**REVIEW ARTICLE**

# Subcutaneous Implantable Cardioverter Defibrillators: An Overview of Implantation Techniques and Clinical Outcomes

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**Abstract:** Sudden Cardiac Death (SCD) is a significant health problem worldwide.

Multiple randomized controlled trials have shown that Implantable Cardioverter Defibrillators (ICDs) are effective life-saving management option for individuals at risk of SCD in both primary and secondary prevention. Although the conventional transvenous ICDs (TV-ICDs) are safe and effective, there are potential complications associated with its use, including localized pocket or wound infection or systematic infection, a vascular access related complication such as pneumothorax, and venous thrombosis, and lead related complications such as dislodgement, malfunction, and perforation.

Furthermore, transvenous leads placement may not be feasible in certain patients like those with venous anomaly or occlusion, or with the presence of intracardiac shunts. Transvenous leads extraction, when needed, is associated with considerable morbidity & mortality and requires significant skills and costs. Totally subcutaneous ICD (S-ICD) is designed to afford the same life-saving benefit of the conventional TV-ICDs while avoiding the shortcomings of the TV-leads and to simplify the implant techniques and hence expand the use of ICDs in clinical practice. It becomes commercially available after receiving CE mark in 2009, and its use increased significantly after its FDA approval in 2012. This review aims to give an overview of the S-ICD system components, implantation procedure, clinical indications, safety, efficacy, and future directions.

## 1. INTRODUCTION

Sudden Cardiac Death (SCD) is a significant health problem worldwide. The SCD is defined as an unexpected natural death due to cardiac causes that occurs within 1 hour of symptoms onset, in a person with known or unknown cardiac disease [1]. The incidence of Emergency Medical Services (EMS)-assessed Out-of-Hospital Cardiac Arrest (OHCA) in people of any age is 57 individuals per 100, 000 population based on the Cardiac Arrest Registry to Enhance Survival (CARES) registry of EMS-treated OHCA [2].

Multiple randomized controlled trials have shown that Implantable Cardioverter Defibrillators (ICDs) are effective life-saving management option for individuals at risk of SCD in both primary [3-6] and [7, 8] secondary prevention.

The first successful ICD implant in human was in 1980 with thoracotomy and [9] implantation of epicardial electrode patches. The first generation of ICD was only capable of defibrillation. Later, the ICD device received FDA approval in 1985. Over the years, the ICD technology evolved further and transvenous ICD (TV-ICD) has been developed with the ability of bradycardia and anti-tachycardia pacing, and biphasic waveform shock. The conventional TV-ICDs utilize a transvenous lead that passed via venous system to the right ventricle for appropriate detection and therapy of ventricular arrhythmias. Despite the proven efficacy and safety of the TV-ICD, there are potential complications associated with its use, including localized pocket or wound infection or systematic infection, a vascular access related complication such as pneumothorax, and venous thrombosis, and lead related complications such as dislodgement, malfunction, and perforation. Furthermore, implantation of these devices requires adequate experience and skills and the use of fluoroscopy. Transvenous leads placement in children is problematic due to small venous capacity and the ongoing growth. It is also problematic in patients with venous anomaly or occlusion, those with no venous access to the heart or with intracardiac shunts due to thromboembolic risk, and patients with high infection risk like those with Human Immune Deficiency (HIV) or dialysis. Transvenous leads extraction, when needed, is

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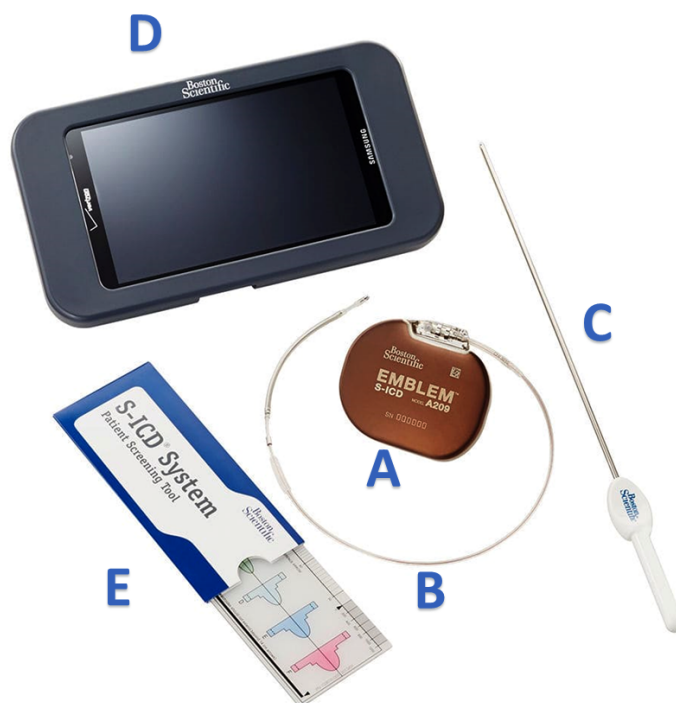
**Fig. (1).** Subcutaneous Implantable Cardioverter Defibrillator (S-ICD) system components.
A: Pulse generator, B: Subcutaneous Electrode, C: Electrode Insertion Tool (EIT), D: Programmer, E: Electrocardiogram (ECG) screening tool. *(Image courtesy of Boston Scientific Corporation, with kind permission to reprint).*

associated with considerable morbidity & mortality and requires considerable skills and costs.

