Journal of Medical Economics

ISSN: 1369-6998 (Print) 1941-837X (Online) Journal homepage: www.tandfonline.com/journals/ijme20

Safety and efficacy of an intrinsic antitachycardia pacing algorithm in patients from Japan and South Korea: results from a cardiac device registry in the Asia Pacific region

Masahiko Goya, Seung-Jung Park, Kenji Ando, Reece Holbrook, Rowan Iskandar, Luke Jacobsen, Joseph D. Mozingo, Boyoung Joung & on behalf of the SPARK Registry Investigators

To cite this article: Masahiko Goya, Seung-Jung Park, Kenji Ando, Reece Holbrook, Rowan Iskandar, Luke Jacobsen, Joseph D. Mozingo, Boyoung Joung & on behalf of the SPARK Registry Investigators (2025) Safety and efficacy of an intrinsic antitachycardia pacing algorithm in patients from Japan and South Korea: results from a cardiac device registry in the Asia Pacific region, Journal of Medical Economics, 28:1, 1307-1318, DOI: 10.1080/13696998.2025.2543213

To link to this article: https://doi.org/10.1080/13696998.2025.2543213

© 2025 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group

View supplementary material

Published online: 13 Aug 2025.

Submit your article to this journal

Article views: 908

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=ijme20

JOURNAL OF MEDICAL ECONOMICS
2025, VOL. 28, NO. 1, 1307–1318
https://doi.org/10.1080/13696998.2025.2543213
Article /2543213

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH

OPEN ACCESS Check for updates

Safety and efficacy of an intrinsic antitachycardia pacing algorithm in patients from Japan and South Korea: results from a cardiac device registry in the Asia Pacific region

Masahiko Goya[a], Seung-Jung Park[b], Kenji Ando[c], Reece Holbrook[d], Rowan Iskandar[e], Luke Jacobsen[d], Joseph D. Mozingo[d] and Boyoung Joung[f]; on behalf of the SPARK Registry Investigators*

[a]Department of Cardiovascular Medicine, International University of Health and Welfare Mita Hospital, Tokyo, Japan; [b]Department of Cardiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [c]Department of Cardiovascular Medicine, Kokura Memorial Hospital, Fukuoka, Japan; [d]Medtronic, Inc., Mounds View, Minnesota, USA; [e]Medtronic International Trading Sàrl, Tolochenaz, Switzerland; [f]Department of Cardiology, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea

ABSTRACT

Background: Antitachycardia pacing (ATP) therapy, available in modern implantable cardioverter defibrillators (ICD) and cardiac resynchronization therapy defibrillators (CRT-D), aims to terminate ventricular arrhythmias without administering high energy shocks. The intrinsic ATP (iATP) algorithm automates ATP programming in real-time, tailoring therapy based on previous ATP attempts. This study evaluated the safety, efficacy, and clinical outcomes of iATP in patients from Japan and South Korea.

Methods: This study was a prospective, observational, multi-site registry that enrolled patients from Japan and South Korea implanted with an ICD or CRT-D device with the iATP algorithm. Patients were followed for a minimum of 12 months. Outcomes included ATP termination success, appropriate shocks, acceleration, arrhythmia-related syncope, and mortality. A post hoc unanchored matching-adjusted indirect comparison (uMAIC) was performed to compare iATP with standard ATP using published literature.

Results: A total of 800 patients were enrolled. The iATP success rate for terminating all episodes was 89.2% (86.2% Generalized Estimating Equation [GEE] estimated) and 82.2% for episodes in the fast VT zone (80.9% GEE estimated). Acceleration occurred in 2.0% of episodes, and arrhythmia-related syncope was observed in 0.5% of patients. The 1-year survival rate was 96.1%, with no device-related deaths or abnormal battery depletions. The uMAIC showed iATP had higher termination efficacy across all episodes (88.1% vs. 79.3%, $p < 0.001$), a lower probability of appropriate shocks per episode (iATP 14.7% and ATP 31.3%, $p < 0.001$), and fewer accelerations per episode (2.1% vs. 4.8%, $p = 0.02$), with similar probability of arrhythmia-related syncope per patient (0.5% vs 0.9%, $p = 0.35$) and mortality (12-month Kaplan Meyer survival estimate iATP 95.4%, ATP 95.3%, $p = 0.43$).

Conclusions: iATP exhibited a high ventricular arrhythmia termination efficacy and a favorable safety profile. Comparison of iATP to standard ATP provides initial evidence of higher termination success, lower incidence of accelerations and appropriate shocks, and similar rates of mortality and arrhythmia-related syncope.

Trial Registration: ClinicalTrials.gov Identifier: NCT01524276; Japan Registry of Clinical Trials Identifier: jRCT1042200049

ARTICLE HISTORY

Received 23 June 2025
Revised 30 July 2025
Accepted 31 July 2025

KEYWORDS

Antitachycardia pacing; implantable cardioverter-defibrillator; cardiac resynchronization therapy-defibrillator; ventricular arrhythmia; registry; matching-adjusted indirect comparison

JEL CLASSIFICATION CODES

I10; I19

CONTACT Boyoung Joung cby6908@yuhs.ac Department of Cardiology, Severance Hospital, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea

*SPARK Registry Investigators members are Kenji Ando (also an author), Eue-Keun Choi, Jong-Il Choi, Woong Gil Choi, Tomoo Harada, Masahide Harada, Naoya Hironobe, KiWon Hwang, Jongmin Hwang, Youmi Hwang, Yasuya Inden, Boyoung Joung (also an author), Ritsushi Kato, Jun Kim, Sung Soo Kim, Takashi Kurita, Kengo Kusano, Heejin Kwon, Shinsuke Miyazaki, Atsushi Mochizuki, Kentaro Nakamura, Nobuhiro Nishii, Il-Young Oh, Yong-Seog Oh, Sou Ohtsuki, Takafumi Oka, Seung-Jung Park (also an author), Jong Sung Park, Jin Kyu Park, Kyoung-Suk Rhee, Seung-Young Roh, Shingo Sasaki, Takeshi Sasaki, Kazuhiro Satomi, Akira Shiose, Kyoko Soejima, Tomoyuki Tani, and Namsik Yoon.

Supplemental data for this article is available online at https://doi.org/10.1080/13696998.2025.2543213.

© 2025 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (http://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

Introduction

Implantable cardioverter-defibrillators with or without cardiac resynchronization therapy (ICD, CRT-D) provide lifesaving high-energy therapy in the event of sudden cardiac arrest and are considered the standard of care for patients at risk of sudden cardiac arrest[1–3]. As an alternative, these devices can also provide low energy antitachycardia pacing (ATP) therapy to terminate episodes of ventricular tachycardia (VT)[4,5]. When successful, ATP achieves the goal of interrupting malignant heart rhythms, particularly monomorphic ventricular tachycardia (MVT), without the clinical and economic burden associated with high-energy shocks[6,7].

