EMBLEM™ S-ICD System

Physician Training

Clinical Evidence
ICD Clinical History
   Historical ICD Challenges

S-ICD™ System
   Clinical Benefits
   Patient Selection

Proof of Concept Studies
   Study Overview
   Sensing Configuration
   Defibrillation Threshold
   Signal Comparisons

START Study
   Study Design
   Sensitivity/Specificity Results

S-ICD™ System IDE Study
   Primary Endpoints
   Baseline Characteristics
   Primary/Secondary Prevention
   Efficacy Results
   Time to Therapy
   Safety Results
   Appropriate vs Inappropriate Shocks

EFFORTLESS Registry
   Registry Design
   Registry Results

Danish Registry
   TV-ICD Results

Pooled Analysis
   Demographics
   Efficacy Results
   Inappropriate Shocks
   Safety Results

EMBLEM™ S-ICD System
   Product Description
   New Features

References
   Clinical Evidence

EMBLEM™ S-ICD System Brief Summary
After completing this module, you should be able to:

- Describe S-ICD™ System technology and its clinical benefits.
- Discuss the purpose, design, and results of the S-ICD System IDE clinical trial, EFFORTLESS Registry.
- Provide an efficacy and safety profile for the S-ICD System based on the pooled study analysis.
Historical ICD Challenges

While effective in preventing SCA, transvenous (TV) ICDs are associated with risks related to implantation, explantation, lead failure, and inappropriate shocks.

- Improvements in transvenous ICD lead technologies have improved the defibrillation and sensing performance of TV-ICD systems. The ICD lead, however, is considered the most fragile component of the ICD system.\(^9\)

- Studies have shown that the risk of:
  - **Lead failure** increases over time as mechanical stresses accumulate.\(^9\)
  - **Infection** increases 2%-7% with each device change.\(^10\)
  - **Incomplete or failed lead extraction** increases with implant duration, less experienced physicians, ventricular leads, and noninfected or younger patients.\(^11\)

- The most common mechanism of lead failure is **insulation disruption** due to subclavian crush or abrasion.\(^9\) Another failure mechanism is **conductor fracture** due to subclavian crush, fatigue or cyclic stress. Lead failure can cause oversensing and inappropriate shock delivery.

**KEY CONCEPT**

The ICD lead is considered the most fragile component of an ICD system. Studies have shown that the risk of lead failure increases over time.\(^9\)

**NOTES**

Boston Scientific (BSC) has a long history of innovation in ICD technologies and a legacy of clinical research.
The S-ICD™ System is designed to:

- Reduce implantation risks because the heart and vasculature remain untouched.
- Reduce lead failure because the S-ICD electrode is not subjected to flexing or motion with each cardiac cycle.
- Reduce inappropriate shocks by accurately discriminating between AF/SVT and VT/VF.
- Be positioned using anatomic landmarks or fluoroscopy.
- Provide greater ICD access to high SCA risk patients who cannot tolerate a transvenous (TV) ICD.

**KEY CONCEPT**

Because the heart and vasculature remain untouched, the S-ICD System reduces the risks associated with transvenous ICDs.

**NOTES**

The S-ICD System provides post-shock pacing, but not long-term pacing, ATP, or CRT therapy. It is contraindicated for patients with unipolar pacing.
Patient Selection

The S-ICD™ System is indicated for treatment of life threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia reliably terminated with anti-tachycardia pacing (ATP).

- The S-ICD System is suitable for a diverse ICD-indicated patient population. See table.
- Additional study is needed to determine the suitability of the S-ICD System in patients without venous access, with congenital abnormalities, or at risk for dialysis infection.

### Key Concept

The S-ICD System is suitable for a diverse ICD-indicated patient population.

