



REVIEW ARTICLE

# The subcutaneous ICD as an alternative to the conventional ICD system: Initial experience in Greece and a review of the literature



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**Abstract** The introduction of an implantable cardioverter defibrillator (ICD) in clinical practice has revolutionized our therapeutic approach for both primary and secondary prevention of sudden cardiac death (SCD), as it has proven to be superior to medical therapy in treating potentially life-threatening ventricular arrhythmias and has resulted in reduced mortality rates. However, implantation of a conventional ICD carries a non-negligible risk of periprocedural and long-term complications associated with the transvenous ICD leads. The entirely subcutaneous implantable cardioverter defibrillator (S-ICD) has recently emerged as a therapeutic alternative to the conventional ICD for patients with various cardiopathies and who are at high risk of SCD. The main advantage is the avoidance of vascular access and thus avoidance of complications associated with transvenous leads. Patients without pacing indications, such as bradycardia, a need for antitachycardia pacing or cardiac resynchronization, as well as those at higher risk of complications from transvenous lead implantation are perfect candidates for this novel technology. The subcutaneous ICD has proven to be equally safe and effective

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compared to transvenous ICD systems in early clinical trials. Further technical improvements of the system will likely lead to the expansion of indications and widespread use of this technology. In the present review, we discuss the indications for this system, summarize early clinical experiences and highlight the advantages and disadvantages of this novel technology. In addition, we present the first two cases of subcutaneous cardioverter defibrillator system implantation in Greece.

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## 1. Introduction

Despite the significant decrease in cardiovascular mortality over the past 20 years, the incidence of sudden cardiac death (SCD) in the general population is currently estimated at 50–100 per 100,000, and it accounts for approximately 300,000 deaths in the U.S. annually, with proportionate numbers in Europe.<sup>1,2</sup> Since 1980, when they were first introduced in clinical practice,<sup>3</sup> implantable cardioverter defibrillators (ICDs) have shown significant survival benefits in individuals at risk of sudden arrhythmic death.<sup>1,4–8</sup>

The widespread use of the conventional ICD,<sup>9</sup> however, is associated with significant procedural and long-term complications that are mainly associated with the use of a transvenous lead within the right ventricle. These include pneumothorax, cardiac perforation, pericardial effusion and tamponade, lead dislodgement, lead malfunction due to insulation failure or lead fractures, venous occlusion and systemic infections.<sup>10</sup> A recent observational study reported a 1.5% rate of major complications.<sup>11</sup> The incidence of complications appears to be higher in the pediatric population and in younger patients, who are expected to undergo multiple procedures. Recent data suggest a significant decrease in transvenous lead longevity from 91–99% at 2 years to 60–72% at 8 years.<sup>12</sup> Moreover, the extraction of transvenous lead systems, which is occasionally required, is associated with significant procedural risks and high morbidity and mortality.

Recently, an entirely subcutaneous ICD system (S-ICD) has been developed to overcome many of the problems associated with conventional transvenous ICDs. In the present review, the current evidence, target population and other important issues regarding the advantages and disadvantages of S-ICDs are discussed.

## 2. Device features and implantation procedure

The S-ICD system is comprised of two basic components, i.e., a generator and an electrode lead (Fig. 1) that are both implanted subcutaneously.<sup>13</sup>

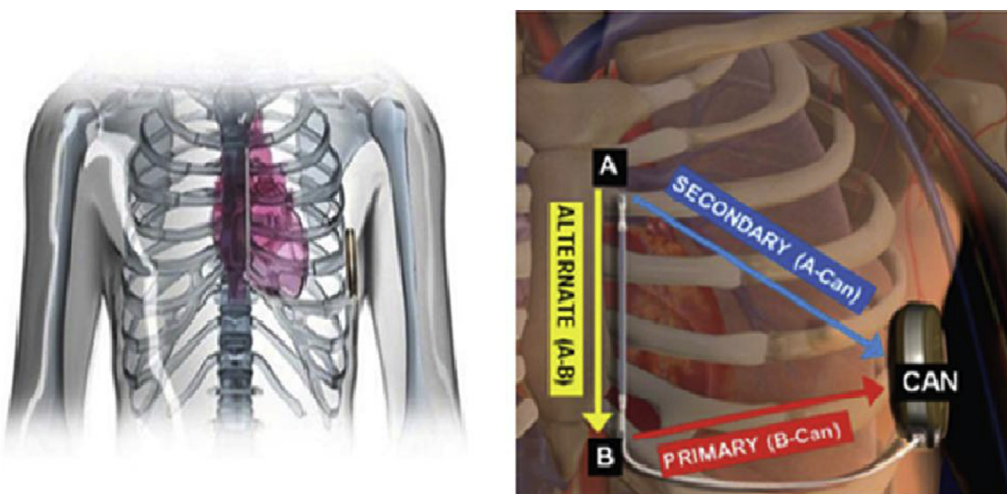
- The pulse generator is placed over the fifth to sixth intercostal space between the left anterior and mid-axillary line (Fig. 2). The device is larger and weighs 145 g, which is approximately double that of a transvenous ICD. The generator is able to (a) provide up to

five high-energy (80 J), non-programmable, defibrillation shocks per episode through the use of a constant tilt of 50° and a biphasic waveform and (b) deliver post-shock bradycardia pacing at 50 beats per minute, using a 200 mA biphasic transthoracic pulse for a period of up to 30 s if >3.5 s of post-shock asystole is detected. The estimated longevity is 5 years for the initial S-ICDs, though it exceeds 7 years for the latest generation models. Additionally, remote follow-up of the device is now available for new S-ICD models.

