

Subcutaneous Implantable Cardioverter Defibrillator in Patients With Hypertrophic Cardiomyopathy: An Initial Experience

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Background—The subcutaneous implantable cardioverter defibrillator (S-ICD) has been developed to avert risks associated with transvenous defibrillator leads. The technology is attractive for younger patients, such as those with hypertrophic cardiomyopathy (HCM). However, there are limited data on S-ICD use in HCM.

Methods and Results—HCM patients identified at risk for sudden death were considered for S-ICD implantation. Patients were screened for potential oversensing by surface electrocardiography (ECG). At implant, defibrillation threshold (DFT) testing was performed at 65, 50, and 35 joules (J). Twenty-seven patients were considered for S-ICD implantation, and after screening, 23 (85%) remained eligible. The presence of a bundle branch block was associated with screening failure, whereas elevated body mass index (BMI) showed a trend toward association. One patient passed screening at rest, but failed with an ECG obtained after exercise. At implant, the S-ICD terminated ventricular fibrillation (VF) with a 65J shock in all 15 implanted patients and a 50J shock was successful in 12 of 15. A 35J shock terminated VF in 10 of 12 patients. DFT failure at 50 J was associated with a higher BMI. There were no appropriate shocks after a median follow-up of 17.5 (3–35) months, and 1 patient received an inappropriate shock attributable to a temporary reduction in QRS amplitude while bending forward, resulting in oversensing, despite successful screening.

Conclusions—In a high-risk HCM cohort without a pacing indication referred for consideration of an ICD, the majority were eligible for S-ICD. The S-ICD is effective at recognizing and terminating VF at implant with a wide safety margin. (*J Am Heart Assoc.* 2016;5:e002488 doi: 10.1161/JAHA.115.002488)

Key Words: defibrillation • hypertrophic cardiomyopathy • implantable defibrillator • sudden death

Patients with hypertrophic cardiomyopathy (HCM) are at variable risk of sudden cardiac death.¹ Over the last several decades the implantable cardioverter defibrillator (ICD) has provided high-risk HCM patients the only reliable treatment for sudden death.^{2–4} Relative to the overall ICD population, largely populated by those with coronary artery disease, HCM patients are younger and thus have a much longer time period during which ongoing protection for sudden cardiac death (SCD) is needed.^{1,3} The risk of transvenous ICD lead failure increases over time and is related to age, activity level and specific lead. Lead failures occur more commonly in young active patients.⁵ Lead failure

results in the potential for additional morbidity and mortality because of the need for additional transvenous leads, with or without lead extraction.

In 2012 the US Food and Drug Administration approved a fully subcutaneous implantable cardioverter defibrillator (S-ICD; Boston Scientific Inc, Marlborough, MA). The S-ICD represents an important evolution in ICD therapy by positioning the lead in the subcutaneous layer of the thoracic cage, thereby avoiding potential complications related to the wear of transvenous leads.⁶ A large implant registry demonstrated the effectiveness of the S-ICD in a diverse group of patients (including HCM); implant success was defined when a single shock of 65 joules (J; the maximum output is 80 J) was effective in terminating ventricular fibrillation (VF). In contrast to the development of transvenous ICDs 20 to 30 years ago, step-down defibrillation threshold (DFT) testing was rarely performed. In the largest S-ICD registry to date, only 10 of 450 patients had any testing done at <65 J.^{6,7}

HCM is a diverse and often unpredictable disease.¹ The efficacy of the S-ICD in patients with HCM remains uncertain. DFT in HCM may be higher than in other cardiomyopathies and may increase over time.^{8,9} In addition, QRS and T-wave oversensing by the S-ICD may be more common in HCM.

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Therefore, we felt it timely to report on our initial experience with S-ICD in patients with HCM, including preimplant screening and step down DFT testing.