### Notes

Based on patient characterization in the Poole and Gold editorial, the S-ICD System is:

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Strongly considered</th>
<th>Not considered</th>
</tr>
</thead>
<tbody>
<tr>
<td>- No venous access (occluded or congenital)  &lt;br&gt;- High risk for TV-ICD complications (dialysis, immunocompromised)  &lt;br&gt;- Channelopathies (LQT, Brugada, HCM)  &lt;br&gt;- Previous device infection/lead failure  &lt;br&gt;- H/O endocarditis</td>
<td>- Younger patients  &lt;br&gt;- Life expectancy &gt; 10 years  &lt;br&gt;- Primary prevention with ischemic / nonischemic heart failure  &lt;br&gt;- Prosthetic valves  &lt;br&gt;- Women (preferred generator placement)  &lt;br&gt;- Selected secondary prevention (survivors of out of hospital VF, no evidence of MVT)</td>
<td>- Brady indicated  &lt;br&gt;- CRT indicated (LBBB, CHF)  &lt;br&gt;- Recurrent monomorphic VT</td>
</tr>
</tbody>
</table>

Source: Poole JE, Gold MR. *Circulation*. 2013

---

**S-ICD™ System**

**Patient Selection**
The S-ICD™ System eliminates the risks associated with venous access and endocardial lead delivery.

- The risks associated with TV-ICD implant include pericardial effusion, cardiac tamponade, systemic infection, pericarditis, deep vein thrombosis, pulmonary, coronary, or systemic embolism, venous occlusion, pneumothorax, tricuspid valve injury, pocket infection/erosion, and lead dislodgement.
- The risks associated with S-ICD System implant include pocket hematoma, pocket infection/erosion, pain, and lead dislodgement.

2005-2012 NCDR data

KEY CONCEPT

The S-ICD System eliminates the risks associated with venous access and endocardial lead delivery.

NOTES

Developed in 1997 by the American College of Cardiology (ACC), the NCDR® is a national cardiovascular data registry that provides evidence-based quality improvement solutions for medical professionals. The ICD Registry™ helps participating hospitals measure and improve care for patients receiving ICDs.
Proof of Concept

Clinical Investigations

Registry

Pooled Analysis

**S-ICD™ System studies** are as follows:

- **Proof of concept** studies demonstrated the feasibility of the S-ICD System, identified the optimal sensing configuration, and tested the subcutaneous defibrillation threshold.

- **Clinical investigation** studies evaluated the safety and efficacy of the S-ICD System in the treatment of life-threatening VF.

- The **EFFORTLESS Registry** provides long-term outcome and efficacy data since the commercial release of the S-ICD System in 2009.

- A **pooled analysis** of IDE and EFFORTLESS data provides long-term efficacy and safety results in a larger study cohort.

**KEY CONCEPT**

The S-ICD was investigated in a number of studies, from early feasibility to a pooled analysis of collected efficacy and safety data.

**NOTES**

Before testing, the S-ICD System underwent comprehensive bench testing and acute and chronic animal studies (ten years development). It meets all FDA standards.
The S-ICD™ System concept was confirmed using a temporary pulse generator and electrode.

- Bardy et al evaluated four S-ICD System configurations in 78 patients. They found that the optimal configuration for converting induced VT/VF was a parasternal electrode and left lateral pulse generator.¹⁴

Note that, in the optimal configuration, the heart is between the distal electrode and device.

KEY CONCEPT

The optimal S-ICD System sensing configuration is a parasternal electrode and left lateral pulse generator.

NOTES

The concept of non-TV-ICDs is not new. In 2005, Grace et al evaluated a subcutaneous coil electrode implanted parallel to the sternum and a can electrode implanted in the left thorax. Burke et al reported on the shock efficacy of a pectoral can and subcutaneous coil electrode placed over the cardiac apex. Their study data proved that multiple configurations provided reliable long-term defibrillation with a lower than expected energy requirement.¹⁵
Defibrillation Threshold

Investigators tested the optimal sensing configuration in 49 patients to determine the **subcutaneous defibrillation threshold (DFT)**.

- Investigators found that, in the optimal configuration, the S-ICD™ System was as effective as a TV-ICD for terminating induced VF. Defibrillation **energy requirements** for the S-ICD System were consistent at 36.6 ± 19.8 joules.\(^5\)

Shocks from coil-to-can are about 35 joules, which is higher than for TV-ICDs.

**KEY CONCEPT**

Defibrillation energy requirements for the S-ICD System were consistent at 36.6 ± 19.8 joules.\(^5\)

**NOTES**

Burke et al originally suggested that surface ECG signals could distinguish VF from the sinus rhythm when using typical TV-ICD sensing and detection algorithms. In 2012, Gold et al showed that VT/VF detection using subcutaneous electrodes did not differ in sensitivity or specificity when compared with intracardiac electrodes.\(^15\)
The S-ICD™ System captures high-resolution ECG signals similar to the surface ECG signal. See Figure A.