Considering the limitations of the TV- ICD system, a totally subcutaneous ICD (S-ICD) is designed to provide the life-saving benefit of the conventional TV-ICDs while avoiding the shortcomings of the TV-leads, and to simplify the implant techniques and hence expand the use of ICDs in clinical practice [10]. It becomes commercially available after receiving CE mark in 2009, and its use has been significantly increased after its approval by United States Food and Drug Administration (FDA) in 2012.

## 2. S-ICD SYSTEM COMPONENTS (Fig. 1)

The S-ICD is comprised of the following four parts [11]:

- Pulse Generator: it is enclosed in a titanium case, and it can provide an 80-Jouls (J) biphasic shock with a charge time of about 10 seconds. The first generation of S-ICD (S-ICD™, SQ-RX 1010, Boston Scientific, Marlborough, Massachusetts, United States) had estimated battery longevity of 5.1 years, which increased to 7.3 years in the second generation (EMBLEM MRI S-ICD, Boston Scientific, Marlborough, Massachusetts, United States). It cannot provide long-term pacing; however, it may deliver post-shock bradycardia pacing for up to 30 seconds if there is 3.5 seconds pause or more.

- Subcutaneous Electrode: It is a single lead-containing both sensing and defibrillating components. It is composed of a proximal, and a distal sensing electrode positioned adjacent to either end of a 3-inch defibrillation coil electrode.

- Electrode Insertion Tool (EIT): It is a tool used to create a subcutaneous tunnel to facilitate implantation of the subcutaneous Electrode [11].

- Programmer: it is a dedicated external programmer that is easily mobilized and has simple programming functions. The malfunctioning company (Boston Scientific, Marlborough, Massachusetts, United States) is planning to unify the S-ICD programmer with its current pacemakers and TV-ICDs devices programmer.

## 3. SENSING OF THE SUBCUTANEOUS SIGNAL

In the S-ICD system, there are three bipolar sensing vectors for arrhythmia detection (Fig. **2**); these consist of the primary vector (proximal electrode ring to can), the secondary vector (distal electrode ring to can) and an alternate vector (distal electrode ring to proximal electrode ring). The S-ICD automatically selects the most appropriate vector for rhythm detection according to the highest R amplitude and the most satisfactory R-wave/T-wave ratio to minimize the risk of double QRS counting and T-wave oversensing [12]. However, polarity can also be switched manually [10].

## 4. IMPLANTATION OF S-ICD

### 4.1. Pre-procedure Electrocardiogram (ECG) Screening:

Screening ECG test using a pre-operative screening tool (Fig. **3**) is an important method to ensure suitable subcutaneous sensing signals. It is crucial to enhance the S-ICD system sensitivity and specificity for rhythm identification and therapy and to reduce the risk of inappropriate shocks. It is usually performed in all patients with two postures (lying down and sitting or standing). The screening test may be performed manually using the ECG machine or automatically (Automated Screening Tool (AST)) by connecting the ECG electrodes to the Boston Scientific programmer. The manual screening is performed by placing the ECG machine
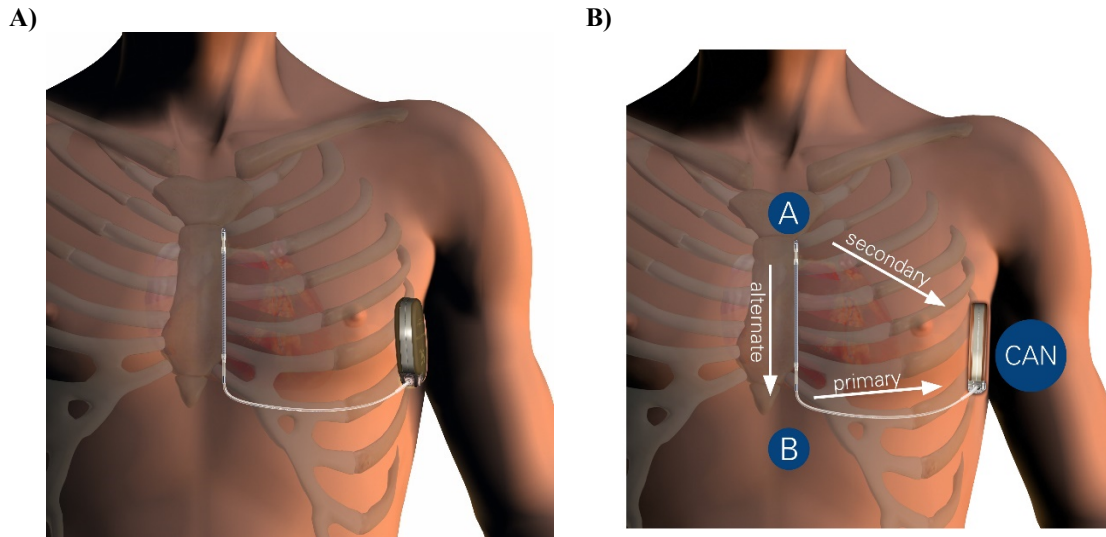
**Fig. (2). A**: Schematic presentation of the S-ICD system position. **B**: Shocking vectors of the S-ICD system: Primary, secondary and alternate. S-ICD – Subcutaneous Implantable Cardioverter Defibrillator – Boston Scientific. *(Image courtesy of Boston Scientific Corporation, with kind permission to reprint).*
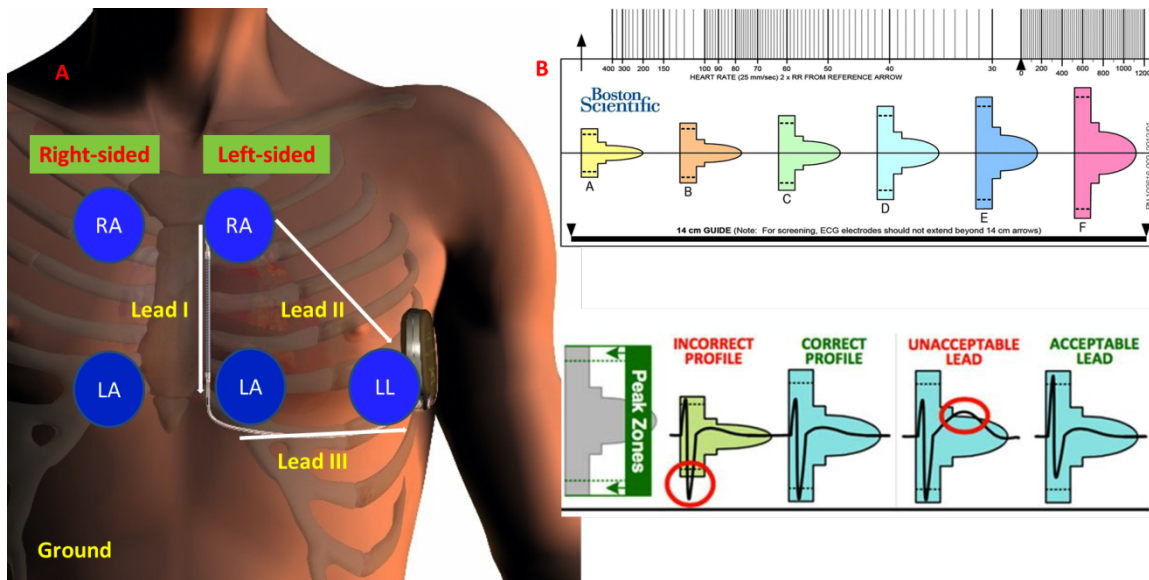