Methods

From January 2012 until May 2015, other than the period from March to October 2013 (because of S-ICD unavailability in the United States), HCM patients presenting to our institution, identified at risk for SCD based on the 2011 American College of Cardiology Foundation/American Heart Association guidelines,⁴ and without a pacing indication were considered for S-ICD implantation. Those patients were screened for potential T-wave oversensing utilizing a manufacturer-provided tool that analyzes surface ECG recordings taken during lying, standing, and immediately after running in place. Surface ECG recordings are obtained from 3 vectors that mimic the sensing vectors of the S-ICD. The “primary” sensing vector is between the electrode at the xyphoid position and the midaxillary S-ICD generator; the “secondary” vector is between the superior parasternal electrode and the generator and the “alternate” vector is between the 2 parasternal electrodes. Screening was not performed in any other alternative electrode position other than the standard 3 configurations available in the S-ICD. Screening was deemed successful if a single ECG vector passed while lying, standing and after exercise. If patients passed screening, they were offered the S-ICD. Patients underwent standard informed consent including for step down DFT testing, which is routine in our laboratory for HCM patients.

At implant, the S-ICD assesses the vector for sensing, and the vector with the greatest distinction between the QRS and the T-wave is chosen. DFT testing was performed in a step-down fashion (Figure 1). VF was induced and a 65 J shock delivered by the S-ICD. If VF was successfully terminated, VF induction was performed again (after 5 minutes) and a 50 J shock was delivered by the S-ICD. If successful, VF induction was repeated again after 5 minutes and treated with a 35 J shock from the S-ICD. If an S-ICD shock failed, the patient was externally defibrillated and no further DFT testing was performed.

Standard informed consent for ICD implantation was obtained. Approval for this retrospective analysis was obtained from the institutional review board of Tufts Medical Center (Boston, MA).

A comparison was made in baseline factors between the group of patients who were successfully screened for the S-ICD and those who failed screening. Age, body mass index (BMI), left ventricular ejection fraction (LVEF), and maximal wall thickness were reported as median (interquartile range; IQR) and compared using the Wilcoxon rank-sum test. The presence of a bundle branch block was compared using the

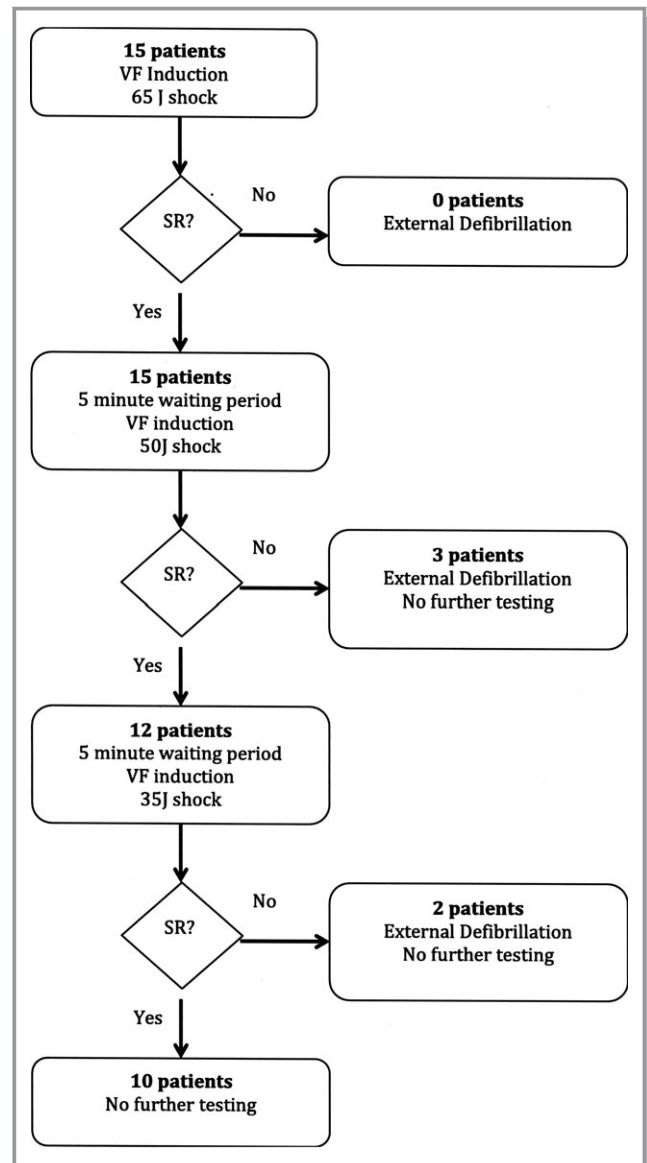


Figure 1. Flow chart of progression of defibrillation threshold (DFT) testing. SR indicates sinus rhythm; VF, ventricular fibrillation.