- The 3-mm lead comprises both sensing and defibrillating properties and is tripolar, consisting of three electrodes; these are the ICD can, a distal electrode on the tip of the defibrillator lead and a proximal electrode located approximately 8 cm from the tip of the lead (Fig. 2).<sup>1</sup> It is positioned such that the distal part is placed parallel and 1 to 2 cm to the left side of the sternum. The distal sensing electrode is localized at the junction of the sternum and the manubrium, while the proximal sensing electrode, which is the anchoring point for the lead, is positioned adjacent to the xiphoid process. Between the two sensing electrodes stands the 8-cm coil for defibrillation against the defibrillator can. Implantation is performed using three incisions (i.e., one for the lateral pocket and two parasternal incisions). The lead is tunneled from the lateral pocket through the parasternal incisions, guided by anatomic landmarks only, without the use of fluoroscopy. The superior parasternal incision is prone to exposure, and subsequently to infection, and it may be aesthetically undesirable to the patient. Thus, alternatively, a two-incision technique



**Figure 1** The subcutaneous ICD system (image courtesy of Boston Scientific Corporation, with kind permission to reprint).



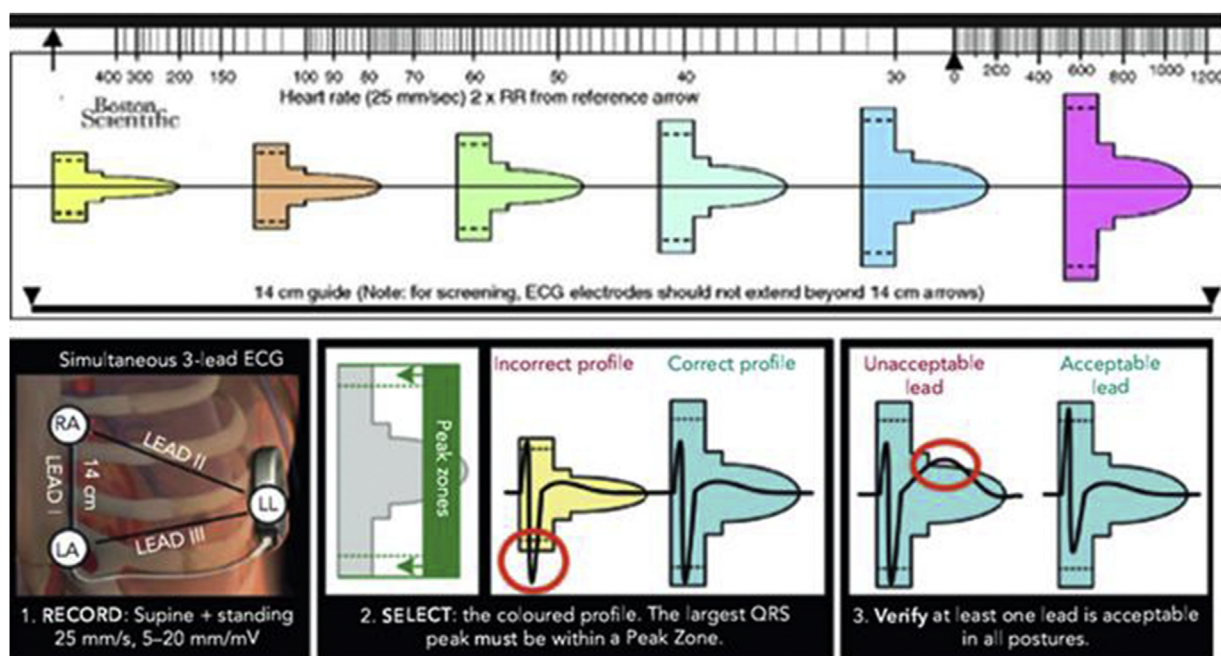
**Figure 2** A, Schematic presentation of the subcutaneous ICD system position (image courtesy of Boston Scientific Corporation, with kind permission to reprint). B, Primary, secondary and alternate shocking vectors of the subcutaneous ICD system (De Maria E, Olaru A, Cappelli S. The subcutaneous defibrillator: who stands to benefit. The e-journal of the ESC Council for Cardiology Practice, Vol 12, No 17, with kind permission to reprint).

avoiding the superior parasternal incision, which was shown to be equally safe and efficacious to the three-incision technique, has been developed.<sup>14</sup> Furthermore, in patients with a more centrally positioned heart, a right parasternal position of the lead may be preferred to include more left ventricular heart muscle in the defibrillation field and achieve optimal sensing.<sup>15</sup>

Arrhythmia detection is performed using 1 of the 3 vectors that are formed between the three sensing poles of the system (Fig. 2)<sup>13</sup>; these consist of the primary vector (i.e., proximal electrode ring-to-can), the secondary vector (i.e., distal electrode ring-to-can) and an alternate vector

(i.e., 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 for double QRS counting and T-wave oversensing.<sup>13</sup> However, polarity can also be switched manually.<sup>13</sup>

In addition, to ensure patient eligibility for an S-ICD, it is recommended to perform a screening electrocardiographic (ECG) template to confirm a satisfactory R-wave/T-wave ratio pre-implantation in no fewer than two postures (Fig. 3).<sup>16</sup> At least one of the three available sensing configurations has to be acceptable in both postures.<sup>13</sup> However, recently it was demonstrated that 15% of candidates



**Figure 3** Screening electrocardiographic ECG template to confirm a satisfactory R-wave/T-wave ratio (image courtesy of Boston Scientific Corporation, with kind permission to reprint).



will not qualify for the S-ICD system due to the lack of an adequate vector.<sup>17</sup>

After the device has been successfully implanted, it is advised to always test the system effectiveness in the lab using a defibrillation test (DFT), although this is no longer necessary for the conventional ICD system.<sup>13</sup> However, this practice is mandatory for the S-ICD because clinical experience and long-term follow-up data are limited and because the studies that established the safety and effectiveness of the system utilized defibrillation testing.<sup>13</sup> During the DFT, conversion of induced ventricular fibrillation (VF) is tested using 65 J, though once implanted the S-ICD delivers a non-programmable 80-J shock to ensure a 15-J safety margin. If the DFT is unsuccessful, the shock vector is reversed. Occasionally, repositioning the generator or lead is necessary, and the defibrillation test is repeated until it is successful.