- The S-ICD System interprets the subcutaneous ECG signal using three far-field sensing vectors. See Figure B.
  - **Primary**: proximal sensing ring to pulse generator surface (can)
  - **Secondary**: distal sensing ring to pulse generator surface (can)
  - **Alternate**: distal to proximal sensing rings

Subcutaneous signals are comparable to surface ECG signals.

“Sensing is the most critical part to solve. ... an entirely new sensing algorithm had to be developed.”

---

**Figure A**: Signal comparisons

**Figure B**: Sensing vectors

---

**KEY CONCEPT**

**NOTES**
The **START study** was a prospective, multicenter trial designed to directly compare the sensitivity and specificity of the S-ICD™ System with that of single and dual chamber TV-ICD systems.\(^{16}\)

- **START** was conducted in two phases: 1) construction of a test library of induced atrial and ventricular arrhythmias using cutaneous and transvenous connections, and 2) comparison of arrhythmia classifications by subjecting the S-ICD and TV-ICDs to the test arrhythmias. *The same set of induced arrhythmias was evaluated by each device.*

- **Non-shockable rate criteria** were selected to ensure the arrhythmia test set was contained *within the programmed discrimination zone*. This permitted testing of arrhythmia episodes that transitioned between the shock and conditional shock zones.

- **Shockable rate criteria** were selected to ensure the arrhythmia test set was contained *above the lower boundary* of the programmed discrimination zone. This prevented classification of an untreated arrhythmia episode as a failure.

**START** = subcutaneous vs transvenous arrhythmia recognition testing. Devices used in the **START** study were from Boston Scientific, Medtronic, and St. Jude.
The START study showed that the S-ICD™ System is equivalent to a TV-ICD in sensitivity and superior to a TV-ICD in specificity.\textsuperscript{16}

- The mean age of START patients was 60 ± 12 years and 78\% were male. The mean LVEF was 31\% and 30\% of patients had a baseline QRS width > 120 ms. An ICD was indicated for primary SCA prevention in 79.7\% of patients and secondary SCA prevention in 20.3\%. Ninety-six (96) episodes (50 non-shockable, 46 shockable) from 64 patients met START’s rate and duration criteria for testing.

- The S-ICD \textbf{delivered appropriate therapy} in 100\% of cases, demonstrating that S-ICD System sensitivity (rhythm detection) is equivalent to that of TV-ICDs.\textsuperscript{16}

- The S-ICD System \textbf{withheld inappropriate therapy for 98\%} of induced arrhythmia episodes, demonstrating that S-ICD System specificity (rhythm discrimination) is significantly better than transvenous ICD specificity (76.7\% for single chamber devices; 68\% for dual chamber devices).\textsuperscript{16}

\begin{table}
\centering
\begin{tabular}{|c|c|c|}
\hline
& Single Chamber & Dual Chamber & S-ICD \\
\hline
Appropriately withheld therapy & 115 & 100 & 49 \\
Inappropriate defibrillation & 35 & 47 & 1 \\
Specificity & 76.7\% & 68\% & 98\% \\
\hline
\end{tabular}
\caption{Primary Results From START Comparing Transvenous and Subcutaneous Discrimination for Induced Ventricular and Supraventricular Anrrhytmias}
\end{table}


\textbf{KEY CONCEPT}

The START study showed that the S-ICD System is equivalent to a TV-ICD in sensitivity and superior to a TV-ICD in specificity.

\textbf{NOTES}

Sensitivity and specificity refinements resulted in the development of a pre-implant screening procedure for identifying patients with a suitable subcutaneous sensing signal.
Primary Endpoints

IDE Primary Endpoints

Primary efficacy: acute VF conversion
Two consecutive successes out of four attempts
Lower bound of two-sided CI > 88%

Primary safety: 180-day complication free rate
Lower bound of two-sided CI > 79%

The S-ICD™ System IDE study was a prospective, single arm study designed to demonstrate the safety and efficacy of the S-ICD.

- The primary efficacy endpoint was acute VT/VF conversion - that is, two consecutive successful conversions out of four attempts at 65 joules.
- The primary safety endpoint was successful device implantation without system complications at 180 days.
- Inclusion criteria: Age ≥ 18 years, indicated for ICD implant or replacement, completed pre-operative ECG evaluation.
- Exclusion criteria: VT reliably terminated with ATP, existing epicardial patches or subcutaneous electrode array, implanted unipolar pacemaker, severe renal dysfunction (GFR ≤ 29).