ATP therapy has been shown to be effective when programmed appropriately[8–11], which creates opportunity as well as challenge. Efforts to implement proven programming strategies in real-world circumstances have been met with limited success[12]. The intrinsic ATP (iATP) algorithm was developed to automate the selection of ATP parameters, ensuring that each subsequent therapy is tailored and refined based on the outcomes observed from the previously delivered therapy. Early experiences with iATP suggest that it safely adjusts therapy progression and terminates a high proportion of arrhythmias without ongoing physician intervention[13].

The goal of this study was to characterize the safety, efficacy, and clinical outcomes associated with iATP in patients from Japan and South Korea. This report includes results on iATP performance local to these healthcare systems and a structured comparison to standard ATP.

Methods

The Surveillance of Automated ATP Algorithm in ICD/CRT Devices with Key Concepts for Assessing Safety and Efficacy (SPARK) registry was conducted to characterize the performance of ICDs and CRT-Ds with the iATP algorithm. The iATP algorithm has been described previously[13]. This manuscript was developed in compliance with the STROBE statement for reporting observational studies[14].

Study population

Patient recruitment was performed at hospitals in Japan and South Korea. Patients included in the study were those who underwent implantation (de novo or replacement) of a Cobalt XT ICD or CRT-D device (Medtronic Inc., Minneapolis, MN) with the iATP algorithm. Patients with either an ICD or a CRT-D device were included as they have similar risk factors for ventricular arrhythmias and iATP will operate in a consistent manner regardless of device type. Patients were excluded if they were inaccessible for follow-up, ineligible according to local law, or enrolled in any concurrent study that might have confounded the results. Enrollment was required prior to or within 30 days of the implant procedure. Patients were followed according to local standard of care for 12 months at minimum.

The SPARK registry was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki and adhered to laws and regulations of the countries and sites involved. Approval was obtained from the ethics committee at each site (Supplement 3), and informed consent was obtained from all participants prior to enrollment.

Study design

The SPARK registry (jRCT1042200049; registered 8 October 2020) was a prospective, observational, multisite registry study conducted within the Medtronic Product Surveillance Registry (NCT01524276). The full set of objectives were to characterize device-related complication-free survival, rate of abnormal battery depletions, device system modifications, patient deaths, termination success rate of iATP in the fast ventricular tachycardia (FVT) zone, arrhythmia-related syncope, and heart failure hospitalizations. This report includes the objectives associated with iATP safety (acceleration, arrhythmia-related syncope, mortality) and efficacy (termination success, appropriate shocks).

iATP algorithm

The iATP algorithm is a real-time automated system designed to reduce implantable cardioverter-defibrillator shocks by using electrophysiological principles to treat ventricular arrhythmias using low energy pulses[13]. It employs a structured sequence of burst pacing plus extra stimuli, where the burst paces aim to reach the re-entrant circuit and the extra stimuli aim to terminate it. The algorithm uses timing information from initial ATP attempts to assess effectiveness and adapt subsequent pacing strategies and also detects changes in episode characteristics to restart therapy if a new circuit forms (Supplementary Figure S1).

Data collection and measures

Data collected at baseline included demographics, clinical characteristics and medical history. At implant, data were collected on the procedure and techniques, adverse experiences and device programming. Data were collected up to the time of study exit. In the case of lost to follow-up, patient follow-up was calculated based on the date of last contact. Adverse events, system modifications, and changes in patient's status (e.g. death and study exit) were reported upon site awareness. All adverse events were adjudicated by a Clinical Events Committee (CEC, Supplement 2), which consisted of independent physician experts who were not related to the study sponsor or a principal investigator in the study, for relatedness to the device and determination of complication or observation. Baseline device programming was collected through CareLink (Medtronic Inc., Minneapolis, MN) remote transmissions and detailed episode data were collected through CareLink or through manual device interrogations.

Ventricular arrhythmia episode data were first adjudicated for morphology and acceleration by two members of an Episode Review Committee (ERC, Supplement 2), with a third review added if there was disagreement between the first two. The ERC included independent physician experts who were not related to the study sponsor or a principal investigator in the study. Eligible episodes were spontaneous episodes detected by the device in the VT, FVT, or ventricular fibrillation (VF) zones that were treated with iATP therapy and were adjudicated by the ERC. Successful episode termination by iATP was defined as an episode with iATP as the last therapy and device-determined success with no shock delivered. Episode acceleration was defined as a reduction in cycle length for a device-treated episode by at least 10% or 30 ms (whichever is larger), or conversion from MVT to polymorphic VT or VF after treatment. A syncope event was defined as a complete loss of consciousness and postural tone as determined by the CEC. A syncope event was considered related to arrhythmia if it had an onset within 24 h of a device-treated ventricular tachyarrhythmia as confirmed by the ERC.

Comparative analysis

The objectives of the post hoc comparative analysis were to compare iATP to ATP in the following metrics: termination success rate (for all treated episodes and for treated episodes detected in the FVT zone), episode acceleration, arrhythmia-related syncope, death, and appropriate shocks. The analysis was structured as an unanchored matching-adjusted indirect comparison (uMAIC)[15]. For the intervention (i.e. iATP), the uMAIC used the individual patient data from the SPARK registry. The comparator was comprised of pooled data from relevant references identified *via* a structured literature review on ATP performance. An unanchored comparison was conducted because of a lack of a common comparator between references. Patient weights for the uMAIC were derived using a generalized linear mixed model, ensuring alignment of key covariates between populations. These weights were then applied to the SPARK data, to ensure that the outcome measures reflected a population more comparable to the comparison literature.

The literature search was performed by one researcher (RH) using PubMed and keywords "((antitachycardia OR anti-tachycardia) AND pacing) AND multicenter" with no restriction on the date of publication. References were excluded if they were limited to a single center, or did not report both raw ATP termination efficacy and efficacy adjusted for multiple episodes per patient, with remaining references included for analysis. For references that included multiple arms comparing variations on application of ATP

therapy, data were extracted separately for each arm, with each arm being referred to as a study in this manuscript. Summary statistics of population baseline characteristics and outcome measures were extracted, including age, gender, device type, indication, left ventricular ejection fraction, QRS width, left bundle branch block, ischemic etiology, New York Heart Association class, myocardial infarction, hypertension, arrhythmia-related syncope, and atrial arrhythmias. Outcome measures included iATP termination success and number of appropriate shocks (efficacy), as well as rate of acceleration, arrhythmia-related syncope, and death (safety). Baseline characteristics and outcomes from the comparison literature were extracted by one researcher (RH) and validated by a second (WM).

