Generating Patient Centric Outcomes with Abbott Technology

Cardiac Rhythm Management
High Voltage Clinical Compendium

Updated August 2021

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Introduction

This document is a collection of relevant clinical publication references that comprise the clinical foundation for Abbott's high voltage, CRM portfolio. Publications are listed by topic and include a background on patient response and its association with survival as well as clinical evidence for unique algorithms including SyncAV™ CRT Technology, VF Therapy Assurance, and DeFT Response™ Technology.

Each publication entry includes its full reference if available, an abstract, and a link to the full article. (This link may require the reader to pay for the full content).

This document will be updated as future publications become available.

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Patient Response and Survival

There are many ways to quantify response. Broadly, they can be classified into three distinct categories:

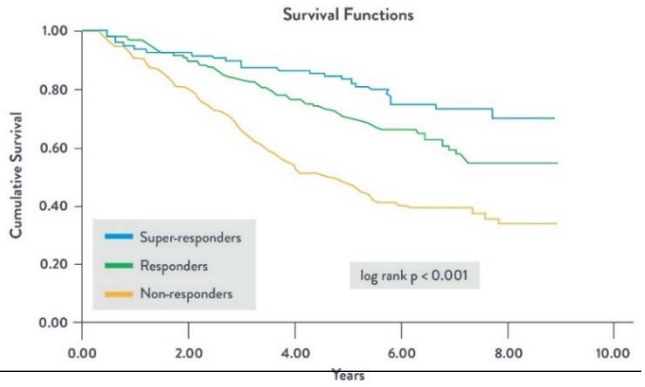
Advancing a patient to the next level of response is associated with decreased mortality rates, reduced heart failure events and a decrease in healthcare expenditures.[1,2]

SURVIVAL AT 5 YEARS[1]

82% Super-Responders

70% Responders

48% Non-Responders

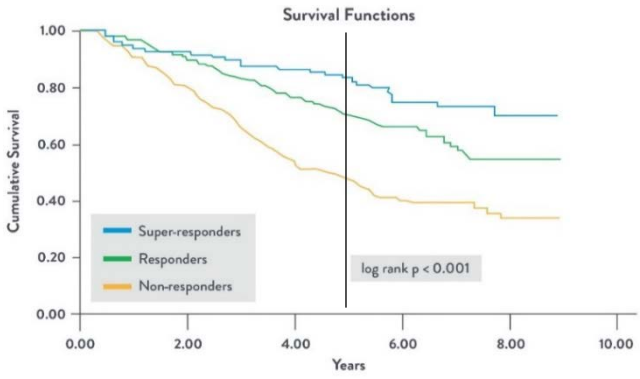


DIFFERENCES IN MORTALITY RATES[1]

34% Super-Responder vs Non-Responder

22% Responder vs Non-Responder

12% Super-Responder vs Responder



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Economic Burden of Non-Response

Responders Cost Less to the Healthcare System

Responders experience

4.81x

less heart failure events than non-responders[2*]

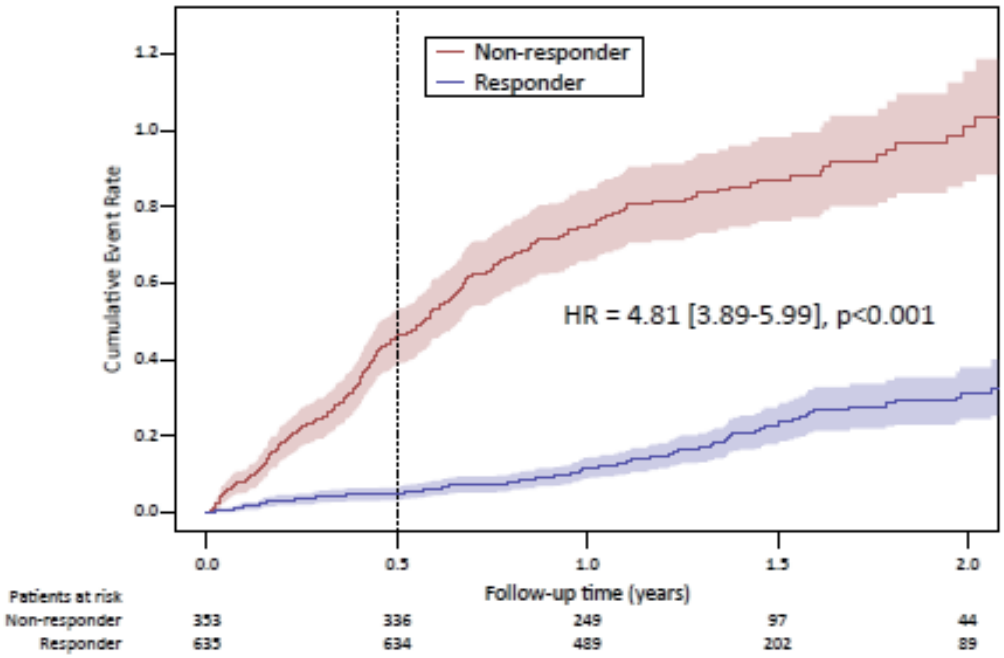
Improving the response rate by

10%

would reduce US health costs by

$26 million annually[2*]