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 120-s of recorded electrograms per event).<sup>13</sup> Except from the shock zone, the system offers the option of programming two-zone therapy as follows<sup>13</sup>: (1) In the shock zone (corresponding to the VF zone of the transvenous ICD), the S-ICD system calculates the heart rate as the average of the last 4 intervals and performs tachycardia analysis using an 18/24 duration criteria. The only criterion for therapy is the actual heart rate. The analysis is repeated to confirm the presence of tachyarrhythmia after capacitor charging (average time of  $14 \pm 2$  s) but before shock delivery. Thus, the presence of non-sustained tachyarrhythmias is excluded. (2) In the optional rhythm discrimination conditional zone, additional electrocardiographic morphology and stability criteria are used to discriminate ventricular tachyarrhythmia from supraventricular tachycardias and to avoid inappropriate shocks. These criteria include correlation waveform analysis of each ventricular complex comparing the current tachycardia beat with the stored template acquired at rest, evaluation of monomorphic or polymorphic relationships in beat-to-beat analysis (i.e., polymorphic relationship indicates ventricular tachyarrhythmia) and QRS width analysis compared with the baseline template (i.e., wide QRS complexes in combination with a monomorphic relationship indicate ventricular tachycardia). Recent data suggest that dual-zone programming reduces inappropriate shocks and thus is recommended for routine programming.<sup>18,19</sup> 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.<sup>18</sup> If ventricular tachyarrhythmia is confirmed, the device is able to deliver up to 5 shocks of 80 J. If the first shock is unsuccessful, polarity is automatically reversed for each successive shock. Of note, in patients who develop bundle branch block during a supraventricular tachycardia episode leading to incorrect classification of the tachyarrhythmia as ventricular, an ECG template recording aberrant beat morphology can be included provided that this was recognized during screening. In these cases, the QRS-complex and T-wave morphology is compared to a template registered and stored by the S-ICD immediately after implantation to discriminate between supraventricular and ventricular arrhythmias.<sup>20</sup>

As mentioned previously, the S-ICD system is able to deliver post-shock bradycardia pacing on demand for up to 30 seconds. However, the system does not provide long-term pacing and therefore is not adequate for patients with symptomatic bradycardia, with frequent ventricular tachycardia episodes that are likely to benefit from anti-tachycardia pacing (ATP), or who require for cardiac resynchronization therapy.<sup>13</sup>

### 3. Current evidence regarding safety and efficacy of the s-ICD: Present and future

Despite the fact that data and experience are still limited compared to conventional transvenous ICDs, S-ICD technology has expanded worldwide since its initial approval in Europe in 2009.

Results from initial trials were published in 2010 by Bardy et al, and they demonstrated short-term safety and efficacy of the S-ICD. In the pilot trial, which consisted of 6 patients, all 18 episodes of induced VF were successfully detected and defibrillated, although the defibrillation threshold was significantly higher than that of conventional ICD.<sup>13</sup>

However, most evidence is currently obtained from the Investigational Device Exemption (IDE) study,<sup>21</sup> a prospective, non-randomized, multicenter, international trial, and the EFFORTLESS (Evaluation of FactORs ImpacTing CLinical Outcome and Cost Effectiveness) S-ICD Registry,<sup>18</sup> an ongoing, non-randomized, multicenter registry in approximately 50 investigational centers in Europe and New Zealand. To provide real world experience, the target sample size of the EFFORTLESS S-ICD Registry is 1,000 patients with at least 60 months of follow-up. In addition, supplementary evidence regarding the safety and efficacy of the S-ICD has been generated in several other trials.<sup>23–27</sup> A recent meta-analysis of the IDE study and EFFORTLESS Registry included 882 patients who underwent S-ICD implantation and were followed for  $651 \pm 345$  days. In that study, 111 spontaneous VT/VF events were treated in 59 patients. Of these, 100 (90.1%) events were terminated with 1 shock, and 109 events (98.2%) were terminated within the 5 available shocks, demonstrating that the S-ICD system has high efficacy.<sup>22</sup> An overview of the different S-ICD trials is presented in Table 1. Although data on the long-term tolerability and safety of the treatment are currently lacking, initial results from these studies provide evidence for the safety and efficacy of the S-ICD system.

The ongoing Prospective Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter-Defibrillator Therapy (PRAETORIAN) trial aims to recruit 700 patients with class I or IIa indication for ICD but without indication for pacing therapy from various centers at the Netherlands (estimated median follow-up: 30 months). This is the first randomized prospective study to compare the safety and effectiveness of the S-ICD to the conventional transvenous ICD system.<sup>28</sup>

### 4. Indications and patient selection

Because current evidence suggests that subcutaneous defibrillators are effective in preventing SCD, most patients