KEY CONCEPT

The IDE study was a prospective, single arm study designed to demonstrate the safety and efficacy of the S-ICD System.

NOTES

Experience acquired during early studies led to the following improvements:
- Development of an anchoring sleeve to prevent electrode migration or dislodgement.
- Adjustment in recommended suture material
- Modification of electrode pin for insertion into device header
- Updated device labeling
Baseline patient demographics and underlying cardiac conditions are listed in the tables.

- The mean age was 52 ± 16, slightly lower than the mean age in most TV-ICD studies.
- 13% of the 321 study patients were previously implanted with a transvenous ICD.
- The mean LVEF was 36%, slightly higher than the mean LVEF in most TV-ICD studies. 70% of patients had an LVEF < 35%.

**KEY CONCEPT**

IDE study patients had a mean LVEF of 36%, which is slightly higher than the mean LVEF in TV-ICD studies.
The distribution of **primary and secondary prevention** patients in the IDE trial was similar to that of the NCDR-ICD Registry, indicating no patient bias.

- **S-ICD™ System IDE study**: 321 patients (79% primary prevention, 21% secondary prevention). Sixty-eight percent were NYHA Class I or II.\(^{17}\)
- **NCDR-ICD Registry**: 486,025 patients (78% primary prevention, 22% secondary prevention).\(^{8}\)
The IDE study met the **primary efficacy endpoint**, exceeding the performance goal of 88%.

**Implant success**
- Of the 330 patients enrolled in the IDE study, 321 were implanted with the S-ICD™ System. In 95% of patients, implant was achieved using only anatomic landmarks (without fluoroscopy).

**Primary efficacy endpoint**
- Effectiveness was analyzed in 304 patients who completed acute induction testing. During testing, the S-ICD System detected 808 of 809 induced VT/VF episodes (99.9%). It converted 100% of VT/VF episodes with a 65 joule shock.
- During the six month follow-up, the S-ICD System detected and recorded 78 spontaneous VT/VF episodes in 21 patients. All arrhythmias either self-terminated or were successfully converted. The device stores 25 treated and 20 untreated episodes, so some episodes may not have been available for analysis.

**Note:** Based on the pre-defined analysis methods, the acute VF conversion efficacy rate of the S-ICD System was 100% in the 304 patients in whom the protocol was **fully implemented**. An unplanned sensitivity analysis of 16 non-evaluable induction tests showed a conversion rate of 94.7%, which still exceeds the performance goal of 88%. Testing was not performed in one patient.

The S-ICD System converted 100% of induced VT/VF episodes, exceeding the performance goal of 88%.

An unplanned sensitivity analysis of non-evaluable induction tests showed a 94.7% conversion rate, which also exceeded the performance goal.

**NOTES**

“The implant success rate applied regardless of implant number.”

Source: Weiss

5
Analysis confirmed **chronic conversion efficacy** and the benefit of a **therapy delay**.

- A subset of 78 IDE study patients underwent testing to confirm conversion efficacy at ≥ 150 days. The test converted VT/VF with a single 65 joule shock in either polarity. Of the **75 patients** who were evaluated, **96%** (n=72) were successfully converted with 65 joules. Three patients were subsequently converted with ≤ 80 joules. Thus, the chronic conversion efficacy was **100%**.

### Chronic Conversion Analysis

<table>
<thead>
<tr>
<th>65 Joules</th>
<th>≤80 Joules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success: n=72</td>
<td>Success: n=75</td>
</tr>
<tr>
<td>Failure: n=3</td>
<td>Conversion: <strong>100%</strong></td>
</tr>
<tr>
<td>Conversion: <strong>96%</strong></td>
<td></td>
</tr>
</tbody>
</table>

- For the chronic conversion analysis, the mean **time to therapy** was 14.6 ± 2.9 seconds. Ninety-five percent (95%) of VT/VF episodes were treated in < 21 seconds and 88% in < 18 seconds, demonstrating the benefit of delaying therapy to allow time for self-termination of non-life-threatening VTs. See images.