As all covariates were not available in all studies for extraction, base case analyses were performed using the maximum number of studies while narrowing the number of covariates. In addition, scenario analyses including a subset of studies that reported a wider set of covariates were performed. Further details are provided in Supplement 6.

Statistical analysis

This study did not have a statistically powered objective, all objectives were descriptive in nature. A total of 800 subjects was determined to be a sufficiently large sample size to represent the local populations and characterize the clinical outcomes. Descriptive statistics are reported as mean ± standard deviation (SD), median [interquartile range (IQR)], number of patients (percentage), or as number of episodes (percentage). Generalized estimating equations (GEE) were used to calculate iATP success rates to adjust event rates for multiple episodes from a single patient. A Cochran's Q test was used to determine whether the observation variation in the comparator study estimates was due to sampling error alone. The Kaplan-Meier method was used to estimate survival probabilities. Survival data were extracted from the comparative studies using PlotDigitizer (version 3.1.6), an online tool for digitizing plots and graphs (https://plotdigitizer.com). All analyses were performed with the use of the R statistical package (R Project for Statistical Computing) or SAS software, version 9.4 (SAS Institute).

Results

Patient characteristics

A total of 800 patients were enrolled at 38 sites in Japan and South Korea between October 2020 and October 2023, having a mean age of 68.0 ± 13.9 years, 75.5% being male, and 68.5% with ICD (31.5% CRT-D) (Table 1). Patients were followed for an average of 16.2 ± 6.6 months.

A total of 370 patients had baseline programming data available, and 619 patients had detailed episode data through at least 90 days of follow-up, enabling complete data for episode adjudication. Programming at baseline was set to enable iATP in the VT zone for 92.7% of patients and in the VF zone for 90.8% of patients. The FVT zone was programmed on for 40.8% of patients, with iATP enabled in the FVT zone in all cases.

Spontaneous episodes and therapy

During follow-up, 631 total arrhythmia episodes from 97 patients were detected and treated by the device (Supplementary Figure S2). Of these, 493 episodes of ventricular arrhythmia from 77 patients were appropriately treated by iATP (median cycle length = 340 [IQR = 320–410] ms). Among these, 369 (74.8%) were detected as VT (median cycle length = 360 [IQR = 330–430] ms) in 61 patients, 73 (14.8%) were detected as FVT (median cycle length = 310 [IQR = 300–320] ms) in 18 patients, and 51 (10.3%)) were detected as VF (median cycle length = 280 [IQR = 270–290] ms) in 11 patients (Figure 1). The morphology of treated episodes was primarily MVT (Table 2).

The application of iATP resulted in termination of 440 of 493 episodes across all detection zones (89.2% unadjusted, 86.2% GEE estimated; 95% confidence interval [CI] = 79.1–91.2%). There were 40 episodes in 18 patients in which iATP was unsuccessful and resulted in at least one shock (66 total shocks). Among episodes detected in the FVT zone, 60 of 73 were successfully terminated by iATP (82.2%

Table 1. Baseline characteristics of SPARK registry patients.

Baseline characteristics	Total ($n = 800$)	CRT-D subjects in Japan ($n = 152$)	CRT-D subjects in South Korea ($n = 100$)	ICD subjects in Japan ($n = 248$)	ICD subjects in South Korea ($n = 300$)
Age (years)	68.0 ± 13.9	71.5 ± 12.6	70.5 ± 12.1	69.0 ± 13.2	64.7 ± 15.0
Male	604 (75.5%)	122 (80.3%)	168 (68.0%)	188 (75.8%)	226 (75.3%)
Primary Prevention Indication	494 (61.8%)	122 (80.3%)	85 (85.0%)	112 (45.2%)	175 (58.3%)
LVEF (%)	38.3 ± 15.3	29.9 ± 10.3	31.4 ± 10.1	43.6 ± 15.7	40.4 ± 15.9
Available	774 (96.7%)	149 (98.0%)	95 (95.0%)	241 (97.2%)	289 (96.3%)
QRS Duration (ms)	126.7 ± 32.7	149.6 ± 28.8	153.4 ± 27.2	118.2 ± 27.5	113.7 ± 29.1
Available	788 (98.5%)	145 (95.4%)	99 (99.0%)	246 (99.2%)	298 (99.3%)
Left Bundle Branch Block	130 (16.3%)	81 (53.3%)	34 (34.0%)	6 (2.4%)	9 (3.0%)
Coronary Artery Disease	166 (20.8%)	50 (32.9%)	16 (16.0%)	49 (19.8%)	97 (32.3%)
Ischemic Cardiomyopathy	174 (21.8%)	38 (25.0%)	17 (17.0%)	44 (17.7%)	75 (25.0%)
Myocardial Infarction	138 (17.3%)	27 (17.8%)	7 (7.0%)	54 (21.8%)	50 (16.7%)
Hypertension	316 (39.5%)	62 (40.8%)	52 (52.0%)	79 (31.9%)	123 (41.0%)
NYHA Class					
No Heart Failure	71 (8.9%)	0 (0.0%)	0 (0.0%)	40 (16.1%)	31 (10.3%)
I	94 (11.8%)	7 (4.6%)	4 (4.0%)	61 (24.6%)	22 (7.3%)
II	274 (34.3%)	67 (44.1%)	33 (33.0%)	91 (36.7%)	83 (27.7%)
III	167 (20.9%)	66 (43.4%)	24 (24.0%)	37 (14.9%)	40 (13.3%)
IV	22 (2.8%)	9 (5.9%)	1 (1.0%)	7 (2.7%)	5 (1.7%)
Not Available	172 (21.5%)	3 (2/0%)	38 (38.0%)	12 (4.8%)	119 (39.7%)
Arrhythmia Related Syncope	86 (10.8%)	11 (7.2%)	2 (2.0%)	45 (18.1%)	28 (9.3%)
Atrial Arrhythmias	275 (34.4%)	67 (44.1%)	30 (30.0%)	84 (33.9%)	94 (31.3%)