**Table 1** Safety and effectiveness of the S-ICD system: overview of the different S-ICD trials.

	Patient number (n)	Age (years)	Follow-up	Underlying heart disease			Primary prevention	Success at conversion test of inducible VT/VF	Success at conversion of clinical VT/VF		Incidence of Inappropriate shocks	Incidence of infection need for explantation)
				Ischaemic CM	Idiopathic dilative CM	Other			1st shock	Overall shocks		
Bardy et al <sup>7</sup> (2010)	55	56 ± 13	10 ± 1m	67%	18%	15%	78%	98% (ttt: 14.0 ± 2.5 s)	N/A	100%	9%	3.6%
Lambiase et al <sup>18</sup> (2014) EFFORTLESS S-ICD Registry	472	49 ± 18	558 d	37%	9.1%	53.9%	63%	99.7% (ttt: 15.1 ± 3.8 s)	88%	100% (ttt: 17.5 ± 4.4 s)	7% (o/s: 5.9%)	4% (2.2%)
Weiss et al <sup>21</sup> (2013) IDE study	314 (implanted/ discharged with device)	51.9 ± 15.5	330 d	N/A (previous MI: 41.4%)	N/A	N/A	79.4%	99.8% (ttt: 14.6 ± 2.9 s)	92.1%	97.4%	13.1% (o/s: 8%)	5.7% (1.3%)
Burke et al <sup>22</sup> (2015) EFFORTLESS/IDE pooled analysis	882	50.3 ± 16.9	651 ± 345 d	37.8%	31.8%	30.4%	69.9%	98.6%	90.1%	98.2%	13.1% (o/s and low amplitude signals: 66% of cases)	1.9% (device & superficial infection)
Olde Nordkamp et al <sup>23</sup> (2012) (Dutch cohort)	118	50	18 ± 7 m	38%	18.5%	43.5%	60%	100%	98%	100%	13%	5.9%
Jarman et al <sup>24</sup> (2013) (UK registry)	111	33	12.7 ± 7.1 m	14%	5%	81%	50%	100%	100%	100%	15% (o/s: 82% of cases)	9.9% (4%)
Köbe et al <sup>25</sup> (2013)	69	45 ± 7	217 ± 138 d	15.9%	36.2%	47.9%	59.4%	95.5%	N/A	100%	5.2% (o/s: 100% of cases)	1.4%
Dabiri Abkenari et al <sup>26</sup> (2011)	31	53 ± 16	286 d	58%	13%	29%	67.7%	100% (ttt: 13.9 ± 2.55 s)	N/A	100%	16% (o/s: 85% of cases)	3.2%
Aydin et al <sup>27</sup> (2012)	40	42 ± 15	229 d (median)	22.5%	22.5%	55%	42.5%	97.5%	57.9%	96.4%	5%	0

M, months; d, days; CM, cardiomyopathy; MI, myocardial infarction; VT, ventricular tachycardia; VF, ventricular fibrillation; ttt, time to therapy; s, seconds; o/s, oversensing.

with an indication for ICD implantation could potentially be considered as candidates for the S-ICD.<sup>1</sup> In the recently released (2015) Clinical Practice Guidelines for the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC), the use of the S-ICD system is recommended as an alternative to transvenous ICDs when pacing therapy for bradycardia, cardiac resynchronization or antitachycardia pacing is not needed (*Class IIaC*).<sup>1</sup> Moreover, the device may be useful, alternatively to the transvenous ICD system, when venous access is difficult, in young patients facing a lifetime of device therapy and in patients after the removal of a transvenous ICD system for infection (*Class IIbC*) (Fig. 4).<sup>1</sup>

Aside from the contraindications related to pacing, at present, only speculation can be made regarding the suitability of the subcutaneous system in different patient groups. Current indications for S-ICD implantation are summarized in Table 2. Firstly, the S-ICD may represent a reliable therapeutic alternative when implantation of the conventional transvenous ICD system is either technically difficult and/or associated with increased procedural risk, such as in patients with complex anatomy (e.g., congenital heart disease), lack of venous access, history of lead infection, or those who are immunocompromised.

Moreover, young patients with a long life expectancy are also suitable candidates, as implantation of transvenous

ICDs is associated with significant long-term risk of lead failure and a need for multiple reinterventions. The system has also been successfully used in children,<sup>18,29</sup> though implantation in patients with low body mass index should be carefully considered due to the relatively large and heavy generator.

Furthermore, patients with ion channelopathies and hypertrophic cardiomyopathy (HCM), who are usually younger, those in whom the mechanism of SCD usually involves polymorphic VT or VF, and those with low risk of bradycardia and monomorphic VT requiring ATP theoretically constitute a group where S-ICD may be the preferable option. However, it should be noted that a higher rate of inappropriate shocks due to T-wave oversensing and double-counting has been recorded in these patients. For example, in patients with Brugada syndrome, although clinical efficacy of S-ICD has been demonstrated, inappropriate shock may be more common due to the characteristic QRS- and T-wave morphology and the frequent presence of supraventricular tachyarrhythmias.<sup>24,30</sup> Moreover, in a recent study, HCM, high body weight, prolonged QRS duration, and R:T ratio <3 in the lead with the largest T wave on 12-lead electrocardiogram were independently associated with screening failure.<sup>31</sup> In the same study, it was demonstrated that 7.4% of patients with ICDs who had no indications for cardiac pacing would not have been