**Fig. (3). A**: Location of the surface electrocardiogram (ECG) electrodes positions during screening for eligibility for subcutaneous implantable cardioverter- defibrillators (S-ICD) in conventional left and right parasternal configurations. **B**: ECG screening tool with examples of acceptable and unacceptable QRS complexes and T-waves.
RA: right arm; LA: left arm; LL: left leg.

Left Arm (LA) electrode at the intended proximal sensing electrode (about 1 cm above the xiphoid process and 1 cm lateral to the left sternal border), placing the Right Arm (RA) electrode at the expected position of the distal sensing electrode (14 cm superior to the LA electrode on the left parasternal line) and placing the Left Leg (LL) at the intended S-ICD device site (at 5th intercostal space laterally along midaxillary line). At least one of the three sensing configurations should be acceptable in both postures with QRS complex fit within the screening template in both supine and sitting or standing positions (Fig. **3**). AST applies the Vector Select algorithm that is used by the S-ICD to sense the cardiac signal and is designed to more closely represent S-ICD device performance. Although validation data from Boston

Scientific showed that AST has 24% more likely to predict the performance of vector select than the manual screening tool with more tolerance of large T-waves than manual screening tool, a recent study showed that the ECG machine screening passes more subjects [13]. There is no data about the rate of inappropriate shock between these two methods.

Cohort studies showed 7% to 11% failure rate of S-ICD screening, and S-ICD implantation is not recommended in these patients because of increased risk of under or oversensing [14-16].

Although S-ICD appears very attractive in young patients with no indication for pacing such as those with Hypertrophic Cardiomyopathy (HCM), inherited arrhythmia syn-

dromes (*e.g.* Brugada Syndrome (BrS), Long QT syndrome, and Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (ARVC/D)), and Congenital Heart Disease (CHD) patients, the S-ICD screening test failure is relatively high in these patients.

HCM patients have a large-amplitude T waves and QRS complexes which may increase the odds of screening failure [15]. Based only on standard screening methodology with left parasternal sensing position, about 38% of HCM patients were ineligible for the S-ICD with 1-vector safety and 71% were ineligible with ≥2-vector safety as recommended in the ESC guidelines [17]. About 10% of total failed ECG screening in HCM patients occurred on exercise [18].

S-ICD screening failure occurs in up to 13% of patients with inherited arrhythmia syndromes with a higher rate of screening failure in BrS patients as compared with other cardiac channelopathies due to the presence of high T wave voltages. Ajmaline challenge unmasked sensing failure in about 14.8% of drug-induced BrS patients previously considered eligible for S-ICD [19, 20]. However, BrS patients are liable to have inappropriate shocks caused by T-wave oversensing even with conventional TV-ICDs [21].

In ARVC/D patients, the negative T-waves (NTWs) in the right precordial leads may partially or entirely revert with exercise in most patients [21]. This may result in the lack of consistency of an appropriate sensing vector both at resting and during exercise [22], or inappropriate ICD detection and therapy [23].

Patients with CHD commonly have conduction system disease with prolonged QRS duration which is one of the predictors of failed S-ICD screening [15]. However, there were no significant differences observed between S-ICD

eligibility in complex CHD patients and controls in a study that evaluated ECG vector screening in 30 patients with CHD and ten control subjects [24].

Consideration of alternative screening positions like right parasternal side, screening during the exercise test, or under drug administration might be helpful in HCM and inherited arrhythmia patients. Furthermore, screening with an external S-ICD to evaluate sensing at rest and during exercise in all three sensing vectors (algorithm-based screening) was shown in a small study to improve patients' selection and reduce the number of false positive and false negative ECG screening of the standard screening method [25].