Fisher’s exact test. A similar comparison of DFT success or failure at 50 J was made, and baseline data are reported as median (IQR) and compared using the Wilcoxon rank sum test.

Results

Patient Selection and Screening

Twenty-seven HCM patients at risk for SCD were considered potential candidates for the S-ICD. After screening for oversensing, 23 patients (85%) remained eligible. In one of the patients who failed screening, the potential for T-wave oversensing was only apparent after exercise in the only sensing vector that passed screening under resting conditions

(Figure 2). Patients who failed screening were more likely to have a bundle branch block on ECG (4 of 4 vs 4 of 23; $P=0.004$) and had a trend toward a higher BMI (33 [27.6–36.9] vs 27.4 [20.8–37.3]; $P=0.07$; Table). Age, LVEF, and maximum wall thickness were not associated with potential for oversensing. Of 23 patients who screened successfully, 7 did not proceed with S-ICD implantation either because of insurance denial (2 patients) or patient decision to have a transvenous device (3 patients). Two patients are awaiting implant. During the same time period, 42 HCM patients underwent implantation of a transvenous ICD, none of which were screened and were thus not included in the current study. Twenty-four patients had a pacing indication, 11 of which had complete heart block after invasive septal reduction therapy. Eight patients expressed a preference for a transvenous ICD and thus were not screened. In addition, 10 patients without a pacing indication were not screened and underwent transvenous ICD implant during a time period of 8 months when the S-ICD was unavailable. The perceived need for antitachycardia pacing was not used in any patient as a reason not to consider an S-ICD.

Baseline Demographics

Among the 16 patients who had an S-ICD implanted, mean age was 39.6 ± 11.0 years (range, 21–57). The indication for S-ICD implant was secondary prevention in 3 patients and

primary prevention, based on the presence of ≥ 1 of the conventional risk factors, in 13 patients. Mean maximal left ventricular (LV) wall thickness was 18.4 ± 5.4 mm (range 11–30) and none of the patients had left ventricular LV outflow tract obstruction >30 mm Hg under basal conditions, including 2 patients who had previous successful invasive septal reduction therapy. Four patients had abandoned transvenous ICD leads. Mean LVEF was $57.2 \pm 10.6\%$ (range, 30–65%).

DFT Testing

One implanted patient did not undergo DFT testing because of the presence of a left atrial thrombus. In the others, VF was terminated by a 65J shock from the S-ICD in all patients and a 50J shock was successful in 12 of 15. A 35J shock terminated VF in 10 of 12 patients (Figure 1). VF was detected appropriately by the S-ICD after all inductions, and in no instance was there significantly delay or lack of detection necessitating external defibrillation. S-ICD defibrillation failure at 50 J was associated with a higher BMI (26.55 [21.50–33.2] vs 33.7 [32.20–37.30]; $P=0.025$). No other baseline patient characteristic showed any association with shock failure at 50 J, including bundle branch block, LVEF, maximum wall thickness, or implant indication (primary vs secondary). The 3 patients with the greatest maximum LV wall thickness of 30, 26 and 24 mm all had an adequate DFT (35, 35 and 50 J, respectively).