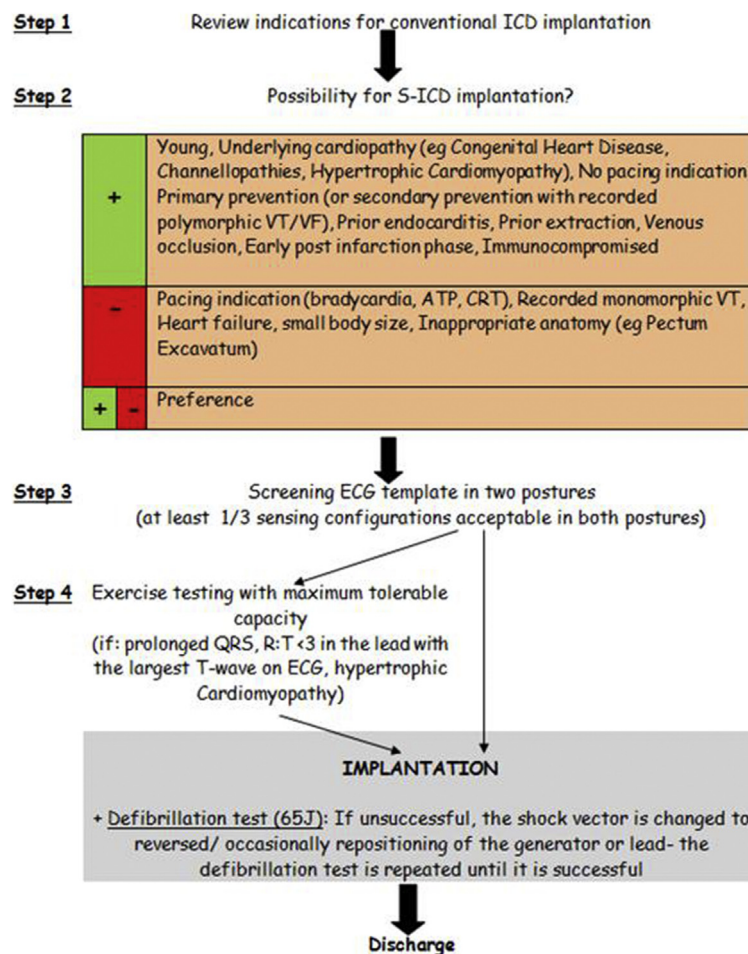


Figure 4 Suggested algorithm for patient selection for implantation of an S-ICD.

**Table 2** Indications for implantation of S-ICDs according to current clinical practice.

Patient group	Comments
Patients with an indication for ICD implantation, when pacing for bradycardia, cardiac resynchronisation or antitachycardia pacing is not needed at the time of implantation and most probably at the future	Any type of underlying heart disease Patient's preference is a determinative factor
Congenital heart disease	Technically difficult with T-ICD
Venous occlusion or thrombosis	Lack of venous access
History of lead infection	Significant risk for infection with T-ICD Possibly, lack of venous access
Previous extraction of a transvenous system	Possibly, lack of venous access
Immunocompromised individuals	Significant risk for infection with T-ICD
Hemodialysis	Significant risk for infection with T-ICD Possibly, lack of venous access
Young patients	Need for multiple re-interventions
Ion channelopathies	Usually young patients SCD usually due to polymorphic VT/VF
Hypertrophic Cardiomyopathy	Usually young patients SCD usually due to polymorphic VT/VF
Early post-myocardial infarction phase (<6 weeks) or early after diagnosis of dilated cardiomyopathy (<3 months)	Bridge therapy

SCD, Sudden Cardiac Death; VT, ventricular tachycardia; VF, ventricular fibrillation; T-ICD, transvenous ICD).

eligible for an S-ICD.<sup>31</sup> Performing an exercise test with maximum tolerable capacity in these patients, as well as adopting a detailed patient screening practice with selection of the optimal sensing vector in different positions, may reduce the risk of T-wave oversensing.

In contrast, in clinical practice, the majority of patients with an indication for ICD suffer from ischemic or idiopathic dilated cardiomyopathy. Clinical studies demonstrated significant safety and effectiveness of the S-ICD in these patients (Table 1), who were mostly recruited in the context of primary prevention of SCD. However, patients with ischemic cardiomyopathy are likely to present with monomorphic VT, for which ATP has proven highly effective at terminating. However, a recent Dutch study of 463 conventional ICD recipients, the majority with ischemic cardiomyopathy, demonstrated that 55.5% did not develop a pacing indication or receive appropriate ATP without subsequent shock from their device, and thus would have been suitable for an initial S-ICD implantation.<sup>32</sup> Patients with a history of sustained monomorphic VT are more likely to need antitachycardia pacing, and thus a conventional ICD system is considered the preferable choice in the context of secondary prevention.<sup>32</sup> Except for secondary prevention, other predictors for the unsuitability of an S-ICD were severe heart failure (NYHA class III/IV) and prolonged QRS duration.<sup>32</sup> In addition, the finding that ICD shocks are associated with higher mortality and a reduction in the quality of life favors the use of ATP therapy. Data from the PainFREE Rx II Trial showed that empirical ATP for fast VT is as effective and safe as an internal shock.<sup>33</sup> Of note, spontaneous termination of VT episodes was observed in 34% of patients in the shock arm. In contrast, all VTs were treated in the ATP group, and no spontaneous termination occurred, suggesting that a considerable proportion of ATP intervention that is delivered before a shock, may be unnecessary.<sup>33</sup>

In patients with the S-ICD system, a significant delay in the initiation and delivery of therapy, due to the more prolonged detection algorithm and charge time compared

to conventional ICDs, has been observed ( $14.6 \pm 2.9$  s compared to  $7.1 \pm 1.6$  s, respectively, in the IDE study).<sup>20,34</sup> In addition, the 5–95% range of the transvenous ICD was narrow at 2.25–7.55 s, whereas for the S-ICD, a positively skewed distribution extending to 24 s of therapy was recorded.<sup>35</sup> It has been suggested that a longer time to detect and deliver a shock likely affords greater leniency for VT events to self-terminate, and because these events would otherwise be treated with a shock and categorized as “appropriate” therapy, this may reduce the number of unnecessary shocks.<sup>20</sup> The MADIT-RIT study demonstrated that both a high-rate programming strategy that treats only high ventricular rates and delayed conventional ICD therapy were associated with significant reductions in the first occurrence of inappropriate therapy, as well as a significant reduction in all-cause mortality.<sup>36</sup> Several S-ICD studies demonstrated that time to therapy for appropriate shocks is within the range of prolongation in detection shown to be beneficial in MADIT-RIT (Table 1).<sup>20,21</sup> Thus, the S-ICD was shown to mimic this programming system by providing high-rate zones of therapy and prolongation of detection-to-shock time to reduce inappropriate shock therapy due to self-termination of VT/VF, likely leading to a consequent reduction in mortality.<sup>20,34</sup> However, debate continues regarding the risks and benefits of prolonged detection allowing for self-termination of VT/VF episodes and potentially reduced mortality from unnecessary ATP and shocks versus potentially higher risk of syncope or avoiding shocks through pace termination of VT.<sup>34</sup>