### 4.2. S-ICD Implantation Procedure

The procedure is typically performed in the electrophysiology laboratory under standard sterile conditions and general anesthesia. However, there is an increase in S-ICD implantations with conscious sedation [12] or Monitored Anesthesia Care (MAC) [26]. The left arm is usually abducted to about 60°, and a dummy of the S-ICD and lead is secured to the patient's chest by adhesive plaster. The positioning of both is guided by anatomical landmarks, as suggested by the manufacturer user's manual [11], in the left thoracic region with the device pocket at the fifth intercostal space between the mid and anterior axillary lines, and the lead position about 1-2 centimeters (cm) to the left of the sternal midline. Although not mandatory, fluoroscopy might be used to ensure the appropriate position of the lead and S-ICD device relative to the heart silhouette. The S-ICD device and lead positions are drawn onto the chest, as well as the incision line for the pocket creation along the chest Langer's lines (Fig. **4**). Following sterile draping, an incision is made at the predefined Langer's lines along the inframammary crease at
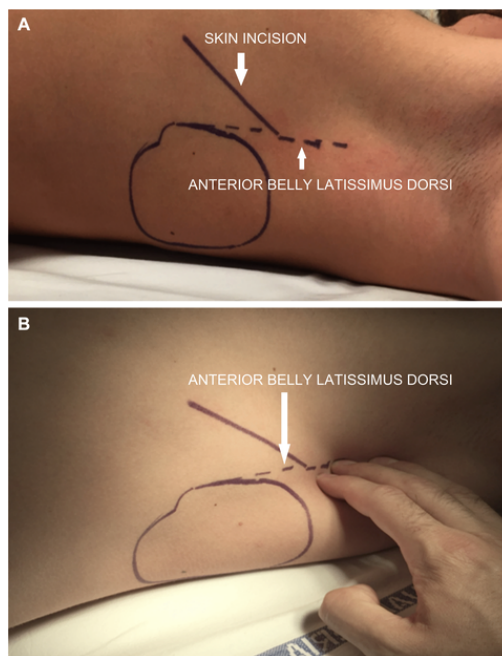


**Fig. (4).** Anatomical landmarks for the intermuscular device pocket. The skin incision is made along the inframammary crease about 2 cm above and tangent to the anterior belly latissimus dorsi (**A**). Note the display of the latisssimus dorsi using the fingers as shown in (**B**). (adapted from reference 30 Migliore F *et al.* Intermuscular Two-Incision Technique for Subcutaneous Implantable Cardioverter Defibrillator Implantation: Results from a Multicenter Registry. Pacing Clin Electrophysiol 2017; 40(3): 278-85).

the anterior edge of the latissimus dorsi. The subcutaneous tissue is dissected directly down to the muscular fascia to create the pocket with ensuring good hemostasis for a subcutaneous pocket positioning [27]. Alternatively, submuscular implantation to place the pulse generator underneath the serratus anterior muscle or subfascial implantation underneath the fascial layer on the anterior side of the serratus anterior muscle [27]. The other approach would be an intermuscular pocket position by blunt dissection between the posterior surface of the latissimus dorsi muscle and the anterior surface of the serratus anterior muscle to have the pocket in the virtual anatomical space between the two muscles [28] (Fig. **5**).

A 2-cm small horizontal incision is made at the level of the xiphoid process (xiphoid incision) in the direction of the pocket incision. The EIT is inserted at the xiphoid incision and tunneled laterally until the distal tip emerges at the device pocket, and then a suture material is used to tie the anchoring hole of the electrode (lead) to the EIT. The EIT is pulled back through the tunnel to the xiphoid incision until the proximal sensing electrode emerges, and then a suture sleeve is placed over the electrode shaft about 1 cm below the proximal sensing electrode. The preformed grooves on the sleeve are used to bind the suture sleeve to the electrode shaft using nonabsorbable suture material. For three incision techniques, a third incision is made at the manubrio-sternal junction 1 to 2 cm left from the midline. The EIT inserted at the xiphoid incision is tunneled to the super parasternal incision, with following the curvature of the sternum by forcing the tip of the EIT directly over the bone tissue of sternum. The lead is then pulled upwards from distal to proximal and fixated.

In the two-incision implantation technique [29, 30] the superior parasternal incision is omitted to reduce the infection risk and to improve the esthetic result. The EIT is covered by an 11-French peel-away sheath and then tunneled from the xiphoid incision in a cranial direction over the sternum approximately 14 cm superior to the xiphoid incision and approximately 1-2 cm to the left or right of the sternal midline. After tunneling, the sheath is advanced over the EIT. The EIT is removed, and the peel-away sheath is left in its subcutaneous position. The electrode is inserted into the subcutaneous sheath until the suture sleeve reaches the opening of the sheath. The sheath is peeled away, leaving the electrode in place. The proximal end of the lead is inserted into the connector port in the device header of the S-ICD, and the screw set tightened. Thus, the device is located in the pocket and anchored to the fascia to prevent possible migration using nonabsorbable suture material. Finally, after device [27] setup, the incisions are closed using intradermal suture.