**KEY CONCEPT**

The chronic conversion efficacy of the S-ICD™ System was 100% at 80 joules or less.

Ninety five percent (95%) of patients were treated within 21 seconds of arrhythmia detection.

**NOTES**

The FDA required acute (induced), spontaneous, and chronic (6 month post implant) conversion testing.
The IDE study met the primary safety endpoint, exceeding the performance goal of 79%.

- The 180-day, device-related (Type 1) complication-free rate was 99%. The 180-day device, procedure, and labeling-related (Type I-III) complication-free rate was 92.1%. These results support the continued safety of the S-ICDTM System.

Deaths

- There were eight deaths. All were adjudicated as unrelated to the device or procedure. The annualized mortality rate was 3.7%, consistent with results of benchmark ICD studies.

Infection

- There were eighteen infections. Four resulted in device explant. Infections requiring explant occurred early in the study and were eliminated with refinements in surgical technique and patient preparation. Fourteen infections were due to suspected incisional or superficial infections. One resolved without treatment; one with wound revision; and twelve with antibiotic management.

Other complications

- No electrode or pulse generator movement was observed during follow-up. Eleven patients reported discomfort, which resolved without repositioning.

**KEY CONCEPT**

The 180-day, Type I-III complication-free rate was 92.1%, exceeding the performance goal of 79%.

**NOTES**

To prevent infection, “...directly observing patient preparation rather than delegating is important...”5

Source: Weiss21
The IDE study showed that **dual zone programming** reduces the rate of inappropriate shocks.

- **Single-zone** programming uses only the detected heart rate to determine if therapy should be delivered or withheld. **Dual-zone** programming enhances AF/SVT vs VT/VF discrimination to determine the appropriateness of therapy.

- Thirty-eight (38) patients received an inappropriate shock for an AT/SVT episode - 24 were due to oversensing; 15 to the programmed rate in the Shock (single) zone. There were no inappropriate shocks in the programmed Conditional (dual) zone.

- Dual-zone programming reduced the rate of inappropriate shocks for oversensing by 54% and for SVT by 74%. See Figure B.

- Sixty-three percent (63%) of VT/VF episodes self-terminated after meeting the criteria to charge, so the patient did not receive shock therapy.

- The first shock clinical conversion rate was 92%.

**KEY CONCEPT**

Dual zone programming reduced the rate of inappropriate shocks by 54% for oversensing and 74% for SVT.

**NOTES**

The rate of inappropriate S-ICD™ System shock therapy is consistent with that of current TV-ICDs.
The **EFFORTLESS Registry** was designed to collect clinical outcome and cost effectiveness data for the S-ICD™ System.

- The EFFORTLESS Registry includes retrospective and prospective patients implanted since the CE mark trial (2009).
- The registry requires enrollment of 1,000 patients at 50 centers in Europe and New Zealand. Patients will be monitored for five years to ensure the collection of robust long-term data.
- Unlike the IDE study, the EFFORTLESS Registry:
  - Does not require implant/defibrillation testing
  - Does not exclude patients with kidney disease
  - Includes patients < 18 years old
  - Permits right-sided electrode placement
  - Includes both two-and three-incision implants (See Module 2)
- Registry patients have a **broad range of underlying cardiac conditions** (Figure A). The S-ICD System is used for primary SCA prevention in 64% of patients and secondary SCA prevention in 36%.
EFFORTLESS registry results from 472 patients followed for 558 days are listed below.\(^\text{18}\) Registry results are consistent with IDE study results.

- The VT/VF clinical conversion rate for spontaneous VT/VF was 100% at \(\leq 80\) joules (sensitivity). The first shock conversion rate was 88% for registry patients and 92% for IDE patients.

- There was one inappropriate shock for AF/SVT within the programmed Conditional Shock (dual) zone (specificity).

- The annual inappropriate shock rate was 6.4% within the programmed Conditional Shock (dual) zone.

- The mean time to therapy was 17.4 \(\pm\) 4.4 seconds for spontaneous VT/VF.

- The Type I-III complication-free rate was 94% at 180 days. This compares to 92.1% at 180 days for IDE patients. As in the IDE study, complications decreased with implanter experience.

**KEY CONCEPT**

One year registry results demonstrate a 100% clinical conversion rate and a 94% complication-free rate.\(^\text{18}\)
The **Danish Registry** was used to collect and analyze complications related to the implantation of cardiac devices (pacemakers, TV-ICDs, CRT systems).