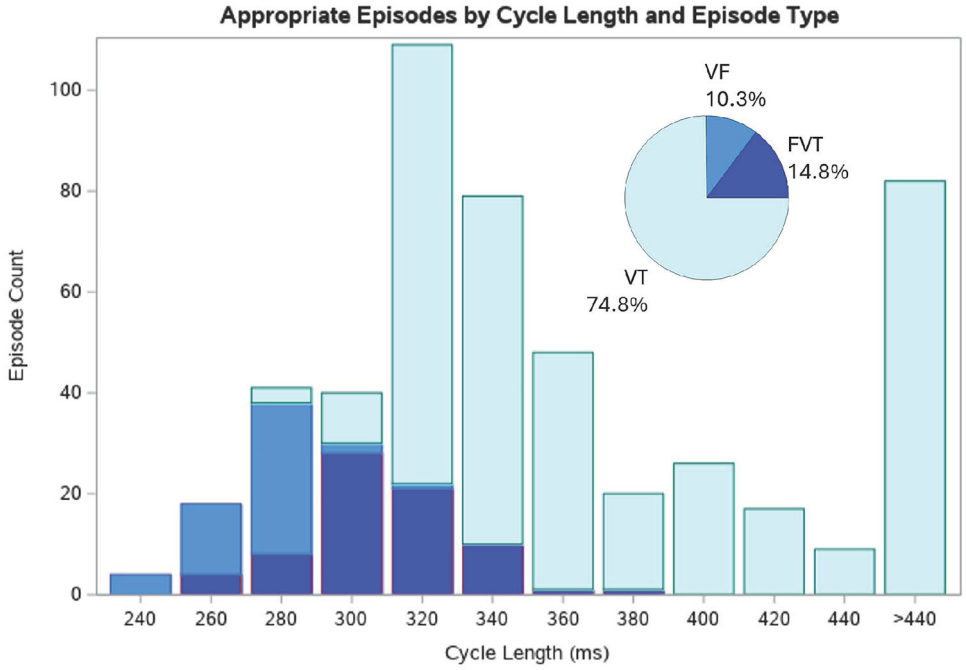

Figure 1. Distribution of iATP treated episodes by detection zone and cycle length at detection.

Table 2. Rhythm classification of iATP treated episodes from the SPARK registry.

	Overall ($n = 526$)	FVT ($n = 81$)	VF ($n = 56$)	VT ($n = 389$)
Rhythm				
Atrial Fibrillation/Flutter	12 (2.3%)	2 (2.5%)	0 (0%)	10 (2.6%)
Mono VT	493 (94%)	73 (90%)	51 (91%)	369 (95%)
Other SVT/Sinus Tach	21 (4%)	6 (7.4%)	5 (8.9%)	10 (2.6%)

unadjusted, 80.9% GEE estimated; 95% CI = 63.3–91.2%). Among the FVT episodes that were not terminated by iATP, 13 episodes in six patients resulted in one shock. There were a small number of episodes that were treated with standard ATP (10 episodes were treated by standard ATP prior to iATP, and five episodes were treated by standard ATP after iATP). There were 1.70 ± 1.97 attempts of ATP or iATP that

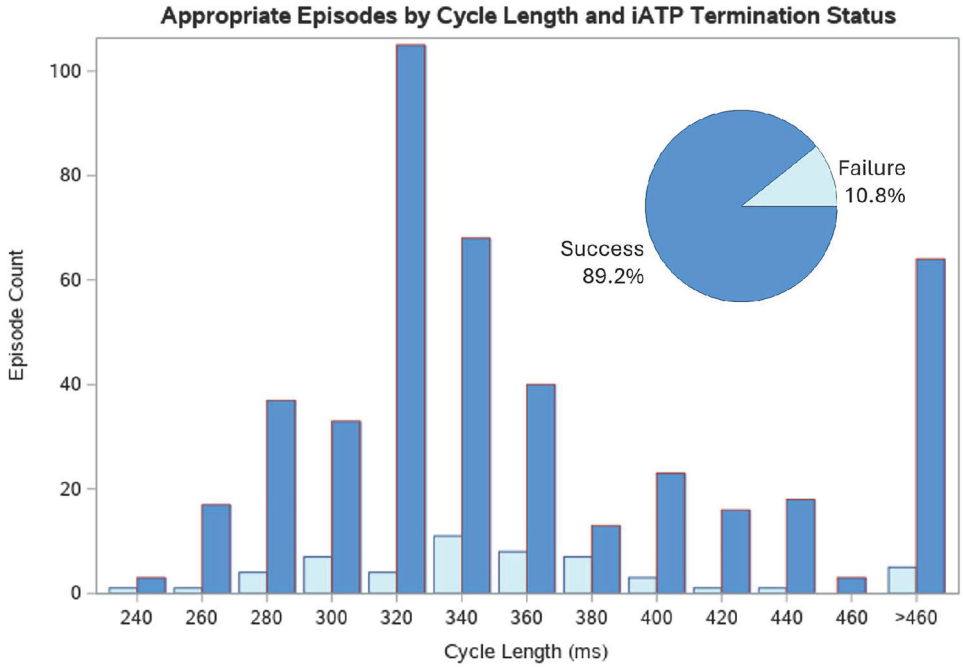

Figure 2. Distribution of iATP success and failure overall and by cycle length at detection.

were delivered per successfully treated episode. The efficacy of iATP to terminate episodes is displayed by cycle length in Figure 2.

Among all shock therapies delivered by the device (whether episode was treated by iATP or not), 32 patients received 120 total shocks. There were 96 appropriate shocks in 25 patients, and 24 inappropriate shocks in seven patients. Among patients with at least 90 days of device follow-up, 98.9% (612 of 619) were inappropriate shock free over the follow-up period.

Safety

Acceleration after iATP was observed in 10 MVT episodes among 493 MVT episodes (2.0%) in six patients. There were three observations of arrhythmia-related syncope in three distinct patients among 619 patients with device data available (0.5%), all three treated with medications and one with device reprogramming. Among the 370 patients with CareLink data available, only one had a manual reprogramming from iATP to standard ATP, and this was in the VF zone. In the VT and FVT zones iATP was never reprogrammed to standard ATP. Death occurred in 36 (4.5%) patients during the study. The Kaplan-Meier survival at 1-year post-implant was 96.1% (95% CI = 94.7–97.5%). Site reported modes of death included non-cardiac (44.4%), non-sudden cardiac (25.0%), sudden cardiac (13.9%), and unknown (16.7%), and all deaths were adjudicated as not related to the ICD system. There were no reported abnormal battery depletions during the SPARK registry follow-up.

Comparative analysis

Individual patient data from all patients enrolled in the SPARK registry were included in the comparative analysis. For the comparator arm, the systematic literature search was performed in March 2025 and resulted in 181 studies. There were 132 exclusions at screening and 37 exclusions after manuscript review, resulting in 12 included for analysis (Supplementary Figure S3). The most common reasons for exclusion were incorrect population or intervention ($n = 64$) and no report of ATP efficacy ($n = 63$). Baseline characteristics from the studies in the comparator arm are summarized in Table 3. Reported mean/median cycle lengths of ATP treated episodes for comparator studies ranged from 290 to 310 milliseconds. The chi-square tests of the Cochran's Q yielded statistically significant results indicating a significant heterogeneity between comparator studies that cannot be explained by sampling uncertainty

Table 3. Baseline characteristics of standard ATP comparator literature.

