Boston Scientific

Advancing science for life™

01

Clinical EVIDENCE

HeartLogic™ Algorithm: Real-World Validation

Prediction of heart failure events with the HeartLogic algorithm: real-world validation (Singh et al.) [1]

S-ICD Performance in Real-World Practice 1

Intermuscular technique for implantation of the subcutaneous implantable defibrillator: a propensity-matched case–control study (Botto et al.) [2]

S-ICD Performance in Real-World Practice 2

Reduction in inappropriate therapies through device programming in subcutaneous implantable defibrillator patients: data from clinical practice (Rordorf et al.) [3]

ISSUE 01 MARCH 2024

Supported by Monica Campari and Mariolina Lovecchio, Boston Scientific

Summary

This Clinical Evidence delves into the most recent real-world data concerning the performance of the HeartLogic algorithm and subcutaneous implantable cardioverter-defibrillators (S-ICD) and their potential application in clinical practice to improve patient outcomes. A new re-validation of the HeartLogic diagnostic tool[1] is explored in order to confirm the performance of the algorithm in clinical practice for implantable cardioverter defibrillators (ICD) and cardiac resynchronisation therapy devices (CRT-D). S-ICD clinical experiences from two retrospective analyses from the observational Rhythm Detect registry are described. One analysis assesses the enhanced outcomes associated with placing the S-ICD generator in the intermuscular space[2]; the other investigates the decrease in inappropriate therapies through device programming[3].

HeartLogic Validation by Using Real-World Data Approach

The HeartLogic algorithm, available in ICD and CRT-D devices, uses sensor data from the devices for the prediction of heart failure (HF) events.

The algorithm combines heart sounds, respiration, thoracic impedance, heart rate, and activity measures into one composite index. The MultiSENSE[4] study validated the HeartLogic index using CRT-D devices and blinded physicians to the index.

Singh et al.[1] published a new analysis to re-validate the index in a real-world setting, including ICD and CRT-D devices. Patients implanted with HeartLogic-enabled ICD/CRT-D were considered for analysis, and the data collected from the LATITUDE NXT remote monitoring system were linked with HF events reported in the Centers for Medicaid and Medicare Services (CMS) Administrative Claims Database.

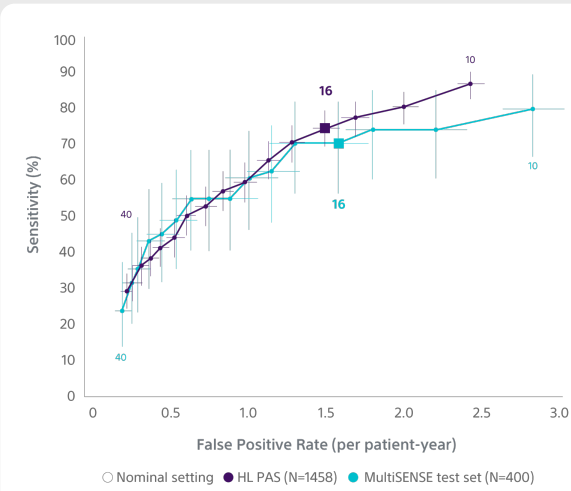


Figure 1: HeartLogic performance: sensitivity vs. false positive rate for the real-world cohort (purple) and MultiSENSE clinical study (blue).

Results

Between 2017 and 2019, a total of 1458 subjects from 567 clinics were considered for the analysis with a total follow-up period of 1570 patient/years.

During the follow-up period, a total of 302 usable HF events (HFE) were observed: 266 (88%) inpatient hospitalisations and 36 (12%) HF outpatient visits with intravenous (IV) decongestive therapy.

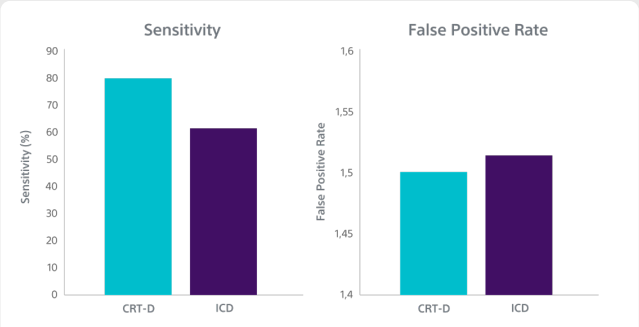
The HeartLogic alerts were 2515 with an average duration of 42 days and the total time in alert state was 18.6%.