- The Danish registry included 784 TV-ICD patients implanted between May 2010 and April 2011. The graph shows the complication rates for the 784 Danish TV-ICD patients along with the complication rates for 369 EFFORTLESS S-ICD patients.\(^2\)

- Registry investigators concluded that complications after cardiac implantable electronic device treatment are "more frequent than generally acknowledged. Both patient- and procedure-related predictors may identify patients with a particularly high risk of complications. This information should be taken into account both in individual patient treatment and planning."\(^2\)

**KEY CONCEPT**

The Danish registry showed that complications after TV-ICD implantation are more frequent than generally acknowledged.\(^2\)
The safety and efficacy of the S-ICD™ System were analyzed in a pooled cohort of patients from the IDE study and EFFORTLESS Registry.

- The pooled database included 889 patients (308 IDE, 568 EFFORTLESS, 13 both). 882 patients were implanted and followed for a mean 22 months.
- The mean age was 50 ± 17. The mean LVEF was 39%. Most patients (70%) were treated for primary SCA prevention. Forty-three percent (43%) of the primary prevention patients had an LVEF ≤ 35%. See tables.
- Fourteen percent (14%) of the 889 patients were previously implanted with a TV-ICD. Most (63%) experienced infection and subsequent TV-ICD extraction. The remainder experienced lead failure or malfunction and subsequent lead removal or abandonment.

### Demographics

<table>
<thead>
<tr>
<th>Poole Demographics²³</th>
<th>Underlying Cardiac Conditions²³ (n=889)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Co-morbidities</td>
</tr>
<tr>
<td>- Range: 7 to 88</td>
<td>- Congestive heart failure (CHF)</td>
</tr>
<tr>
<td>- <strong>Mean: 50 ± 17</strong></td>
<td>- Hypertension</td>
</tr>
<tr>
<td>Gender</td>
<td>- Myocardial infarction (MI)</td>
</tr>
<tr>
<td>- Male: 72.5%</td>
<td>- Diabetes</td>
</tr>
<tr>
<td>- Female: 27.5%</td>
<td>- Atrial fibrillation (AF)</td>
</tr>
<tr>
<td>Body type</td>
<td>- Valve disease</td>
</tr>
<tr>
<td>- Height: 175 ± 10 cm</td>
<td>- COPD</td>
</tr>
<tr>
<td>- Weight: 86 ± 23 kg</td>
<td>- Stroke</td>
</tr>
<tr>
<td>- BMI: 28 ± 7 kg/m</td>
<td><strong>Primary Prevention</strong> 27%</td>
</tr>
<tr>
<td></td>
<td><strong>Primary Prevention (low LVEF) 43%</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Secondary Prevention</strong> 30%</td>
</tr>
<tr>
<td><strong>LV ejection fraction (LVEF)</strong></td>
<td><strong>Mean: 39%</strong></td>
</tr>
</tbody>
</table>

**Pooled Analysis**

**KEY CONCEPT**

The objective of the pooled analysis was to assess the long term efficacy and safety of the S-ICD System in a larger study cohort.
Efficacy Results

The pooled analysis of S-ICD™ System data showed high shock efficacy for spontaneous VT/VF.

- The S-ICD™ System detected 111 discrete VT/VF episodes in 59 patients. **First shock efficacy** was > 90%. **Overall shock efficacy** was > 98%. One episode self-terminated after the final (5th) shock. Another was undersensed, but subsequently detected and converted with the first shock. The data show that the S-ICD System is as effective as TV-ICDs in treating spontaneous VT/VF. See table.

- The mean **time to therapy** was 19.2 ± 5.5 seconds. The stored data showed that VT/VF self-terminated in a majority of patients (4.6% untreated, 4.1% treated). This data supports the time delay strategy for preventing unnecessary shocks.