## 5. Inappropriate shock therapy

Despite the fact that prophylactic ICD implantation improved outcomes in patients with heart disease, inappropriate shocks, which have an incidence of 12–17%, remain a significant clinical problem.<sup>4–8,34</sup> In addition, in the MADIT II trial, inappropriate shocks, but not



inappropriate ATP, were associated with increased mortality risk.<sup>37</sup> Furthermore, studies interestingly demonstrated increased mortality in patients who received appropriate shocks, but not appropriate ATP.<sup>38–40</sup> Supraventricular arrhythmias appear to be the commonest causes of inappropriate therapy in patients with transvenous ICD systems.<sup>6,7,20,39</sup>

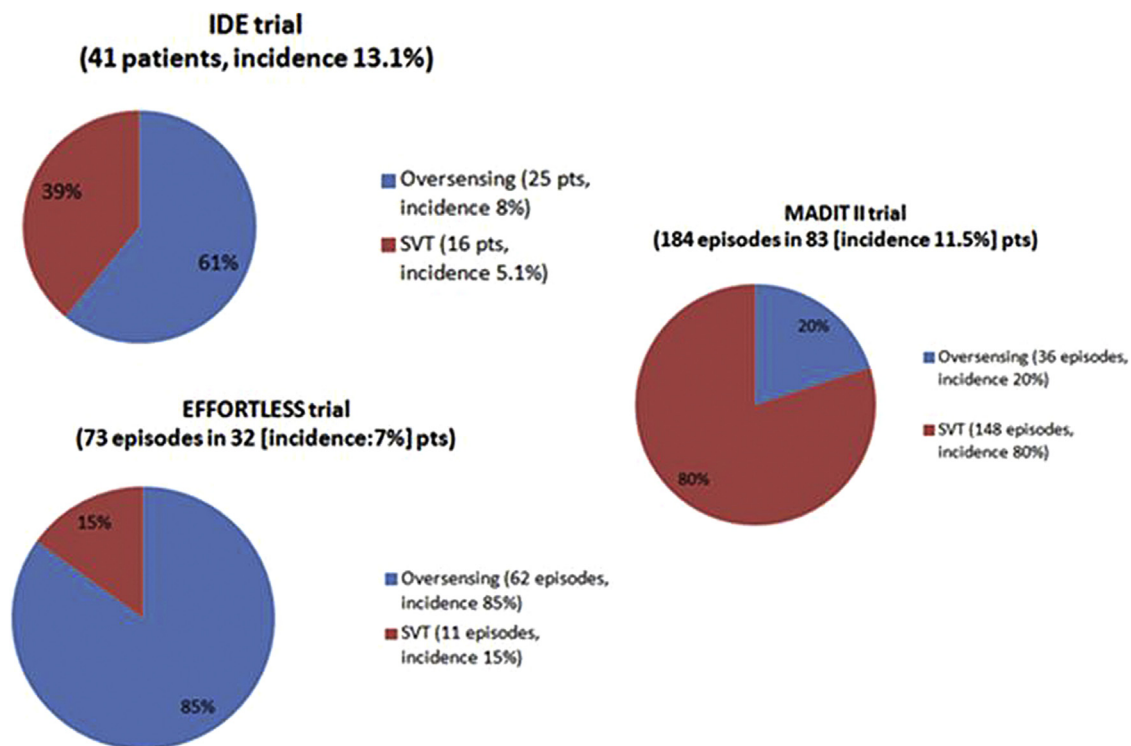
Regarding the subcutaneous ICD system, current data demonstrate a comparable rate of inappropriate shocks with transvenous ICDs (Fig. 5). Reported rates range between 7% and 16% (Table 1).<sup>13,18,21,23–27</sup> In the IDE trial, the incidence of inappropriate therapy was 13.1% (41 patients) over a mean follow-up of 11 months.<sup>21</sup> Oversensing was the commonest cause of inappropriate shocks, which occurred in 25 patients (8%), 22 of whom experienced T-wave oversensing. In 5.1% (16 patients), a shock was delivered due to supraventricular tachycardia. However, none of these inappropriate shocks were delivered in the conditional zone, indicating that programming of a conditional zone significantly reduces the risk of inappropriate shocks for supraventricular tachycardia (70% relative risk reduction).<sup>21</sup> Moreover, in a cohort from the IDE trial, 226 subjects with dual-zone programming were compared with 88 subjects with single-zone programming. The 2-year inappropriate shock-free rates were 89.7% and 73.6% in the dual- and single-zone programming subgroups, respectively, suggesting that the use of dual- rather than single-zone programming is preferable.<sup>19</sup> In patients with HCM and inherited channelopathies, the risk of inappropriate shocks was increased due to T-wave changes, particularly during exercise.<sup>29,34</sup> An exercise stress test is

recommended in these cases to assess the R-wave/T-wave ratio template changes and detect T-wave oversensing during exertion, and the sensing vector should be manually adjusted as necessary.<sup>28,41</sup> In general, T-wave oversensing can be minimized by optimizing the sensing vector prior to implantation and by performing an exercise test examining this vector.<sup>34</sup> Amelioration of the risk of T-wave oversensing could also be achieved by increasing the pre-implantation requisite of satisfactory R-wave/T-wave ratio templates to more than 1.<sup>23,28</sup>

In the EFFORTLESS registry, 73 inappropriate shocks were recorded in 32 patients over an average follow-up of 18 months (inappropriate shock rate: 7%).<sup>18</sup> Oversensing was the major cause of inappropriate shocks in 85% of the cases. Similarly to the IDE study, single-zone programming resulted in a higher inappropriate shock rate than dual-zone programming (12% versus 6.4%).<sup>18</sup>

In summary, the existing data demonstrate a relatively high rate of inappropriate ICD shocks with the S-ICD system, though it is comparable to that of transvenous ICDs. In contrast to the transvenous ICDs, most of the inappropriate therapies appear to occur due to T-wave oversensing resulting in double counting (Fig. 5). The susceptibility to T-wave oversensing was demonstrated in a study utilizing a screening template designed to identify patients who are vulnerable to oversensing prior to insertion and showed that 8% of patients who already had an ICD would fail the screening test.<sup>16</sup>