Study[a]	Arm	*N*	Age	Male	ICD	Primary prevention	LVEF	QRS	Ischemic history	HTN	NYHA III-IV	Atrial arrhythmia
Wathen et al. (2001)[5]	ATP	220	67	78.0%	100%	37.0%	33.0%	NR	100%	51.0%	25.0%	NR
Wathen et al. (2004)[4]	ATP	313	67	80.0%	100%	48.0%	32.0%	NR	83.0%	56.0%	18.0%	NR
Santini et al. (2010)[10]	8 pulse ATP	475	64	86.1%	100%	42.7%	33.7%	NR	76.6%	NR	31.6%	NR
Santini et al. (2010)[10]	15 pulse ATP	450	63.4	89.3%	100%	39.6%	34.2%	NR	72.7%	NR	30.7%	NR
Gasparini et al. (2010)[11]	BiV ATP	266	66.6	86.8%	0.0%	81.6%	24.9%	155.7	66.5%	NR	NR	NR
Gasparini et al. (2010)[11]	RV ATP	260	66.8	83.8%	0.0%	80.4%	26.0%	153.9	61.2%	NR	NR	NR
Saeed et al. (2010)[25]	ATP	830	67.2	72.5%	76.4%	100.0%	25.2%	NR	71.1%	56.5%	28.6%	32.0%
Anguera et al. (2015)[26]	Single ATP Burst	42	64.1	85.7%	73.8%	59.0%	NR	NR	61.9%	45.2%	45.2%	26.2%
Anguera et al. (2015)[26]	Successive ATP	112	62.5	90.2%	75.9%	58.2%	NR	NR	51.8%	52.7%	40.2%	31.2%
Auricchio et al. (2015)[27], Sterns et al. (2023)[16]	ATP	2770	64.8	79.4%	61.3%	69.2%	32.2%	125.9	44.0%	52.1%	32.2%	32.0%
Watanabe et al. (2014)[28]	ATP	715	65.3	76.9%	60.0%	42.1%	42.9%	124.6	41.0%	47.7%	21.8%	30.0%
Chinushi et al. (2020)[29]	ATP	85	65.4	81.2%	61.0%	52.9%	35.8%	135.1	27.1%	NR	33.0%	17.7%
Gulizia et al. (2009)[30]	Ramp ATP	103	66	79.0%	100%	59.0%	30.0%	120	57.0%	49.0%	55.0%	23.0%
Gulizia et al. (2009)[30]	Burst ATP	103	67	84.0%	100%	46.0%	33.0%	119	68.0%	49.0%	57.0%	28.0%
Knops et al. (2022)[31], Olde Nordkamp et al. (2024)[32]	Transvenous ICD	423	64	81.6%	100%	80.1%	30.0%	105	69.2%	57.3%	15.2%	22.1%
Schuger et al. (2024)[9]	ATP + Shock	1302	64	78.7%	100%	100.0%	27.4%	107	58.1%	71.7%	29.7%	26.2%

NR, Not reported.
[a]See Supplement 5 for detailed information on included publications.

alone. Therefore, we adopted random-effect models to pool the study estimates. After individual patient data reweighting, there was close matching between SPARK registry and comparator arm baseline characteristics (Supplementary Table S4).

In the base case analysis, the use of iATP in all treated episodes was associated with a significant higher termination efficacy (iATP = 88.1% and ATP = 79.3%, $p < 0.001$), and the results are presented in Figure 3. The use of iATP in treated episodes in the FVT zone was also associated with a significantly higher termination efficacy (iATP = 85.6% and ATP = 73.5%, $p < 0.001$). The results for iATP efficacy were otherwise directionally consistent when adjusted for multiple episodes within patients, and when performed for subsets of studies with wider covariate inclusion (Supplementary Table S3). The termination efficacy of iATP remained high across a wide range of cycle lengths (Supplementary Figure S4).

When compared to standard ATP, iATP was associated with a lower probability of shock given an appropriate detection, inclusive of episodes treated with shock only or ATP and shock (iATP = 14.7% and ATP = 31.3%, $p < 0.001$). The use of iATP was associated with a lower rate of accelerations per treated episode (2.1% vs 4.8%, $p = 0.02$). There was no significant difference in the probability of arrhythmia-related syncope per patient (0.5% vs 0.9%, $p = 0.35$). The results for shocks, accelerations, and arrhythmia-related syncope are presented in Figure 3. When compared to a single comparator study with detailed survival analysis available[9], no significant difference in mortality was observed (12-month Kaplan Meyer survival estimate iATP = 95.4%, ATP = 95.3%, $p = 0.43$, Supplementary Figure S5).

Discussion

In the prospective SPARK registry including Japanese and South Korean patients, iATP successfully terminated 89.2% (86.2% GEE estimated) of all treated episodes, and 82.2% (80.9% GEE estimated) of episodes detected in the FVT zone. In addition, iATP had a favorable safety profile as characterized by episode acceleration (1.9% of episodes), arrhythmia-related syncope (0.4% of patients), and overall mortality (96.1% survival at 1 year) with no observation of abnormal battery depletion. A post hoc comparative analysis found that the use of iATP was associated with a significantly higher termination efficacy across zones as compared to standard ATP (iATP = 88.1% and ATP = 79.3%, $p < 0.001$), and significantly higher termination efficacy for episodes detected in the FVT zone (iATP = 85.6% and ATP = 73.5%, $p < 0.001$). The use of iATP was associated with a lower incidence of episode acceleration (iATP = 2.1% and ATP = 4.8%, $p = 0.02$) and a similar probability of arrhythmia-related syncope per patient (iATP = 0.5% and ATP = 0.9%, $p = 0.35$), with no significant difference in mortality ($p = 0.43$). A substantial number of patients remained inappropriate shock-free (98.9%) over the follow-up period.