## 5. DEFIBRILLATION THRESHOLD TESTING AND S-ICD PROGRAMMING

The term Defibrillation Threshold (DFT) testing refers to the minimum shock strength that defibrillates the heart [31]. After the successful implantation of the S-ICD system and before closure of the pockets, DFT is performed -if there is no contraindication- with induction of Ventricular Fibrillation (VF) by 50- Hertz (Hz) stimulation. The DFT is generally considered successful if the device detects and terminates VF using a 65-J shock.
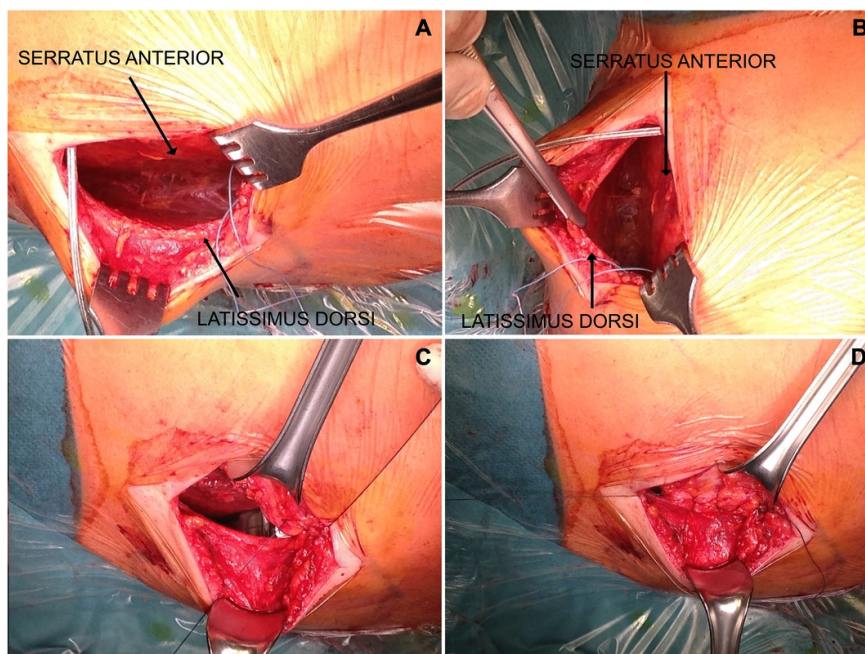


**Fig. (5).** Intermuscular pocket is created by blunt dissection between the anterior surface of the serratus anterior muscle and the posterior surface of the latissimus dorsi muscle, over the left sixth rib between the midline and anterior axillary line (**A** and **B**). The pulse generator is placed into the virtual anatomical space between the two muscles and anchored to the fascia to prevent possible migration. Subsequently, the two muscles are sutured using conventional absorbable suture (**C** and **D**).
(adapted from reference 30 Migliore F *et al*. Intermuscular Two-Incision Technique for Subcutaneous Implantable Cardioverter Defibrillator Implantation: Results from a Multicenter Registry. Pacing Clin Electrophysiol 2017; 40(3): 278-85.)

DFT is currently not required in all cases of TV-ICD. The Cardioverter defibrillator implantation without induction of ventricular fibrillation: a single-blind, non-inferiority, randomised controlled trial (SIMPLE) has shown that DFT is not necessary for TV-ICD systems [32]. However, DFT is still recommended for S-ICD devices. S-ICD implantation in intermuscular space and more posteriorly showed a high success rate of DFT [28] and S-ICD implantation without DFT using this approach seems to be safe in one small study without performing DFT [33].

The detection zone is programmed from 170-250 beats per minute (bpm) with the device having a total storage capacity of 24 episodes (*i.e.*, maximum of 120s of recorded electrograms per event) [10]. The S-ICD device programming features included two tachyarrhythmia detection zones: (1) in the shock zone, detection and therapy are based on the heart rate only. The S-ICD system calculates the heart rate as the average of the last four intervals and performs tachycardia analysis using an18/24 duration criteria. The analysis is repeated to confirm the presence of tachyarrhythmia after capacitor charging (average time of $14 \pm 2$ s) but before shock delivery. (2) In the conditional zone, morphology analysis algorithm and stability are applied in addition to the heart rate [10]. Rate cutoffs are individualized for each patient based on the clinical indications. In the non-randomized multicenter EFFORTLESS S-ICD registry, the inappropriate shock rate was reduced with dual-zone programming to 6.4% compared to 12% with single-zone programming [34]. If the Ventricular Arrhythmia (VA) is confirmed, the device can deliver up to 5 shocks of 80 J. The polarity is automatically reversed for each successive shock if the first shock is unsuccessful [35].

The sensing vector (primary, secondary, or alternate) is automatically selected by the device at the time of implantation and optimized during supine and upright positions before discharge.

## 6. THE S-ICD EFFICACY

The main function of the ICD is to appropriately detect and treat life-threatening VAs.

DFT performed at the time of device implant, is used to predict shock efficacy in the event of VA. The S-ICDs have been shown to be effective in terminating VAs during DFT.

Although the mean DFT is higher in S-ICDs compared to TV-ICD (36.6+/-19.8 J *vs*. 11.1+/-8.5 J) as shown in a study with 49 patients, the absolute DFT safety margin is slightly greater in the S-ICD [10]. The same study reported 100% sensitivity for detection of induced VF and 98% shock efficacy [10]. Data from the IDE and EFFORTLESS studies with eight hundred eighty-two patients who underwent S-ICD implantation with a mean follow up of 651±345 days showed spontaneous VAs termination with one shock in 90.1% and within the five available shocks in 98.2% [36]. These VAs conversion rates are comparable to those observed with TV-ICDs.

## 7. THE S-ICD SAFETY

The S-ICD is mainly developed to avoid the risks associated with intravascular leads implantation in the TV-ICD procedures. To achieve this purpose, the side effects of the S-ICD must be acceptable and not higher than TV-ICD. Significant problems associated with early S-ICD implants included device infection, lead migration, and to a lesser extent, implant-site hematoma and device erosion. There is a decreasing incidence of these complications with more operator experience and improving device profile.