In contrast, a reduced inappropriate shock rate due to incorrect characterization of a supraventricular arrhythmia has been demonstrated with the S-ICD system compared to



**Figure 5** Inappropriate shock rates among patient populations with the subcutaneous ICD system in the IDE and EFFORTLESS trials and the transvenous ICD system in the MADIT II trial (pts: patients, SVT: supraventricular tachycardia, comprising atrial fibrillation, sinus tachycardia and other forms of supraventricular arrhythmias).



conventional ICDs.<sup>6,7,18,20,21,39</sup> These clinical data are compatible with findings from the Subcutaneous versus Transvenous Arrhythmia Recognition Testing (START) trial, which compared arrhythmia detection by the S-ICD with single- or dual-chamber transvenous ICDs using simultaneous arrhythmia recordings. There was no significant difference in the sensitivity of detecting ventricular tachyarrhythmias between the S-ICDs and transvenous ICDs. However, specificity of the subcutaneous system for discriminating supraventricular arrhythmias was significantly better (98% in S-ICD vs 76.7% in single-chamber transvenous ICD vs 68% in dual-chamber transvenous ICD), suggesting a potential reduction in inappropriate therapies with S-ICDs compared to transvenous ICDs.<sup>42</sup>

## 6. Complications with the S-ICD system

The main advantage of the S-ICD system compared to conventional ICDs is the fact that it avoids vascular access (Table 3). Subsequently, perioperative complications are rare, and several complications associated with the implantation of a conventional ICD system and the presence



**Figure 6** The electrocardiogram of a 48-year-old female, revealing a characteristic spontaneous type 1 Brugada pattern (case 1).

of the transvenous lead, such as pneumothorax, cardiac tamponade and perforation, vascular lesions, and electrode dislocation, are avoided.<sup>43</sup>

In IDE, the 180-day complication-free rate relating to the device, labeling and the insertion procedure was reported at

**Table 3** Advantages and disadvantages of S-ICDs.

Advantages	Comments	Disadvantages	Comments
No vascular access required	Specific potential procedural complications omitted (eg cardiac tamponade, pneumothorax, vascular lesions) Suitable for patients with complex anatomy (eg congenital heart diseases) or no venous access	Pacing for bradycardia, ATP and CRT functions not available	
No fluoroscopy required		Pulse generator larger/heavier, compared to conventional ICD	New generation devices are significantly smaller/lighter
No risk of bacterial endocarditis		Longevity shorter (~5 years) compared to conventional ICD	Longevity of new generation devices >7 years
Better discrimination of supraventricular arrhythmias		Longer charge time & time-to-therapy	Prolongation of detection-to-shock time may reduce inappropriate shocks
Simpler extraction procedure		Simpler diagnostic and therapeutic algorithms	
		Remote monitoring not available	Available in new generation models
		Limited clinical experience	Up-to-date evidence suggests efficacy and safety
		Significant incidence of inappropriate shocks (mostly due to oversensing)	Equivalent to conventional ICD
		Significant incidence of pocket infection	Equivalent to conventional ICD
		Defibrillation test mandatory	
		Pre-implantation ECG screening required	
		Higher cost compared to conventional ICD	

92.1% (lower confidence limit: 88.9%).<sup>21</sup> In addition, in EFFORTLESS, 15 system-related complications occurred in 14 patients (3%) in the first 30 days post-implant, which accounts for a peri-operative complication-free rate of 97%.<sup>18</sup> At 360 days post-implantation, the documented system or implantation-related complication-free rate was 94%.<sup>18</sup> Moreover, it has been reported that more complications occurred with the first implants, suggesting a physician-related learning curve.<sup>23,29,44</sup> In accordance, in the Dutch cohort, the investigators observed that relatively more inappropriate shocks and device-related complications occurred in the first patients. Complication rates then improved with increased operator experience, optimization

of screening for T-wave oversensing on exercise, use of a suture sleeve to prevent lead migration and reductions in implant time.<sup>23</sup> Subsequently, they concluded that both physician-related and device-related learning curves existed.

The main complications associated with the S-ICD system were infection and suboptimal lead position.<sup>20,34</sup> The rate of infection of the generator pocket ranges in trials from 2–10% (Table 1) and occasionally leads in explanation of the system.<sup>43</sup> Interestingly, the incidence of infections may also be related to initial inexperience. In the IDE study, three of 4 cases of infection that required explanation of the system occurred in the first third of the study, a finding that was attributed to a learning curve.<sup>21</sup>



**Figure 7** Implantation of a subcutaneous ICD system in a 48-year-old female (case 1). Initially, an incision was made at the mid-axillary line between the 5th and 6th intercostal spaces (B). The lead was then tunneled from the lateral incision (C) through the two parasternal incisions (i.e., the xiphoid incision and from the xiphoid to the superior incision), and positioned parallel to the left edge of the sternum (D, E). The pulse generator was eventually connected to the subcutaneous electrode and secured in a pocket created at the level of the lateral incision (F, G). After implantation, a defibrillation test was performed and demonstrated inducible VF that was interrupted with a 65-J DC shock (I).

## 7. Conclusions

The subcutaneous ICD has emerged as a promising alternative to conventional ICD systems, as it avoids the potential periprocedural and long-term complications associated with the transvenous leads. Current evidence suggests that S-ICD is a highly effective and safe modality with comparable defibrillation success rate and similar rates of inappropriate shock delivery to conventional ICDs. Thus, a wide range of patients without pacing requirements, and particularly younger patients, may benefit. Ongoing clinical studies will help establish the S-ICD system's long-term safety and efficacy and better define target patient groups. Recent developments in the field of leadless electrodes may expand the indications for S-ICDs.

## 8. Initial experience with the S-ICD system in Greece

We report the first two cases of a subcutaneous ICD implantation in Greece that took place in the electrophysiology laboratory of Hippokrateion General Hospital of Athens in October 2015.