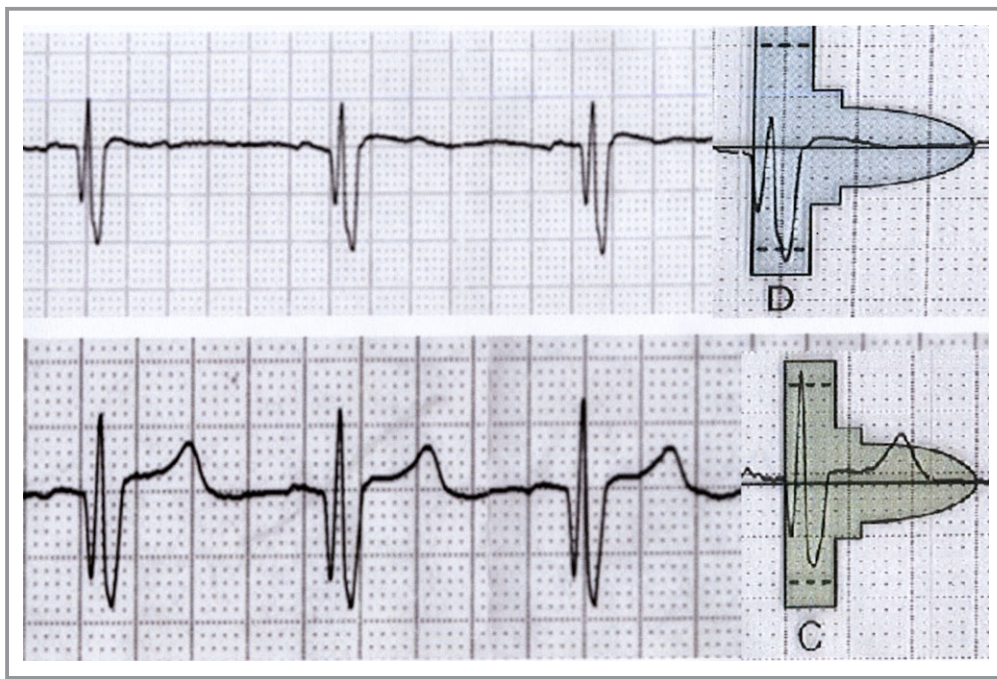


Figure 2. Single lead III electrocardiogram (ECG) pre-exercise in the upright position (top panel) and postexercise (lower panel) showing change in T-wave amplitude. The pre-exercise ECG passed ECG screening whereas the postexercise ECG did not. Failure of screening is indicated by a portion of the T-wave outside the shaded area on the superimposed screening tool. The 2 other leads failed screening at rest.

Table 1. Comparison of Baseline Characteristics of Patients who Passed and Failed Screening for S-ICD

	Successful Screening (n=23)	Screening Failed (n=4)	P Value
Age, y			
Mean±SD	38.2±12.3	39.7±14.0	
Median (IQR range)	37 (17–57)	38 (24–59)	0.71
BMI			
Mean±SD	27.7±4.4	32.6±3.9	
Median (IQR range)	27.4 (20.8–37.3)	33.0 (27.6–36.9)	0.07
ECG			
LBBB or RBBB	4/23	4/4	0.004
LBBB	2/23	3/4	0.013
RBBB	2/23	1/4	0.35
LVEF (%)			
Mean±SD	59±9.6	55±10.0	
Median (IQR range)	60 (30–70)	57 (40–65)	0.42
Maximal wall thickness, mm			
Mean±SD	17.2±5.5	18.5±7.8	
Median (IQR range)	16.0 (9.0–30.0)	15.5 (13.0–30.0)	0.89

BMI indicates body mass index; IQR, interquartile range; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; RBBB, right bundle branch block.

Follow-up

Follow-up data after a median of 17.5 (3–35) months was available for all 16 patients; there were no appropriate shocks, and 1 patient received an inappropriate shock attributable to a temporary reduction in QRS amplitude in the device chosen sensing vector, which resulted in oversensing of other ECG elements (Figure 3). This occurred despite successful preimplant ECG screening in all 3 vectors. The patient was bending over at the time. Interrogation of that device after the inappropriate shock showed normal sensing without any oversensing in the same vector (alternate) that the device had automatically chosen for sensing in both an upright and bending-over position. The alternate sensing vector was the active sensing vector during the inappropriate shock. The sensing channel was then manually set to a different vector, and the patient has not received any further shocks.

Discussion

These data suggest that the majority of HCM patients who are at risk of SCD and do not have a pacing indication are eligible

for S-ICD implantation, and that the device appears effective at recognizing and terminating induced VF at implant. Screening these patients is important to avoid inappropriate shocks. High BMI and presence of a bundle branch block were associated with failure of screening. Although no past study has specifically looked at S-ICD use in this patient population, 2 previous studies on the subject have included HCM patients. In 1 study, 2 of 18 (11%) patients with HCM failed screening,¹⁰ 4 of 18 (22%) patients in a similar study,¹¹ whereas 15% patients failed in our study. The overall failure rate of screening in all patients, with varying ICD indications in various studies is 7.4% to 14.5%.^{10–12} In the study by Olde-Nordkamp et al., screening failure among the larger group of patients was independently associated with HCM, elevated BMI and prolonged QRS duration, which is similar to our findings.