The possible complications of S-ICD include (Table **1**):

Infection: Although S-ICD device infection has been reported as high as 9.9% [37], the rate of documented or suspicion of infection related to the S-ICD procedure ranges from 1.3 to 5.9% in the S-ICD registries. Fortunately, infection is superficial in most cases, and the need to explant the device is 1.2 to 2.1%.

The infection rate currently is comparable to that of TV-ICDs reported as 0.13% to 1.9% [38-41].

None of the S-ICD infections reported in the IDE trial and EFFORTLESS registry were associated with endocarditis or bacteremia [34, 38]. As with TV-ICDs, S-ICD–related infections require individualization of care to determine in which circumstances device explant or other invasive management is necessary.

Hematoma: Multiple cohorts, including the IDE trial, report no implant-related hematomas [38]. The reported hematoma rate is 0.2 to 1.4 % [34, 42]. Hematoma formation rate with TV- ICD is 0.86% in the National Cardiovascular

**Table 1.    Comparison between TV-ICD and S-ICD complications.**

| | **TV-ICD** | **S-ICD** |
|---|---|---|
| Infection | 0.13% to 1.9%<br>Risk of bacteremia and IE | 1.3 - 5.9% (device explanation rate is 1.2 - 2.1%)<br>Very low risk of bacteremia and IE |
| Hematoma | 0.86 - 2.4% | 0.2 -1.4 % |
| Device erosion | Usually reported with infection | 1.7% -1.8% |
| Lead-related complications | 20% leads failure rate over 10-years | 0.86% lead migration |
| Inappropriate shocks | < 5% | 5-25% |

S-ICD: Subcutaneous of Implantable Cardioverter Defibrillator.
TV-ICD: transvenous Implantable Cardioverter Defibrillator.

Data Registry, and about 1.2% to 2.4% in randomized clinical trials [43-45].

Device erosion: An early experience with S-ICD reported a high rate of device erosion of 18.8% [37]. However, it is much less in the following studies. The rates range from 1.7% to 1.8% in the trials reporting pulse generator erosion [39]. The reduction in the size of S-ICD pulse generator may help reducing device erosion complication.

S-ICD Lead migration: In early studies with S-ICD system, lead migration was identified as a worrisome problem. It often requires lead revision. Lead migration exposes the patient to inappropriate ICD shocks due to myopotentials and T-wave oversensing [10, 46]. With the introduction of the suture sleeve that secures the lead at the lower sternal (xiphoid) incision by the manufacturer, lead migration has been reduced significantly. Lead migration in the EFFORT-LESS registry was 0.85% [34]. The S-ICD lead has no central lumen, which provides higher tensile strength, and does not require a stylet for placement [47]. The S-ICD lead has less exposure to environmental stress due to its subcutaneous location. In the European Regulatory Trial with a follow-up of 5.8 years, there were no reported lead malfunctions or failures [48]. In comparison, the traditional TV-leads failure rate is approximately 20% over 10-years [49].

Inappropriate shocks: In the first trials and patient cohorts, the inappropriate shock rate ranges from 5% to 25% [10, 45]. Currently, the TV-ICDs have inappropriate shock rates of <5% [50]. The S-ICD inappropriate shocks are often due to T-wave oversensing, but may occur due to lead migration, or Supraventricular Tachycardias (SVTs). The lead migration as a cause of inappropriate shocks has been reduced significantly with the introduction of the lead suture sleeve, as mentioned earlier. Software update to improved SVT discrimination and device reprogramming are expected to reduce the inappropriate shocks due to SVT. ECG screening pre-implantation aims to reduce T-wave oversensing and double counting. T-wave oversensing after implant can most often be managed noninvasively through device programming [34, 42]. A novel discrimination algorithm to reduce T-wave oversensing without compromising tachyarrhythmia discrimination should further reduce such inappropriate shocks [51]. Changes in QRS morphology after the sinus rhythm template is acquired at the time of S-ICD implantation, such as the development of right or left bundle branch block, which is a less common cause of inappropriate shocks. This can typically be managed noninvasively by acquiring a new QRS morphology template that the device uses for comparison during arrhythmia episodes. Furthermore, the introduction of two zones with a conditional zone, which applies SVT discriminators, and a shock zone for rates >220 bpm reduces inappropriate shocks.

These changes reflect the findings of the prospective, multicenter START (Subcutaneous *versus* Transvenous Arrhythmia Recognition Testing) trial, which compared discrimination algorithms of the S-ICD with TV-ICD systems [35]. In this study, both transvenous and cutaneous (S-ICD sensing vectors) were recorded simultaneously during atrial and ventricular arrhythmia induction. Signals were interpreted offline by the S-ICD and traditional TV–ICDs from 3 manufacturers [35]. Appropriate detection of VAs for S-ICD