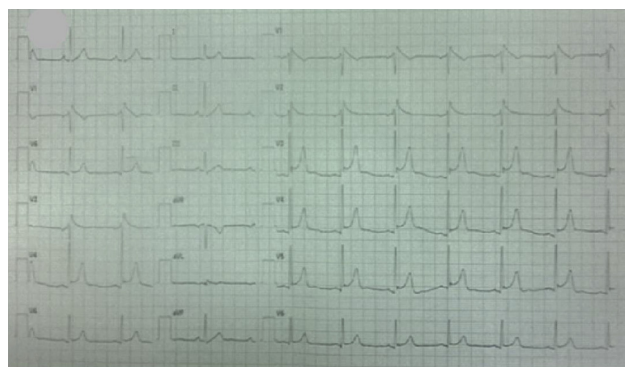
The first patient was a 52-year-old Caucasian female who presented in the Emergency Department of our hospital due to relapsing syncope. The patient reported at least 3 syncopic episodes within a period of 3 months. The electrocardiogram revealed a characteristic spontaneous type 1 Brugada pattern of a coved ST segment elevation of 4 mm in leads V1 and V2 followed by a negative T wave (Fig. 6). Physical examination and blood tests were insignificant. The echocardiographic examination was normal. Thus, the diagnosis of Brugada syndrome was established. According to the current recommendations, the patient was considered to be at high risk of SCD, and the decision was made to implant a subcutaneous ICD (Class IIa) (Fig. 6).<sup>1</sup> Before implantation, a three-lead surface electrocardiogram was performed to assess the appropriateness of surface signals. The patient underwent ICD implantation (Boston Scientific Emblem S-ICD™ System) using the standard three-incision technique. Initially, an incision was made at the mid-axillary line between the 5th and 6th intercostal spaces. The lead was then tunneled from the lateral incision through the two parasternal incisions (i.e., the xiphoid incision and from the xiphoid to the superior incision), and positioned parallel to the left edge of the sternum. The pulse generator was eventually connected to the subcutaneous electrode and secured in a pocket created at the level of the lateral incision. After implantation, a defibrillation test was performed that demonstrated inducible VF that was interrupted with a 65-J DC shock (Fig. 7). A post-implant chest radiography demonstrated optimal placement of the pulse generator and subcutaneous electrode (Fig. 8). The patient underwent an uneventful hospital stay and was discharged 3 days later in stable condition.

The second patient was a 48-year-old Caucasian male. He presented at the outpatient department of our hospital with 2 syncopic episodes, recurrent palpitation, pre-syncope, chest discomfort and dyspnea in the prior weeks. Prior medical history and physical examination were



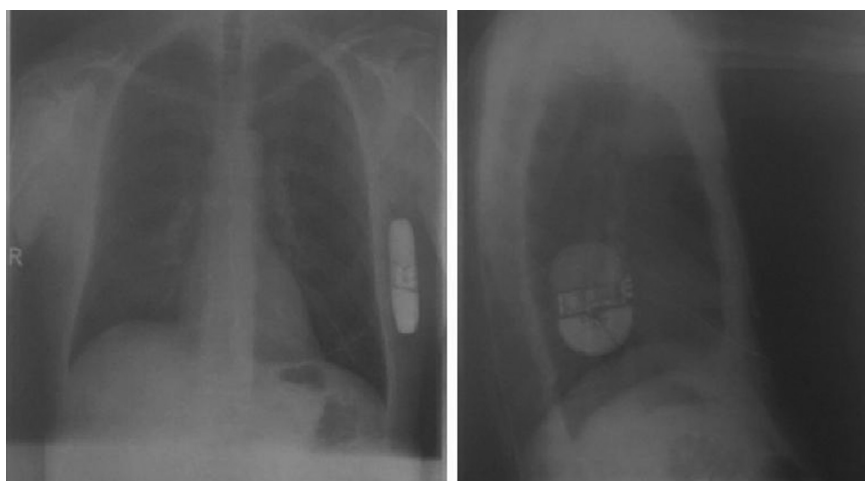
**Figure 8** A post-implant chest radiography demonstrated optimal placement of the subcutaneous ICD system (case 1).

unremarkable. His electrocardiogram was consistent with typical type 1 Brugada changes, showing a coved ST segment elevation of maximum 5 mm in the right precordial leads V1-V3 followed by a negative T wave (Fig. 9). Laboratory tests were all normal. Echocardiography did not reveal any abnormal features. A 24-hour ambulatory-ECG monitoring period revealed frequent premature ventricular beats and multiple runs of non-sustained VT of the same morphology. Recent ESC Clinical Practice Guidelines for the Prevention of Sudden Cardiac Death recommend ICD implantation in patients with a diagnosis of Brugada syndrome and syncopic episodes (class IIa) (Fig. 9).<sup>1</sup> The patient underwent a three-lead surface electrocardiogram screening followed by a subcutaneous ICD system implantation (Boston Scientific Emblem S-ICD). The procedure was similar to the previous patient, though this case used the two-incision technique, during which the parasternal part of the electrode was positioned using an 11 French peel-away sheath. The generator was, similarly to the previous patient, connected to the subcutaneous electrode and placed in a pocket created at the level of the lateral incision. A defibrillation test was performed post-procedurally that demonstrated inducible VF that was interrupted with



**Figure 9** The electrocardiogram of a 22-year-old male, revealing a characteristic spontaneous type 1 Brugada pattern (case 2).





**Figure 10** A post-implant chest radiography demonstrated optimal placement of the subcutaneous ICD system (case 2).

a 65-J DC shock. A chest-X-ray demonstrated optimal placement of the pulse generator and subcutaneous electrode (Fig. 10). The patient had an uneventful hospital stay and was discharged 3 days after the implantation.

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## Disclosures/relationship with industry

None.

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