Based on our experience, in addition to the manufacturer-recommended screening supine and standing, performance of screening after exercise should be considered, given that T-wave amplitude and morphology can change dramatically and introduce the potential for inappropriate shocks. Despite successful preimplant screening, inappropriate shocks for oversensing remain a possibility.

Defibrillation was achieved with a wider safety margin than has been deemed to be adequate in the largest S-ICD registry to date, which included patients with other types of heart disease. These results were present across a diverse phenotypic expression of HCM including a subset with substantial LV wall thickening. Although DFT testing has fallen out of favor in the majority of patients undergoing ICD implantation, HCM remains a unique condition in which DFT testing should still be strongly considered for both transvenous and S-ICDs.¹³ The DFT with transvenous ICDs in HCM, in general, can be expected to be higher than in other cardiomyopathies, thus reducing the margin between the maximum output and the DFT.⁸ In addition, HCM is a progressive process with increasing LV wall thickness and mass, which can potentially adversely affect the DFT over time. An adequate safety margin for defibrillation is especially relevant for patients with HCM given that many patients will live for decades with the need for SCD protection. It is reassuring to find that, based on our data, there is a wider DFT safety margin at implant than had been previously documented in a large S-ICD registry where testing was only performed at 65 J. Though potentially important, the actual clinical significance of the width of the DFT safety margin for an individual patient is unclear and could only be answered by longer follow-up in a large cohort of HCM patients.

In this series, there was significant association between a higher BMI and S-ICD defibrillation failure at 50 J. The vector of an S-ICD shock is between the midaxillary, apical subcutaneous defibrillator and the parasternal lead coil. It is

