICD were 9 times more likely to experience an inappropriate shock for over sensing, these patients had the first generation S-ICD without the benefit of SMART Pass Technology, which has been shown to reduce T-wave over sensing by 82%. ¹

- In the two studies that reported data on appropriate shocks, ATP did not result in a lower rate of appropriate therapy for the TV-ICD patients.

¹Theuns, D, et al. Evaluation of a Novel Algorithm Designed to Reduce Oversensing in the S-ICD. HRS 2016; AB05-01

The new SMART Pass Technology in S-ICD shown to reduce IAS for oversensing by 82%

S-ICD was shown in early studies to have superior AF/SVT discrimination. ¹ With SMART Pass, the overall IAS rate is projected to be comparable to or lower than TV-ICDs due to a reduction in cardiac oversensing. ²

Superior AF/SVT Discrimination

In the 2012 START study, the authors noted: “specificity of supraventricular arrhythmia detection varied considerably among devices and was best for the S-ICD system” ¹

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S-ICD vs TV-ICD Meta-Analysis
Selected Studies


**Emblem™ MRI S-ICD System from Boston Scientific CRM**

(1 of 2)

### 6.4. Emblem™ MRI S-ICD System

#### Indications for Use

The S-ICD System is intended to provide defibrillation therapy for the treatment of life-threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia that is reliably terminated with anti-tachycardia pacing.

#### Contraindications

Unipolar pacing and impedance-based features are contraindicated for use with the S-ICD System.

#### Warnings

Read the manual thoroughly before using the S-ICD System to avoid damage to the pulse generator and/or subcutaneous electrode. Such damage can result in patient injury or death. For single patient use only. Do not reuse, reprocess, or resterilize. All Boston Scientific S-ICD implantable components are designed for use with the Boston Scientific S-ICD System only. Connection of any S-ICD System components to a non-compatible component will result in failure to deliver life-saving defibrillation therapy. Always have external defibrillation equipment and medical personnel skilled in CPR available during implant and follow-up testing. Using multiple pulse generators could cause pulse generator interaction, resulting in patient injury or a lack of therapy delivery. Test each system individually and in combination to help prevent undesirable interactions. Concomitant use of the S-ICD System and implanted electromechanical devices (for example a ventricular assist device, VAD; or implantable insulin pump or drug pump) can result in interactions that could compromise the function of the S-ICD, the co-implanted device, or both. Electromagnetic (EMI) or therapy delivery from the co-implanted device can interfere with S-ICD sensing and/or rate assessment, resulting in inappropriate therapy or failure to deliver therapy when needed. In addition, a shock from the S-ICD pulse generator could damage the co-implanted device and compromise it's functionality. To help prevent undesirable interactions, test the S-ICD system when used in combination with the co-implanted device, and consider the potential effect of a shock on the co-implanted device. Handle the components of the SICD System with care at all times and maintain proper sterile technique. Do not modify, cut, kink, crush, stretch or otherwise damage any component of the S-ICD System. Use caution handling the subcutaneous electrode connector. Do not directly contact the connector with any surgical instruments such as forceps, hemostats, or clamps. Use appropriate anchoring techniques as described in the implant procedure to prevent S-ICD System dislodgement and/or migration. Do not implant in MRI site Zone III. Use caution when placing a magnet over the SICD pulse generator because it suspends arrhythmia detection and therapy response. In patients with a deep implant placement (greater distance between the magnet and the pulse generator) magnet application may fail to elicit the magnet response. Do not expose a patient with an implanted S-ICD System to diathermy. EMBLEM S-ICD devices are considered MR Conditional. Unless all MRI Conditions of Use are met, MRI scanning of the patient does not meet MR Conditional requirements for the implanted system. The Programmer is MR Unsafe and must remain outside the MRI site Zone III. During MRI Protection Mode the Tachycardia therapy is suspended. MRI scanning after ERI status has been reach may lead to premature batter depletion, a shortened device replacement window, or sudden loss of therapy. The Beeper may no longer be usable following an MRI scan. It is strongly recommended that patients are followed on LATITUDE NXT after an MRI scan if they are not already. Advise patients to seek medical guidance before entering environments that could adversely affect the operation of the active implantable medical device, including areas protected by a warning notice that prevents entry by patients who have a pulse generator. The pulse generator may be more susceptible to low frequency electromagnetic interference at induced signals greater than 80 uV. The S-ICD System has not been evaluated for pediatric use.
Precautions
For specific information on precautions, refer to the following sections of the product labeling: clinical considerations, sterilization and storage, implantation, device programming, environmental and medical therapy hazards, hospital and medical environments, home and occupational environments, follow-up testing, explant and disposal and supplemental precautionary information. Advise patients to avoid sources of EMI because EMI may cause the pulse generator to deliver inappropriate therapy or inhibit appropriate therapy.

Potential Adverse Events
Potential adverse events related to implantation of the S-ICD System may include, but are not limited to, the following: Acceleration/induction of atrial or ventricular arrhythmia, adverse reaction to induction testing, allergic/adverse reaction to system or medication, bleeding, conductor fracture, cyst formation, death, delayed therapy delivery, discomfort or prolonged healing of incision, electrode deformation and/or breakage, electrode insulation failure, erosion/extrusion, failure to deliver therapy, fever, hematoma/seroma, hemothorax, improper electrode connection to the device, inability to communicate with the device, inability to defibrillate or pace, inappropriate post shock pacing, inappropriate shock delivery, infection, keloid formation, migration or dislodgement, muscle/nerve stimulation, nerve damage, pneumothorax, post-shock/post-pace discomfort, premature battery depletion, random component failures, stroke, subcutaneous emphysema, surgical revision or replacement of the system, syncope, tissue redness, irritation, numbness or necrosis. Patients who receive an S-ICD System may develop psychological disorders that include, but are not limited to, the following: depression/anxiety, fear of device malfunction, fear of shocks, phantom shocks. Refer to the product labeling for specific indications, contraindications, warnings/precautions and adverse events. Rx only.