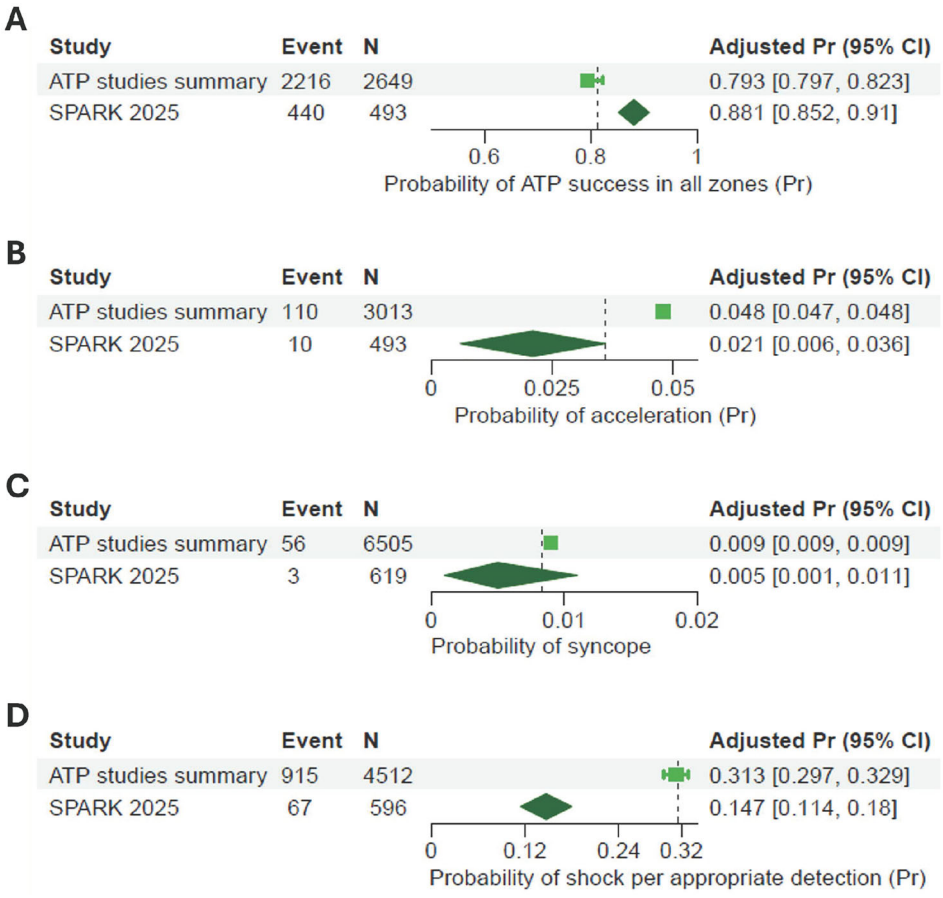

Figure 3. Comparative results for termination efficacy in all zones (Panel A), acceleration (Panel B), arrhythmia-related syncope (Panel C), and shocks (Panel D).

Several previous investigations have reported on the performance of standard ATP. The studies that qualified for the comparative analysis represent a wide date range (2001[5] to 2024[9]) and technology from different manufacturers[9,16]. The median of the termination success rate of 70.4% across the studies in the comparative analysis represents a reasonable real-world performance expectation.

There is emerging evidence to corroborate the observations in the individual patient data from the SPARK registry. A virtual heart modeling study found that iATP was able to terminate episodes that were not terminated by standard ATP, with better efficacy attributed to closing the excitable gap and reaching the critical isthmus of the VT[17]. In a feasibility study of 144 patients, Yee and colleagues observed a raw termination efficacy for iATP of 82.8% across all detection zones[13]. Yanagisawa et al. performed a novel study randomizing the order of application of either standard ATP or iATP and found that, in episodes where initial standard ATP failed to terminate, iATP was significantly more likely to terminate those episodes as compared to applying standard ATP after iATP failure to terminate, implying that iATP has broader effectiveness[18]. In a propensity matched analysis, Onuki et al. found that iATP was associated with a higher termination rate (84.1% vs. 53.6%, $p < 0.001$) and lower rate of acceleration (0.0% vs. 10.1%, $p = 0.013$) compared to standard ATP[19]. Finally, a recently published analysis of iATP performance found the overall termination success rate in MVT episodes to be 87.1%[20].

There is biological plausibility to the observation that iATP had an improved termination efficacy and reduction in accelerations. The iATP algorithm was designed to address previously observed failure modes of standard ATP in episode termination. Insufficient prematurity is addressed in iATP by providing rapid pacing *via* extra stimuli that is tuned with learnings from failed initial termination attempts if necessary. The ability to first try one extra stimulus and switch to two if needed is a difference from standard ATP, where the entire series of burst paces are made more rapid to achieve the same result, increasing the potential for episode acceleration. Finally, iATP enables automaticity in tailoring treatment

to the specific needs of each patient and each VT episode without manual effort, which is important as real-world programming lags consensus recommendations. The findings of the Shock-Less study[12] found even after distribution of programming reports, optimal programming was still achieved in less than 50% of patients.

To further characterize the safety profile of iATP there are a few other considerations. Compared to standard ATP, use of iATP was associated with no difference in arrhythmia-related syncopal episodes. In addition, the rate of inactivation of iATP therapy was low, indicating that patients rarely experienced symptoms driving physician modification of therapy settings. Finally, there were no observations of premature battery depletion in the SPARK registry. There is no quantitative analysis of the number of ATP therapies delivered, but this observation can be explained by the principle of operation. Low energy pacing pulses that are infrequently delivered such as those delivered by iATP have minimal impact on battery depletion. For example, a typical ATP sequence involves eight pulses at 8 volts for 1.5 milliseconds, which cumulatively requires less than one part in 9 million of the energy from a battery with a capacity of 1 amp-hour.

Programming in the SPARK patients may have been driven by a therapeutic goal to treat slower VT episodes. This might be due to unmeasured differences in patient characteristics, such as cardiac sarcoidosis[21]. This is evidenced by the median cycle length difference between SPARK (340 ms) and the comparator studies (290–310 ms) and by noting the large number of episodes with cycle length $>$440 ms (Figure 1). As a result, the analyses of the SPARK registry data may include episodes of different pathologies (slow ordinary monomorphic VT and very slow sarcoidosis mediated episodes) being considered together. Overall, the improved termination rate associated with iATP could benefit all patients, especially those expected to have more VT episodes, such as patients with a secondary prevention indication or those with ischemic cardiomyopathy and significant myocardial scarring. Additionally, treatment of VTs with very long cycle lengths (i.e. $>$400 ms) is a therapeutic focus in these countries, and the success rate of iATP terminations was observed to be strong in episodes with cycle length $>$460 ms.

The use of uMAIC in this study was employed because iATP is a new algorithm and direct comparative data is not yet fully developed *via* traditional clinical trials. Unlike a naïve meta-analysis, which aggregates findings without accounting for differences in patient populations, uMAIC adjusts individual patient-level data from one study to match the aggregate characteristics of another, thereby minimizing bias and improving comparability. Its adaptability and methodological rigor make it a valuable tool for health technology assessment organizations[22], and it has been widely used in oncology research with more recent applications in cardiovascular medicine[23,24].