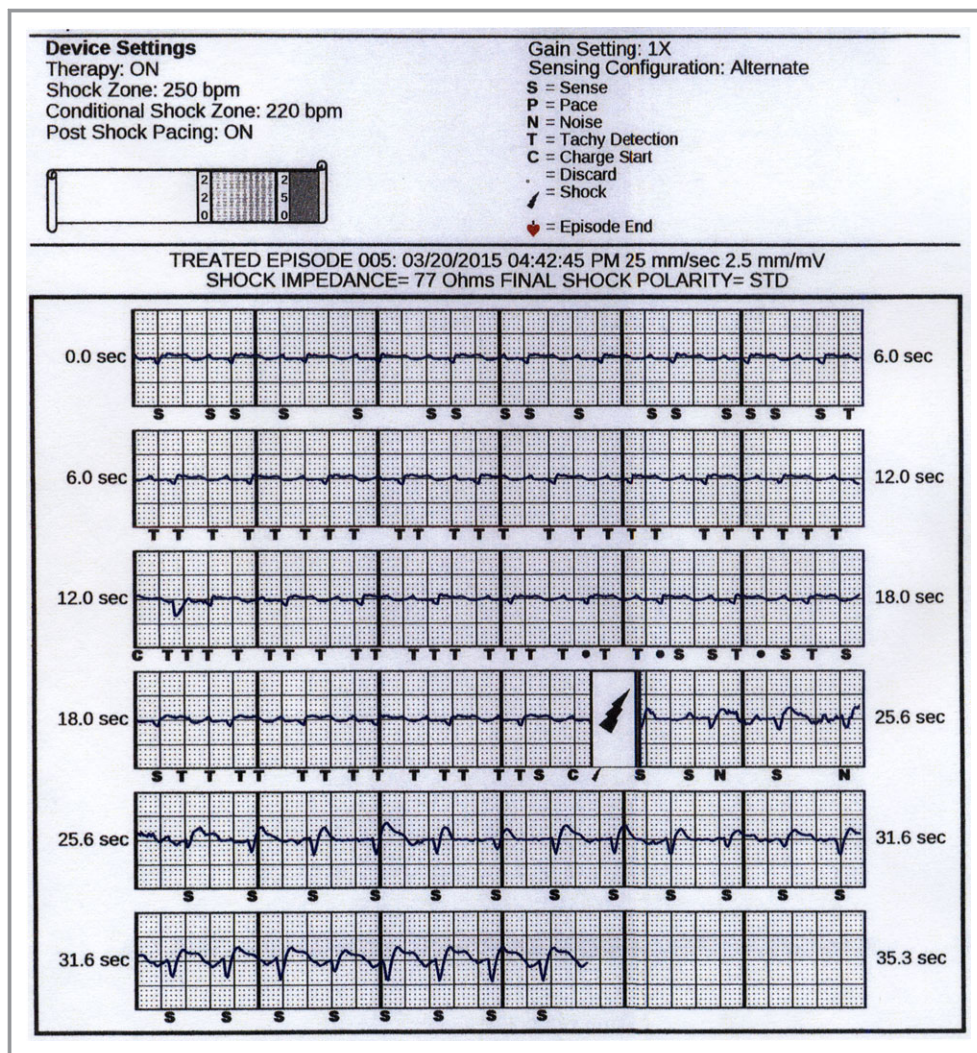


Figure 3. Stored electrogram of alternate vector recording from an S-ICD. This patient who passed screening for an S-ICD, received a shock resulting from oversensing on non-QRS elements of the recording. This oversensing occurred when the patient bent over to clip his toenails. S-ICD indicates subcutaneous implantable cardioverter defibrillator.

possible that the presence of a greater amount of body fat between those 2 positions could be responsible for less energy delivery to the myocardium. This would be in contrast to a transvenous ICD, which typically rests over the pectoralis muscle and shocks by a vector between that position and an endocardial right ventricular coil and, in some cases, a superior vena cava coil as well. This finding would be similar to data showing body weight predicting failure of external cardioversion of atrial fibrillation.¹⁴ This finding is likely not unique to HCM, and should be validated in a larger group of patients.

Long-term studies of transvenous ICD leads show that lead failure is an important issue, particularly for young individuals. In a pediatric HCM registry, lead failure occurred in 15 of 224 patients (6.6%) in a 4.3-year average follow-up.³ Seven of these individuals had inappropriate shocks attributable to lead

failure. In an early HCM ICD series, 12 of 128 (9.4%) individuals followed for an average of 3.1 years had a lead fracture.² Nine of these had an inappropriate shock. Certain leads are even more prone to failure. The Medtronic Fidelis (Medtronic Inc, Minneapolis, MN) lead has failed at a rate of 2.8% a year, with a higher incidence in the younger individual.¹⁵ In a Canadian series the failure rate for the Fidelis lead at 5 years was 16.8%.¹⁶ All transvenous leads are subjected to repetitive shoulder and cardiac motion. Thus, it is generally accepted that no transvenous lead will last the lifetime of a young individual. The S-ICD lead, by contrast, is not subject to the same stresses as a transvenous lead. In addition, the absence of a lumen in the S-ICD lead should theoretically reduce the risk of lead failure. Therefore, survival of an S-ICD lead can be expected to be longer than a transvenous lead, making it a particularly good option for the

young individual. Moreover, the consequences of lead failure or infection are far less serious with an S-ICD compared to a transvenous system, because removal of an S-ICD lead is of much lower risk compared to a transvenous lead.

The S-ICD has some functional limitations when compared to a transvenous ICD. The S-ICD has no bradycardia pacing capability. In addition, there is no antitachycardia pacing (ATP) available in the S-ICD. Patients who have a pacing indication at the time of ICD implant should not be considered for the S-ICD and they were not included in this series. Patients who are being considered for an ICD for secondary prevention who have had multiple past episodes of sustained monomorphic ventricular tachycardia that may be amenable to ATP may be best served by a transvenous ICD. Otherwise, the lack of ATP, in our opinion, should not be an argument for favoring a transvenous device. ATP has never been shown, in a prospective, randomized trial, to affect mortality, and its absence is far outweighed by the much larger potential benefit of avoiding transvenous leads and the associated potential future morbidity and mortality in this typically younger population. Our approach is to consider any patient with HCM in need of sudden cardiac death protection who does not have a current pacing indication as a candidate for an S-ICD. The majority of HCM patients undergoing ICD implant are young, and the younger the patient, the stronger our preference for the S-ICD.

Limitations

Follow-up in this study is relatively short. Further longitudinal studies with larger cohorts and longer follow-up are necessary to determine the efficacy of the S-ICD in treating life-threatening ventricular arrhythmias in HCM.

Conclusion

In this single-center series of S-ICD in patients with HCM, the S-ICD appropriately recognized and terminated induced VF at implant testing, with a wide safety margin. T-wave oversensing may be an issue, necessitating stringent preoperative testing. Longer-term experience is necessary for further confidence in this system, but the current short-term results are promising.

Disclosures

None.

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