*In this study response was defined using a clinical composite score



Cumulative event rate over time for all types of HF events. Vertical dashed line indicates when response was characterized by CCS. Shaded areas are 95% confidence intervals.

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Response, Survival, and Economics Information Sources

1 Durability of the survival effect of cardiac resynchronization therapy by level of left ventricular functional improvement: fate of "non-responders."

Link to publication

Citation: Rickard J, Cheng A, Spragg D, et al. Durability of the survival effect of cardiac Resynchronization therapy by level of left ventricular functional improvement: fate of "non-responders." Heart Rhythm. 2014;11(3):412-416. https://doi.org/10.1016/j.hrthm.2013.11.025. Accessed July 31, 2018.

Background: Although improvement in left ventricular (LV) function has been shown to portend superior short-term outcomes in patients with heart failure undergoing cardiac resynchronization therapy (CRT), the durability of this effect at 5 years has not been established.

Objective: To determine the long-term outcomes of patients undergoing CRT on the basis of the degree of echocardiographic response.

Methods: We extracted clinical data on a cohort of 880 consecutive patients undergoing the new implantation of a CRT device between September 30, 2003, and August 6, 2007. Patients with an ejection fraction (EF) ≤35% undergoing initial CRT implantation, with an available pre-CRT and follow-up echocardiogram, were included in the final cohort. On the basis of changes in LVEF, patients were categorized into "non-responders" (change in EF ≤4%), "responders" (EF change 5%–20%), and "super-responders" (change in EF >20%). A Cox multivariate model was performed to determine the effect of response on long-term survival free of LV assist device or heart transplant.

Results: A total of 526 patients met inclusion criteria, of whom 196 (37.3%) were classified as non-responders, 236 (44.9%) as "responders," and 94 (17.9%) as "super-responders." In multivariate analysis, "super-responders" had the best survival and non-responders the worst over a mean of follow-up of 5.3 ± 2.4 years. At 5 years, survival free of LV assist device or heart transplant among super-responders was 82%; responders, 70%; and non-responders, 48%.

Conclusions: In patients with heart failure undergoing CRT, survival benefit is durable at 5 years follow-up and its degree intimately tied to the level of improvement in ventricular function. The prognosis of non-responders is exceptionally poor.

2 The cost of non-response to CRT: analysis from the ADVANCE-CRT registry

Citation: Varma N, et al. The cost of non-response to CRT: Analysis from the ADVANCE-CRT registry. Poster presented at Heart Rhythm Society. 2018.

Background: A large minority of patients (pts) receiving cardiac resynchronization therapy (CRT) according to current guidelines do not benefit, and may suffer costly repeated hospitalizations.

Objective: Quantify the healthcare resource utilization of CRT non-response.

Methods: The ADVANCE-CRT registry monitored pts from 69 centers worldwide receiving Abbott CRT devices from 2013- 2015. Response to CRT (CRT-R) therapy was measured at 6 months using a clinical composite score (inclusive of NYHA class, patient global assessment, HF events, and cardiovascular death). Inpatient hospitalizations for heart failure (HFH) were reported during follow up of up to 2 years (yr). HFH rates were modeled with Poisson regression
and costs over time estimated assuming published HFH event costs ($16,770 Medicare, $30,100 private insurance).

Results: Of 988 US pts included in the analysis (31% female, LVEF 31 ± 12%, ischemic disease 46%, age 70 ± 11 yrs), 353 (35%) were non-responders (CRT-NR) at 6 months. HFH occurred in 96 (27%) CRT-NR and 32 (5%) CRT-R over 2 years. Length of stay of each HFH was similar between the two groups (6.8 ± 7.3 days). Number of HFH per pt was significantly higher for CRT-NR at both 1 yr (0.42 ± 0.05) and 2 yrs (0.62 ± 0.08) after implant, compared to CRT-R (0.04 ± 0.01 and 0.13 ± 0.03 respectively).

Conclusions: CRT-NR had 11X more HFH at 1 yr and 5X more HFH at 2 yrs than CRT-R. Given ≈40,000 CRT US implants every year, reducing CRT non-response rate by only 10% would save the healthcare system more than $25 million/yr.