### Conversion Efficacy

<table>
<thead>
<tr>
<th>Study</th>
<th>First Shock</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled S-ICD data</td>
<td>90.1%</td>
<td>98.2%</td>
</tr>
<tr>
<td>ALTITUDE First Shock</td>
<td>90.3%</td>
<td>99.8%</td>
</tr>
<tr>
<td>SCD-HeFT</td>
<td>83%</td>
<td>--</td>
</tr>
<tr>
<td>PainFree Rx</td>
<td>87%</td>
<td>--</td>
</tr>
<tr>
<td>MADIT-CRT</td>
<td>89.8%</td>
<td>--</td>
</tr>
<tr>
<td>LESS Study</td>
<td>--</td>
<td>97.3%</td>
</tr>
</tbody>
</table>

Source: Burke 2015

---

**KEY CONCEPT**

The pooled analysis of S-ICD System data showed high shock efficacy for spontaneous VT/VF.

The study data showed the S-ICD System was as effective as TV-ICDs in treating spontaneous VT/VF.

---

**NOTES**

“The main findings of the pooled cohort confirm that the favorable outcomes achieved with the S-ICD continue up to three years post implant.” Burke 2015
The pooled analysis of S-ICD™ System data showed a trend toward a lower **inappropriate shock rate**.

- The decreasing incidence of inappropriate shocks is associated with improvements in patient screening and increased adoption of **dual zone programming**. The Kaplan Meier rate of inappropriate shock was 11.7% for dual zone programming and 20.5% with single zone programming. See Figure A.

- In the most recent quartile of patients, the **inappropriate shock rate** was 4.5% at six months, a 34% reduction from the first to the last quartile. During this time, dual zone programming increased from 51% to 95%.

**S-ICD vs TV-ICD comparison**

- The data showed that the one year inappropriate shock rate for the S-ICD System (dual zone programming) was similar to or lower than the inappropriate shock rate observed in TV-ICD studies. See Figure B. Note that S-ICD System settings were at physician discretion and not controlled programming.

**KEY CONCEPT**

The pooled analysis of S-ICD System data showed a trend of fewer inappropriate shocks with increased adoption of dual zone programming.

The study data showed that the inappropriate shock rate for the S-ICD System was similar to or lower than that for TV-ICDs.

**NOTES**

The pooled analysis was divided into four enrollment quartiles to account for changes in implanter technique and programming, system software, and the implant screening process.23
Pooled Analysis

The pooled analysis of S-ICD™ System data showed a reduction in complication rates over time.

- The six-month complication rate decreased from 8.9% in the first enrollment quartile to 5.5% in the last quartile (see graph). The acute major complication rate was lower with the S-ICD™ System than TV-ICDS, possibly because the S-ICD System does not require vascular access.

- The six-month infection rate decreased from 2.5% in the first enrollment quartile to 0.2% in the last quartile (Figure A). Improvements in patient prep, implant technique, and infection management appear to have positively affected the rate of infection. The development of an alternative two-incision technique decreases the incisional surface area and the infection risk.

S-ICD vs TV-ICD comparison

- The data showed that the complication rate for the S-ICD System was similar to or lower than the complication rate for TV-ICDs. See Figure B.

Safety Results

<table>
<thead>
<tr>
<th>Complication</th>
<th>S-ICD&lt;sub&gt;A&lt;/sub&gt; (Pooled data)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>*Ezzat&lt;sup&gt;2&lt;/sup&gt;</th>
<th>**Danish Registry&lt;sup&gt;4&lt;/sup&gt;</th>
<th>***JAMA&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>1.7</td>
<td>1.5</td>
<td>0.8</td>
<td>0.67</td>
</tr>
<tr>
<td>Haematoma</td>
<td>0.4</td>
<td>1.2</td>
<td>2.3</td>
<td>0.24</td>
</tr>
<tr>
<td>Lead&lt;sup&gt;6&lt;/sup&gt;</td>
<td>1.8</td>
<td>3.1</td>
<td>2.4</td>
<td>1.79&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0.1</td>
<td>1.1</td>
<td>0.9</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Figure B: S-ICD vs TV-ICD complication rates

4. EHJ. doi:10.1093/eurheartj/eht511
5. 90 days follow-up
6. Includes suboptimal lead position or movement

**18 month data**
**6 month data**
***3 month data

Figure A: Complication rates over time
Source: Burke 2015

KEY CONCEPT

The pooled analysis of S-ICD™ System data showed a reduction in complication rates over time.

The study data showed that the complication rate for the S-ICD System was similar to or lower than that for TV-ICDs.