The SPARK Registry and the comparative analysis have limitations that should be acknowledged. The registry had no control arm for direct comparison to standard ATP. The comparison to standard ATP was a post hoc analysis that used the uMAIC method to account for differences in patient characteristics. Undocumented prognostic or effect-modifying factors, particularly in the comparator arm, may have impacted the validity of uMAIC results. The registry was limited to devices from a single manufacturer which could limit generalizability, though the iATP algorithm is only available from this manufacturer. Device programming, such as detection parameters, discrimination algorithms, and therapy delivery strategies differ among the comparison literature and are not consistently reported. Therefore, these are not directly accounted for in the comparative analyses. Primary prevention indications were not collected directly in the SPARK registry and were instead derived from reported arrhythmia history. The iATP performance data was exclusive to patients from Japan and South Korea and was compared to standard ATP data, of which only two studies were in patients from Japan, with the others not isolated to these populations. For example, the cycle lengths for episodes in the registry were longer on average than those reported in the comparison literature and may reflect region-specific treatment practices. However, the efficacy of iATP in the registry data did not seem to vary greatly over different cycle lengths. The definition of arrhythmia-related syncope and acceleration were not consistent across the data being compared. The uMAIC analysis was unanchored as there were no individual studies that met the selection criteria that compared iATP to standard ATP directly. To address this issue, an effort was made to include a broad set of comparator literature, patient characteristics for adjustment, and scenarios for sensitivity analysis. While this analysis did not stratify outcomes by study type, the inclusion of both randomized controlled trial and real-world data was intended to ensure a robust comparator

reflective of variation in ATP application. The comparator studies from the literature did not uniformly report the same patient baseline characteristics and outcome measures, so each analysis may have used unique subsets of the comparator studies based on availability of the applicable characteristics and outcomes. The results of this analysis are most applicable to the Japanese and South Korean healthcare systems and may not be generalized to other systems.

Conclusion

The results from this prospective registry provide evidence that the iATP algorithm had a high success rate of termination of device-detected ventricular arrhythmias, a low rate of accelerations, and a low rate of arrhythmia-related syncope. An unanchored matching-adjusted indirect comparison to literature on standard ATP provides initial evidence that iATP was associated with a higher termination efficacy and a favorable safety profile.

Transparency

Declaration of funding

This work was supported by Medtronic Japan Co., Ltd. The funder/study sponsor played a role in the study design, data analysis, and preparation of the manuscript.

Declaration of financial/other interests

MG: Lecture fees – Japan Lifeline, Abbott Medical Japan, Johnson & Johnson. SJP: None. KA: Lecture fees – Medtronic Japan, Japan Lifeline, Abbott Medical Japan, Biotronik Japan, Novartis Pharma. RH: Medtronic employee and shareholder. RI: Medtronic employee. LJ: Medtronic employee and shareholder. JM: Medtronic employee. BJ: None. A reviewer on this manuscript has disclosed that they are affiliated with a department that has been sponsored by Medtronic Japan. The other peer reviewers on this manuscript have no other relevant disclosures. All the reviewers received an honorarium for their peer review work.

Author contributions

LJ contributed to the study conception and methodology for the registry and RH, RI contributed to the conception and methodology of the comparative analysis. MG, SJP, KA, and BJ, along with the study investigators, collected the study data and LJ performed the analysis. RH collected the comparative analysis data and RI performed the comparative analysis. All authors interpreted the results and contributed to the discussion. RH drafted the manuscript, with critical revisions provided by all authors. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Acknowledgements

The authors express their gratitude to Yoshiko Ishiwatari, Yewon Lee, Michelle Kim, So-Jeong You, Vu Huynh, and Shauna Johnson (Medtronic, Inc.) for their pivotal roles in executing the SPARK Registry. Appreciation is also extended to Waruiru Mburu and Hyung-Deuk Park (Medtronic, Inc.) for their meticulous validation of data extracted from the comparator literature and the uMAIC analysis. Additionally, the authors acknowledge Troy Jackson and Bob Taepke for their expertise in ATP and iATP, which contributed significantly to this study. This research was supported by Medtronic Inc.

Data availability statement

Data are not publicly available due to the sensitive nature of the research. Relevant data can be made available upon reasonable request.

ORCID

Masahiko Goya http://orcid.org/0000-0002-7210-0671
Seung-Jung Park http://orcid.org/0000-0002-9187-5405

Kenji Ando http://orcid.org/0000-0003-0699-4248
Reece Holbrook http://orcid.org/0000-0001-8995-3024
Rowan Iskandar http://orcid.org/0000-0001-8680-4824
Luke Jacobsen http://orcid.org/0000-0002-1906-4421
Joseph D. Mozingo http://orcid.org/0000-0003-1609-1421
Boyoung Joung http://orcid.org/0000-0001-9036-7225