and TV-ICD in single- and dual-zone configurations was 100% and >99%, respectively. Specificity for SVTs was significantly better for the S-ICD system compared to 2 of 3 TV-ICD systems, as well as the composite of TV devices (98.0%[S-ICD] *vs.* 76.7% [single chamber device range: 64.0-92.0%] *vs.* 68.0% [dual chamber device: 32.7-89.8%; P < 0.001]) [35]. Dual-zone programming increased with experience of the individual implanter, which reduced inappropriate shock rate significantly [52]. The specificity of TV-ICDs was inferior to that of the S-ICD [35, 52, 53]. Currently, the inappropriate shock rate appears comparable to that of TV-ICDs due to the software and programming updates in the recent versions of the S-ICD. However, one should keep in mind that there has been no head-to-head comparison in equivalent patient populations. The inappropriate shock rate of 7% was seen in EFFORTLESS registry with primarily using dual-zone programming and higher shock cutoff rates [34]. TV-ICD registries report inappropriate shock rates of 4% to 18% [54-56]. However, newer TV-ICDs device algorithms have shown lower inappropriate shock rates. The ADVANCE III (Avoid Delivering Therapies for Non-sustained Arrhythmias in ICD Patients III) trial, randomized ICD patients to a long detection setting (30 of 40 intervals) and nominal setting (18 of 24 intervals) for VAs with cycle length ≤ 320 ms in both primary and secondary prevention populations and demonstrates a reduction of overall therapies and shocks in the subgroup of secondary prevention patients [57]. Over a median follow up period of 12 months, the long detection period was associated with a 25% reduction in the number of overall therapies and a 34% reduction in the number of shocks [57].

Rarely inappropriate S-ICD therapy may occur due to oversensing arising from artifact due to subcutaneous air in a newly implanted S-ICD. Air entrapment within the parasternal or device pockets may produce S-ICD system malfunction. These caused by the insulation of the sensing contact ring by the accumulation of air in the pocket. Recovery of sensing vector is expected in few days with the disappearance of the subcutaneous air [58, 59].

Anecdotally, inappropriate S-ICD shock may occur due to noise generated by S-ICD electrode contact with sternotomy wires [60].

## 8. THE APPROPRIATE CANDIDATES FOR SUBCUTANEOUS ICD THERAPY AND THE S-ICD RECOMMENDATIONS IN THE CURRENT CLINICAL GUIDELINES

First, it should be clear that patients who need bradycardia pacing, Cardiac Resynchronization Therapy (CRT), or likely to benefit from ATP therapy are not candidates for S-ICD at present.

The S-ICD therapy may be best for patients at a young age with an anticipated long-term need for the defibrillation function, patients with primary prevention indication, those with poor vascular access, previous CIED infection, or a higher infection risk (*e.g.*, Patients with mechanical valves, diabetes, or renal dysfunction).

In the 2015, European Society of Cardiology (ESC) guidelines for the management of patients with ventricular

arrhythmias and the prevention of sudden cardiac death, it is stated that S-ICD 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 anti-tachycardia pacing is not needed (Class IIa, Level of evidence C) [61].

The Canadian Cardiovascular Society/Canadian Heart Rhythm Society (CCS/CHRS) 2016 Implantable Cardioverter-Defibrillator (ICD) Guidelines [62] recommend S-ICD in patients with limited vascular access or pocket sites in whom an ICD therapy is indicated (Strong Recommendation; Low-Quality Evidence). The implantation of an S-ICD might be considered in patients in whom an ICD is recommended who have one of the following conditions:

- Congenital Heart Disease patients with no access to the ventricles.

- Congenital Heart Disease patients with shunt resulting in increased risk of thromboembolic events with TV-ICD.

- The absence of a pocket site due to either prior device-related infection and/or chronic indwelling catheters [46].

In the 2017 American heart association/ American College of Cardiology/ Heart Rhythm (AHA/ACC/HRS) guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death, the S-ICD is recommended in patients who meet criteria for an ICD who have inadequate vascular access or are at high risk for infection, and in whom pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated, a subcutaneous implantable cardioverter-defibrillator (Class I, Level of evidence B-NR) [63] (Table **2**).

## 9. HOME MONITORING

Automatic remote home monitoring has been shown in large randomized prospective trials of all types of CIEDs to have superior performance to conventional care [64].

The current S-ICD system has the feature of remote monitoring (LATITUDE™ Home Monitoring System) which provides S-ICD patients with all the advantages of home monitoring.

## 10. THE COMBINATION OF S-ICD WITH OTHER CARDIAC IMPLANTABLE ELECTRONIC DEVICES (CIEDS)

The combination of S-ICD with a transvenous pacemaker when bradycardia pacing indication emerged in patients with S-ICD is shown to be successful in small case series [65, 66]. Combination of S-ICD with cardiac Contractility Modulation device (CCM) in cardiomyopathy patients with heart failure and narrow QRS complex has been reported [66-68].

Careful assessment for "cross-talk" between the devices is required at the time of device implantation. As there have been no significant studies of the safety and feasibility of this approach, it should be used cautiously at this time [47].

## 11. THE COMBINATION OF S-ICD AND LEADLESS PACING

The lack of pacing function is a major drawback of the S-ICD. However, the need of implanting bradycardia or CRT pacing devices in S-ICD patients is not high. In one study, the need for bradycardia pacing over 5.8 years of follow up was 1.8%, and the need to upgrade to a CRT device was 3.5% [48]. It seems that previous TV-ICD trials may have overestimated the incidence of ATP therapy. An analysis of SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) [6] patients suggests that approximately 15% of patients with New York Heart Association functional class II to III heart failure will experience monomorphic VT necessitating ATP therapy over almost 45.5 months of follow-up [69]. Additionally, studies with TV-ICD showed a reduction in the need for therapies with prolonged detection intervals, due to spontaneous termination of arrhythmia [50, 57]. To overcome this limitation, incorporating leadless pacemaker with S-ICD *via* wireless communication between the two devices is under investigation.

The preclinical acute and chronic performance (3 months) of the combined function of an ATP-enabled LP and S-ICD with appropriate VVI functionality, successful wireless device-device communication, and ATP delivery were demonstrated in one recent study [70].

Clinical studies on safety and performance in human are needed.