Among the HFEs, 225 (75%) were predicted by HeartLogic with an alert lead time of 49 days.

A high concordance across configurable thresholds was also seen with the original MultiSENSE observations (Figure 1).

The performance goals were also exceeded by both the CRT and the ICD subgroups.

At the nominal threshold, the observed sensitivity was higher for patients with CRT (79.9% [95% confidence interval [CI], 73.9–85.1%]) devices than those with ICDs (61.4% [95% CI, 50.4–71.6%]; P<0.001), although there was no difference between the subgroups for false-positive alert rates (1.50 [95% CI, 1.40–1.60] vs. 1.51 [95% CI, 1.37–1.67]; P=0.91) (Figure 2).



Sensitivity: **74.5%**

False Positive Rate: **1.48 alerts/patient-year**

Average alert lead time: **49±40 days**

Figure 2: HeartLogic performance for CRT-D and ICD devices.

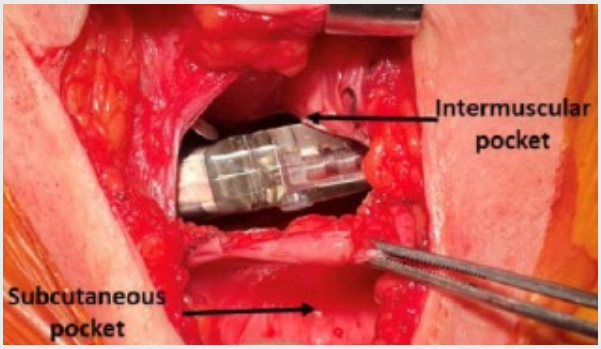
This analysis confirmed the HeartLogic performance in terms of sensitivity, false positive rate and early HF worsening detection in a real-world setting, including ICD patients, not included in the approval study.

Improved safety profile of the S-ICD with intermuscular technique

The Prospective Randomised Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator (PRAETORIAN) Trial has demonstrated that S-ICD was non-inferior to transvenous ICD with respect to the composite endpoint of device-related complications and inappropriate shocks[5].

However, the results of the trial cannot be fully extended to the S-ICD therapy in current clinical practice. Indeed, the traditional S-ICD implantation technique adopted in the trial, which involves the insertion of the pulse generator under the subcutaneous (SC) tissue, has significantly changed over time.

In a retrospective analysis, Botto et al.[2] aimed to analyse the mid-term outcome of patients enroled in the Italian Rhythm Detect registry, who underwent S-ICD implantation with the generator positioned in an IM position in comparison with a SC pocket.



Device-related complications at 1 year
4.6% vs **1.0%**
Subcutaneous Intermuscular

Inappropriate shocks at 1 year
4.2% vs **1.4%**
Subcutaneous Intermuscular

Composite endpoint at 1 year
8.4% vs **2.4%**
Subcutaneous Intermuscular

Figure 3: Rate at 1 year of device-related complications, inappropriate shocks and the composite endpoint of inappropriate shocks or complications in the SC-group versus the IM-group.

Outcome analysis

A total of 1577 consecutive patients who had undergone S-ICD implantation from 2013 to 2021 were followed up until December 2021. SC patients (n=290) were propensity-matched with patients of the IM group (n=290), and their outcomes were compared.

- The risk of device-related complication was lower in the matched IM group than in the SC group (unadjusted hazard ratio [HR] 0.41, 95% CI, 0.17–0.99; P=0.041).

1.4% Inappropriate Shocks

The rate of inappropriate shocks at 1 year was 1.4% (95% CI, 0.1–2.7) in the IM group and 4.2% (95% CI, 1.8–6.7) in the SC group

- The rate at 1 year of the combined endpoint of inappropriate shocks or complications, with the IM positioning of the generator, decreased from 8.4% (95% CI, 5.1–11.7) to 2.4% (95% CI, 0.6–4.2), as well as the rate of inappropriate shocks (from 4.2% [95% CI, 1.8–6.7] to 1.4% [95% CI, 0.1–2.7]) and device-related complications (from 4.6% [95% CI, 2.1- 7.1] to 1.0% [95% CI, 0.0–2.2]).
- During follow-up, 46 patients (7.9%) received appropriate shocks, all events **(100%)** were successfully converted, in agreement with previous findings[5, 6-8].

This analysis demonstrated the superiority of the IM S-ICD generator positioning in reducing device-related complications and inappropriate shocks, affirming the already established safety and efficacy of the subcutaneous defibrillator.