NOTES

A Cleveland Clinic study found a three fold higher mortality risk in patients with endovascular infection compared to pocket infection.23
The **EMBLEM™ S-ICD System** provides defibrillation therapy via a completely subcutaneous defibrillation system. It provides an alternative for treating life-threatening ventricular tachyarrhythmias in patients at risk for sudden cardiac arrest (SCA).

- The **pulse generator** is implanted in a pocket at the mid-axillary line. The **electrode** is inserted via an incision at the xiphoid process; then tunneled to the device pocket and superior sternum. The **proximal sensing ring** is placed near the xiphoid; the **distal sensing ring** in the superior sternum.

- Before implant, the acceptability of the patient’s subcutaneous ECG signal is verified. After implant, the EMBLEM S-ICD System uses a proprietary **rhythm discrimination algorithm** in the Conditional zone to identify and classify the subcutaneous ECG signal.

- The **EMBLEM S-ICD System** automatically delays therapy to allow time for self-termination of nonsustained VT.

### KEY CONCEPT

The EMBLEM S-ICD System provides defibrillation therapy via a completely subcutaneous defibrillation system.

### NOTES

The EMBLEM S-ICD System can be programmed to a Shock zone or Conditional Shock zone (default).

Upon VT/VF detection, the EMBLEM S-ICD System delivers an 80 joule biphasic shock to restore the normal sinus rhythm.

The EMBLEM S-ICD System provides post shock pacing at 50 bpm for thirty seconds.
The EMBLEM S-ICD is **20% thinner** than the first generation S-ICD (12.7 mm vs 15.7 mm).

The edges of the pulse generator are rounded to make pocket placement easier and improve patient comfort. The **header is centered** to make electrode wrap easier.

---

The EMBLEM S-ICD is projected to last **40% longer** than the first generation S-ICD (projected longevity 7.3 vs 5.1 years).

---

The EMBLEM S-ICD is enabled for **remote patient management**.

Latitude NXT for use with the EMBLEM S-ICD is an investigational device not available for sale.

---

The pulse generator has **two suture holes** through the header. This feature gives implanters flexibility when anchoring the pulse generator in the pocket.
References: Clinical Evidence


8. Boston Scientific data


References: Clinical Evidence


17. IDE# G090013. Manuscript publication pending.


22. Johansen JB. Presented at BSC meeting AB05-04 HRS, 2013; Denver, CO.


EMBLEM™ S-ICD Brief Summary

EMBLEM™ S-ICD System from Boston Scientific CRM

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 this 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 or Cameron Health S-ICD System only. Connection of any S-ICD System components to a noncompatible 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 coimplanted 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 coimplanted device and compromise its functionality. To help prevent undesirable interactions, test the S-ICD system when used in combination with the coimplanted device, and consider the potential effect of a shock on the coimplanted device.

Handle the components of the S-ICD 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. 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. Do not expose a patient to MRI scanning. 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.
EMBLEM™ S-ICD System Brief Summary

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. (Rev. A)
S-ICD™ System Brief Summary

S-ICD™ System from Boston Scientific RM

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 pacemakers are contraindicated for use with the S-ICD System.

Warnings and Cautions

The S-ICD System contains sterile products for single use only. Do not resterilize. Handle the components of the SICD System with care at all times and maintain proper sterile technique. All Cameron Health implantable components are designed for use with the Cameron Health S-ICD System only. Connection of any S-ICD System components to any other ICD system will result in failure to deliver lifesaving defibrillation therapy.

General

• External defibrillation equipment should be available for immediate use during the implantation procedure and follow-up.
• Placing a magnet over the SQ-RX Pulse Generator suspends arrhythmia detection and therapy response. Removing the magnet resumes arrhythmia detection and therapy response.
• Battery depletion will eventually cause the SQ-RX Pulse Generator to stop functioning. Defibrillation and excessive numbers of charging cycles shorten the battery longevity.
• The S-ICD System has not been evaluated for pediatric use.
• The S-ICD System does not provide long-term bradycardia pacing, Cardiac Resynchronization Therapy (CRT) or Anti-Tachycardia Pacing (ATP).

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; 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 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.

S-ICD™, SQ-RX® and Q-TRAK® are registered trademarks of Cameron Health, Inc. Q-TECH™, Q-GUIDE™ and INSIGHT™ are trademarks of Cameron Health, Inc.

Refer to the product labeling for specific indications, contraindications, warnings/precautions and adverse events. Rx only. (Rev.C)