**Table 2.** **S-ICD indications in the current clinical guidelines.**

| Guidelines | S-ICD Therapy Recommendation | Recommendation Class | Level of Evidence |
|---|---|---|---|
| 2015 ESC | S-ICD should be considered as an alternative to transvenous defibrillators in patients with an indication for an ICD when pacing therapy for bradycardian support, cardiac resynchronization or antitachycardia pacing is not needed. | IIa | C |
| 2016 CCS/CHRS | S-ICD to be considered in patients with limited vascular access or pocket sites in whom an ICD is recommended. | Strong Recommendation | Low-Quality Evidence |
| 2017 AHA/ACC/HRS | S-ICD is recommended in patients who meet criteria for an ICD who have inadequate vascular access or are at high risk for infection, and in whom pacing for bradycardia or VT termination or as part of CRT is neither needed nor anticipated. | class I | B-NR |

AHA/ACC/HRS: American heart association/ American College of Cardiology/ Heart Rhythm Society; CCS/CHRS: Canadian Cardiovascular Society/Canadian Heart Rhythm Society; ESC: European Society of Cardiology.
Level of evidence: C; Consensus of opinion of the experts and/ or small studies, retrospective studies, registries. B-NR; Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies/ Meta-analyses of such studies. S-ICD: Subcutaneous implantable cardioverter defibrillator.

**Table 3.**   **S-ICD advantages and disadvantages compared to TV-ICD.**

| S-ICD System | |
|---|---|
| **Advantages** | **Disadvantages** |
| It is extravascular (preserves venous access) | Does not provide bradycardia pacing or anti-tachycardia pacing (ATP) |
| Low risk of systemic infection | Lack of advanced diagnostics |
| Avoids risks associated with TV- lead extraction if required | Large Size (Twice that of current TV-ICD) |
| Less or no fluoroscopy | Shorter battery life of 5 -7 years |
| Cosmetic considerations | The need for pre-implantation ECG screening |
|  | It requires DFT testing |

DFT: Defibrillation Threshold.
S-ICD: Subcutaneous Implantable Cardioverter Defibrillator.
TV-ICD: Transvenous Implantable Cardioverter Defibrillator.

## 12. ONGOING CLINICAL STUDIES ON S-ICD

There are currently several ongoing clinical studies that are going to provide more information on the safety and efficacy of S-ICD with a head-to-head comparison to the conventional TV-ICD system in randomized controlled trials. The first study is the randomized prospective PRAETO-RIAN trial [71] which aims to recruit 700 patients from various centers from the Netherlands with class I or IIa ICD indication and without indication for pacing therapy, with 1:1 randomization to S-ICD or TV-ICD systems. The primary study objective is to demonstrate non-inferiority of the S-ICD to the TV-ICD regarding the composite of inappropriate shocks and ICD-related complications. The follow-up is estimated at a median of 30 months. The S-ICD will be programmed with the conditional zone activated with the discriminator rate cutoff between 180 and 250 bpm. The TV-ICDs will be programmed with a monitor zone (> 167 bpm), fast VT zone (> 182 bpm) with one sequence of ATP followed by shocks, and a VF zone with high-energy shocks only (> 250 bpm).

The second study is the Avoid Transvenous Leads in Appropriate Subjects (ATLAS S-ICD) [72], which is Canadian multi-center, randomized open-label parallel group clinical trial. It aims to recruit 500 patients with 1:1 randomization to VVI TV-ICD *vs*. S-ICD, with the assessment of perioperative and long-term device-related complications, and the rate of failed appropriate clinical shocks and arrhythmic death.

The MADIT S-ICD study [73] is designed to test the hypothesis that post-myocardial infarction diabetes patients with relatively preserved ejection fraction of 36%-50% will have a survival benefit from a subcutaneous implantable cardioverter defibrillator.

## CONCLUSION

The S-ICD is an attractive alternative to TV-ICD in patients with an indication for primary or secondary prevention

of SCD and without the need for pacing. It has the advantages of saving the venous system and avoids risks related to vascular access, like pneumothorax and hemothorax, the possibility of device implant without fluoroscopy, less risk of lead-related acute and chronic complications, and less risk of systematic infection. However, it has the limitations of lack bradycardia and anti-tachycardia pacing, larger size with less battery life compared to single chamber TV-ICD, and lack of long-term follow-up (Table **3**).

S-ICD has a favorable efficacy and safety profile, and there is a potential to improve the system functionality by integrating it with leadless pacing.

## LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| ACC | = | American College of Cardiology |
| AHA | = | American Heart Association |
| ATP | = | Anti-tachycardia Pacing |
| CRT | = | Cardiac Resynchronization Therapy |
| CCS | = | Canadian Cardiovascular Society |
| CHRS | = | Canadian Heart Rhythm Society |
| CM | = | Centimeters |
| DFT | = | Defibrillation Threshold |
| ECG | = | Electrocardiogram |
| EIT | = | Electrode Insertion Tool |
| ESC | = | European Society of Cardiology |
| FDA | = | Food and Drug Administration |
| HRS | = | Heart Rhythm |
| Hz | = | Hertz |
| HIV | = | Human Immune Deficiency |
| ICD | = | Implantable Cardioverter Defibrillator |
| J | = | Joules |
| S | = | Subcutaneous |
| SCD | = | Sudden Cardiac Death |
| TV | = | Transvenous |
| U.S. | = | United States |
| VA | = | Ventricular Arrhythmia |
| VF | = | Ventricular Fibrillation |

## CONSENT FOR PUBLICATION

Not applicable.

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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