Enhancing Patient Outcomes through Optimal Device Programming

Previous studies have highlighted the crucial role of device programming[7, 9] in the S-ICD's ability to discriminate among arrhythmias.

Specifically, the UNTOUCHED Trial documented a remarkably low inappropriate shock rate in S-ICD recipients when standardised programming with high arrhythmia detection cut-off rates (conditional zone between 200–250 bpm and a shock zone for arrhythmias >250 bpm) was employed [7].

According to Gold et al., the programming approach in UNTOUCHED – discrimination algorithms active from 200–250 bpm – should be routinely adopted in S-ICD patients to prevent unnecessary shocks.

Nevertheless, the programming approach utilised in routine clinical practice remains unknown, as is its impact on the rates of inappropriate and appropriate therapies.

Rordorf et al.[3] assessed S-ICD programming on implantation and during follow-up in a cohort of 1468 consecutive S-ICD recipients, measuring the occurrence of shocks during follow-up.

- On implantation, the median programmed conditional zone cut-off was set to 200 bpm (IQR: 200–220) and the shock zone cut-off was 230 bpm (IQR: 210–250).
- During follow-up, the conditional zone cut-off rate was not significantly changed, while the shock zone cut-off was changed in 42% of patients and the median value increased to 250 bpm (IQR: 230–250; P<0.001).
- "UNTOUCHED-like programming" was independently associated with fewer inappropriate shocks (HR 0.50, 95% CI, 0.25–0.98; P=0.044), and had no impact on appropriate and ineffective shocks.

29% vs **49%**
After implantation / At the last follow-up

UNTOUCHED-like programming immediately after device implantation, and at the last follow-up.

UNTOUCHED-like programming adoption at baseline in the first and in the last 734 devices (P<0.001).

5% vs **53%**
First 734 Patients / Last 734 Patients

The present findings (Figure 4) not only elucidate how the S-ICD should be used in order to obtain a better outcome, but also portray that the achievable performance of the S-ICD is even better than that observed in the first trials, which suffered from the limitations of an immature technology and an amendable programming strategy.

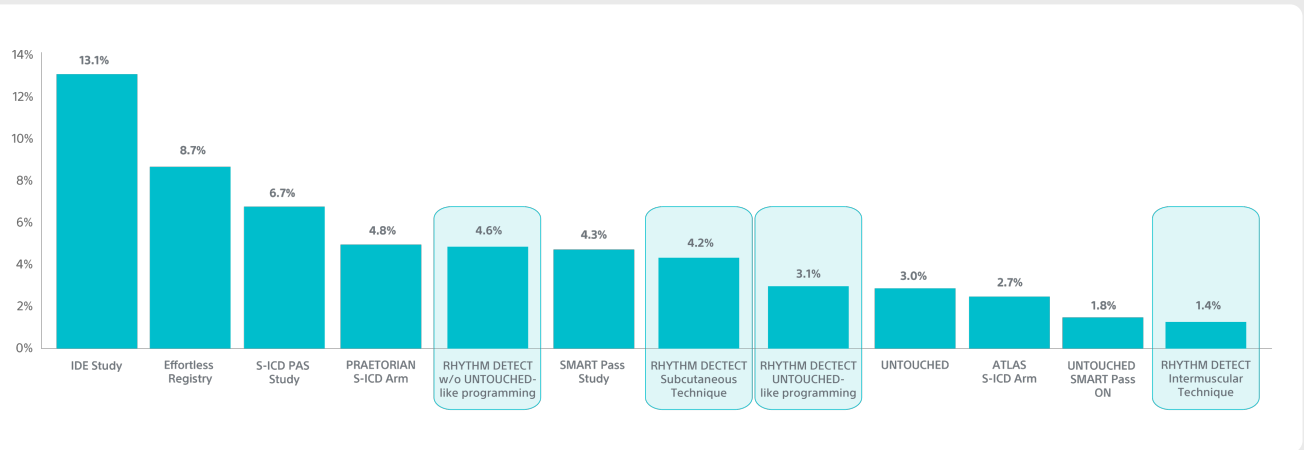


Figure 4: One-year inappropriate shock rates throughout studies.

"Implanting a Recalled Device — Choices for Patients, Physicians, and Public Health" [10]

Kramer DB, Hauser RB

When an ICD model is recalled because of a defective component or feature, the devices are usually no longer implanted, and patients living with these permanent implants undergo either prophylactic replacement or, more commonly, close follow-up to monitor for problems related to the device.