References

[1] Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation. 2018;138(13):e210–e271.
[2] Iwasaki YK, Noda T, Akao M, et al. JCS/JHRS 2024 guideline focused update on management of cardiac arrhythmias. Circ J. 2025;89(7):1012–1073. doi:10.1253/circj.CJ-24-0073.
[3] Zeppenfeld K, Tfelt-Hansen J, de Riva M, et al. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J. 2022;43(40):3997–4126. doi:10.1093/eurheartj/ehac262.
[4] Wathen MS, DeGroot PJ, Sweeney MO, et al. Prospective randomized multicenter trial of empirical antitachycardia pacing versus shocks for spontaneous rapid ventricular tachycardia in patients with implantable cardioverter-defibrillators: Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (PainFREE Rx II) trial results. Circulation. 2004;110(17):2591–2596. doi:10.1161/01.CIR.0000145610.64014.E4.
[5] Wathen MS, Sweeney MO, DeGroot PJ, et al. Shock reduction using antitachycardia pacing for spontaneous rapid ventricular tachycardia in patients with coronary artery disease. Circulation. 2001;104(7):796–801. doi:10.1161/hc3101.093906.
[6] Turakhia MP, Zweibel S, Swain AL, et al. Healthcare utilization and expenditures associated with appropriate and inappropriate implantable defibrillator shocks. Circ Cardiovasc Qual Outcomes. 2017;10(2):e002210.
[7] Li A, Kaura A, Sunderland N, et al. The significance of shocks in implantable cardioverter defibrillator recipients. Arrhythm Electrophysiol Rev. 2016;5(2):110–116. doi:10.15420/AER.2016.12.2.
[8] Wilkoff BL, Ousdigian KT, Sterns LD, et al. A comparison of empiric to physician-tailored programming of implantable cardioverter-defibrillators: results from the prospective randomized multicenter EMPIRIC trial. J Am Coll Cardiol. 2006;48(2):330–339. doi:10.1016/j.jacc.2006.03.037.
[9] Schuger C, Joung B, Ando K, et al. Assessment of antitachycardia pacing in primary prevention patients: the APPRAISE ATP randomized clinical trial. JAMA. 2024;332(20):1723–1731. doi:10.1001/jama.2024.16531.
[10] Santini M, Lunati M, Defaye P, et al. Prospective multicenter randomized trial of fast ventricular tachycardia termination by prolonged versus conventional anti-tachyarrhythmia burst pacing in implantable cardioverter-defibrillator patients-Atp DeliVery for pAiNless ICD thErapy (ADVANCE-D) trial results. J Interv Card Electrophysiol. 2010;27(2):127–135. doi:10.1007/s10840-009-9454-z.
[11] Gasparini M, Anselme F, Clementy J, et al. BIVentricular versus right ventricular antitachycardia pacing to terminate ventricular tachyarrhythmias in patients receiving cardiac resynchronization therapy: the ADVANCE CRT-D trial. Am Heart J. 2010;159(6):1116–1123.e2. doi:10.1016/j.ahj.2010.02.007.
[12] Silver MT, Sterns LD, Piccini JP, et al. Feedback to providers improves evidence-based implantable cardioverter-defibrillator programming and reduces shocks. Heart Rhythm. 2015;12(3):545–553. doi:10.1016/j.hrthm.2014.11.002.
[13] Yee R, Fisher JD, Birgersdotter-Green U, et al. Initial clinical experience with a new automated antitachycardia pacing algorithm: feasibility and safety in an ambulatory patient cohort. Circ Arrhythm Electrophysiol. 2017;10(9):e004823.
[14] von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344–349. doi:10.1016/j.jclinepi.2007.11.008.
[15] Signorovitch JE, Sikirica V, Erder MH, et al. Matching-adjusted indirect comparisons: a new tool for timely comparative effectiveness research. Value Health. 2012;15(6):940–947. doi:10.1016/j.jval.2012.05.004.
[16] Sterns LD, Auricchio A, Schloss EJ, et al. Antitachycardia pacing success in implantable cardioverter-defibrillators by patient, device, and programming characteristics. Heart Rhythm. 2023;20(2):190–197. doi:10.1016/j.hrthm.2022.10.015.
[17] Swenson DJ, Taepke RT, Blauer JJE, et al. Direct comparison of a novel antitachycardia pacing algorithm against present methods using virtual patient modeling. Heart Rhythm. 2020;17(9):1602–1608. doi:10.1016/j.hrthm.2020.05.009.
[18] Yanagisawa S, Inden Y, Sato Y, et al. Comparison of novel intrinsic versus conventional antitachycardia pacing for ventricular tachycardia among implantable cardioverter-defibrillator recipients. J Cardiovasc Electrophysiol. 2024;35(4):821–831. doi:10.1111/jce.16232.

[19] Onuki K, Nagashima M, Fukunaga M, et al. The efficacy and safety of intrinsic antitachycardia pacing. J Arrhythm. 2025;41(1):e13221.
[20] Jackson T, Yee R, Taepke R, et al. Real world performance of an individualized antitachycardia pacing algorithm. J Cardiovasc Electrophysiol. 2025. doi:10.1111/jce.16747.
[21] Terasaki F, Azuma A, Anzai T, et al. JCS 2016 guideline on diagnosis and treatment of cardiac sarcoidosis – digest version. Circ J. 2019;83(11):2329–2388. doi:10.1253/circj.CJ-19-0508.
[22] Farinasso CM, Ferreira VL, Medeiros FC, et al. Matching-adjusted indirect comparison studies in oncology: a scoping review focused on reporting quality. Value Health Reg Issues. 2025;47:101088. doi:10.1016/j.vhri.2025.101088.
[23] Kasner SE, Sondergaard L, Nakum M, et al. A matching-adjusted indirect comparison of results from REDUCE and RESPECT-two randomized trials on patent foramen ovale closure devices to prevent recurrent cryptogenic stroke. J Med Econ. 2024;27(1):337–343. doi:10.1080/13696998.2024.2320604.
[24] Hussein A, Gupta D, De Potter T, et al. Treatment of Atrial fibrillation using ablation index-guided contact force ablation: a matching-adjusted indirect comparison to cryoballoon ablation. Adv Ther. 2020;37(2):785–799. doi:10.1007/s12325-019-01173-4.
[25] Saeed M, Neason CG, Razavi M, et al. Programming antitachycardia pacing for primary prevention in patients with implantable cardioverter defibrillators: results from the PROVE trial. J Cardiovasc Electrophysiol. 2010;21(12):1349–1354. doi:10.1111/j.1540-8167.2010.01825.x.
[26] Anguera I, Dallaglio P, Martínez-Ferrer J, et al. Shock reduction with multiple bursts of antitachycardia pacing therapies to treat fast ventricular tachyarrhythmias in patients with implantable cardioverter defibrillators: a multicenter study. J Cardiovasc Electrophysiol. 2015;26(7):774–782. doi:10.1111/jce.12699.
[27] Auricchio A, Schloss EJ, Kurita T, et al. Low inappropriate shock rates in patients with single- and dual/triple-chamber implantable cardioverter-defibrillators using a novel suite of detection algorithms: painFree SST trial primary results. Heart Rhythm. 2015;12(5):926–936. doi:10.1016/j.hrthm.2015.01.017.
[28] Watanabe T, Inoue K, Kashiwase K, et al. Efficacy of anti-tachycardia pacing for terminating fast ventricular tachycardia in Japanese implantable cardioverter defibrillator patients. Primary results of the SATISFACTION study. Circ J. 2014;78(11):2643–2650. doi:10.1253/circj.cj-14-0146.
[29] Chinushi M, Furushima H, Saitoh O, et al. Patient-by-patient basis anti-tachycardia pacing for fast ventricular tachycardia with structural heart diseases. Pacing Clin Electrophysiol. 2020;43(9):983–991. doi:10.1111/pace.13980.
[30] Gulizia MM, Piraino L, Scherillo M, et al. A randomized study to compare ramp versus burst antitachycardia pacing therapies to treat fast ventricular tachyarrhythmias in patients with implantable cardioverter defibrillators: the PITAGORA ICD trial. Circ Arrhythm Electrophysiol. 2009;2(2):146–153. doi:10.1161/CIRCEP.108.804211.
[31] Knops RE, van der Stuijt W, Delnoy P, et al. Efficacy and safety of appropriate shocks and antitachycardia pacing in transvenous and subcutaneous implantable defibrillators: analysis of all appropriate therapy in the PRAETORIAN trial. Circulation. 2022;145(5):321–329. doi:10.1161/CIRCULATIONAHA.121.057816.
[32] Olde Nordkamp LRA, Pepplinkhuizen S, Ghani A, et al. Inappropriate therapy and shock rates between the subcutaneous and transvenous implantable cardiac defibrillator: a secondary analysis of the PRAETORIAN trial. Circ Arrhythm Electrophysiol. 2024;17(12):e012836.