Between 2022 and 2023, the Food and Drug Administration (FDA) categorised the recall of two Medtronic ICDs, relating to the possibility of the devices not delivering a full-energy shock in response to ventricular arrhythmias, as a Class I recall.

Despite these active recalls, these devices continue to be implanted, even though the underlying issue is not fully corrected. Patients and the medical community are therefore confronted with an important clinical decision, without independent science to guide them.

Breaking News
Read what the experts have to say.

What do the authors suggest doing?

Independent Studies

To allow patients and physicians to make more informed decisions, the FDA, the manufacturer, and cardiology professional societies should urgently coordinate an independent, multistakeholder study to better define the risk of malfunctions and associated patient harm.

Quarterly Product Performance Report

The manufacturer should publish quarterly performance updates regarding the recalled devices. Such updates could include a summary of adverse events reported to the FDA that are related to the recalls.

Shared Decision Making

The clinical community should carefully consider the ongoing use of recalled devices. If physicians continue to implant recalled devices, they should adhere to the principles of informed consent and talk with patients about the Class I recalls and why a particular device is preferred over alternatives.

Key Messages

- **HeartLogic Algorithm: Real-World Validation:** HeartLogic performances were validated in a real-world setting: high performance in terms of sensitivity and false positive rate were confirmed for ICD and CRT-D patients[1].

- **S-ICD Performance in Real-World Practice 1:** Placing the S-ICD generator in the intermuscular space instead of the standard subcutaneous pocket results in fewer device-related complications and inappropriate shocks over a medium-term follow-up[2].

- **S-ICD Performance in Real-World Practice 2:** In clinical practice, there has been a trend in recent years towards the wider adoption of optimised programming. The standardised programming proposed by the UNTOUCHED study reduced the rate of inappropriate shock in the S-ICD population, without affecting therapy effectiveness[3].

1. Singh JP, Wariar R, Ruble S, et al. Prediction of Heart Failure Events With the HeartLogic Algorithm: Real-World Validation. J Card Fail. 2023;S1071-9164(23) 00868-0.

2. Botto GL, Ziacchi M, Nigro G, et al. Intermuscular technique for implantation of the subcutaneous implantable defibrillator: a propensity-matched case-control study. Europace. 2023;25(4):1423–1431.

3. Rordorf R, Viani S, Biffi M, et al. Reduction in inappropriate therapies through device programming in subcutaneous implantable defibrillator patients: data from clinical practice. Europace. 2023;25(5):euac234.

4. Boehmer JP, Hariharan R, Devecchi FG, et al. A multisensory algorithm predicts heart failure events in patients with implanted devices: results from the MultiSENSE study. JACC Heart Fail. 2017;5(3):216–225.

5. Knops RE, Olde Nordkamp LRA, Delnoy PHM, et al. Subcutaneous or transvenous defibrillator therapy. N Engl J Med. 2020;383(6):526–536.

6. Burke MC, Aasbo JD, El-Chami MF, et al. 1-Year prospective evaluation of clinical outcomes and shocks: the subcutaneous ICD post approval study. JACC Clin Electrophysiol. 2020;6(12):1537–1550.

7. Gold MR, Lambiase PD, El-Chami MF, et al. Primary results from the understanding outcomes with the S-ICD in primary prevention patients with low ejection fraction (UNTOUCHED) trial. Circulation. 2021;143(1):7–17.

8. Lambiase PD, Theuns DA, Murgatroyd F, et al. Subcutaneous implantable cardioverter-defibrillators: long-term results of the EFFORTLESS study. Eur Heart J. 2022;43(21):2037–2050.

9. Gold MR, Weiss R, Theuns DA, et al. Use of a discrimination algorithm to reduce inappropriate shocks with a subcutaneous implantable cardioverter-defibrillator. Heart Rhythm. 2014;11(8):1352–1358.

10. Kramer DB, Hauser RG. Implanting a Recalled Device - Choices for Patients, Physicians, and Public Health. N Engl J Med. 2023;389(20):1832–1834.

CAUTION:

The law restricts these devices to sale by or on the order of a physician. Indications, contraindications, warnings, and instructions for use can be found in the product labelling supplied with each device, or at www.IFU-BSCI.com. Products shown for INFORMATION purposes only and may not be approved or for sale in certain countries. This material not intended for use in France.

Boston Scientific

Advancing science for life™

www.bostonscientific.eu

CRM-1797902-AA CE 2797