CRT Optimization

Clinical Significance of QRS Narrowing

Cardiac resynchronization therapy-induced acute shortening of QRS duration predicts long-term mortality only in patients with left bundle branch block3
Jastrzebski, Marek, et al. Ep Europace 21.2 (2019): 281-289

Link to publication

This single-center, longest retrospective mortality study is the first to demonstrate that shortening of QRS duration predicts favorable prognosis in patients with left bundle branch block (LBBB); reinforcing the importance of QRS shortening with initiation of cardiac resynchronization therapy.

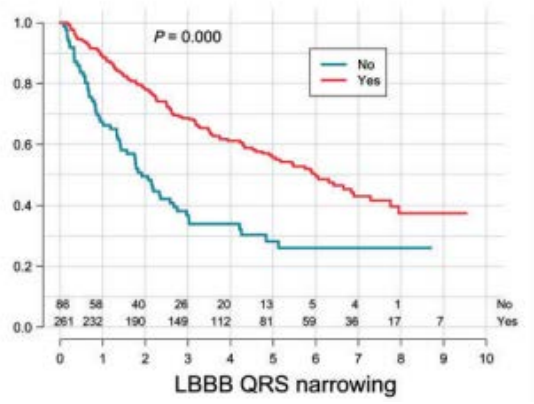
Methods Summary

Included 552 consecutive patients who underwent CRT device implantation

Study Endpoints:
Primary – Death from any cause or urgent heart transplantation
Secondary – Hospital admission for heart failure

Observation period of 9 years

Results Summary



- Patients with QRS narrowing were found to have significantly better prognosis
- Statistical significance was observed for QRS narrowing in the whole group and in LBBB sub-group

2x lower mortality rate
only in patients with LBBB who demonstrated QRS narrowing after CRT implantation

Conclusions

This study showed that immediate shortening of QRS duration with initiation of CRT in patients with LBBB strongly predicts favorable prognosis.

CRT Optimization (cont'd)

SyncAV™ CRT Technology

SyncAV™ CRT Technology is an Abbott-exclusive, device-based cardiac resynchronization therapy (CRT) algorithm which individualizes therapy by dynamically adjusting timing (AV delays) based on the patient's intrinsic rhythm and has demonstrated improved electrical synchrony and narrower QRS. The algorithm adjusts the AV delay for the next 256 cycles using the following equation:
AV_{Delay} = [Intrinsic Conduction Time] – [SyncAV™ CRT Delta]

SyncAV™ CRT Technology is Proven to Narrow QRS

Programming Cardiac Resynchronization Therapy for Electrical Synchrony: Reaching Beyond Left Bundle Branch Block and Left Ventricular Activation Delay[4]
Varma et al. J Am Heart Assoc. 2018

Link to publication

Hypothesis
Since CRT aims to restore electrical synchrony in dyssynchronous ventricles with a prolonged QRS, programming to reduce this seems intuitive.

Optimized SyncAV™ CRT Settings
Programming with a delta that delivers the narrowest QRS complex

MODE	MODE I	MODE II	MODE III	MODE IV
PACING METHOD	BIV ONLY	SyncAV™ DEFAULT	SyncAV™ OPTIMAL	LV ONLY
AV OFFSET	NOMINAL SETTINGS	-50 MS; DEFAULT SyncAV™	OPTIMAL	-50MS
PERCENT QRS REDUCTION	11.8%	**17.8%**	**23.9%**	**15.6%**
		Nominal SyncAV™ Settings		LV only pacing

100% of patients
were shown to have a narrower QRS duration
when SyncAV™ CRT technology was optimized

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SyncAV™ CRT Technology significantly reduces heart failure hospitalizations

Gain in real-world cardiac resynchronization therapy efficacy with SyncAV dynamic optimization: Heart failure hospitalizations and costs[5]

Varma, Niraj et al. Heart Rhythm. 2021

Link to publication

This large, retrospective study evaluated the impact of SyncAV on heart failure hospitalizations (HFHs) and related cost in a real-world CRT cohort. It showed that HFHs were significantly reduced after CRT implantation and the effect was more pronounced in patients receiving SyncAV CRT (SyncAV ON) compared to standard CRT (SyncAV OFF).

Methods Summary

Study cohort: N = 13,006 (SyncAV OFF: n = 12,269; SyncAV ON: n = 737)

- 4:1 propensity score matching was used to ensure all patient characteristics were similar
- Cohort after propensity matching: N = 3,630 (SyncAV OFF: n = 2,904; SyncAV ON: n = 726)

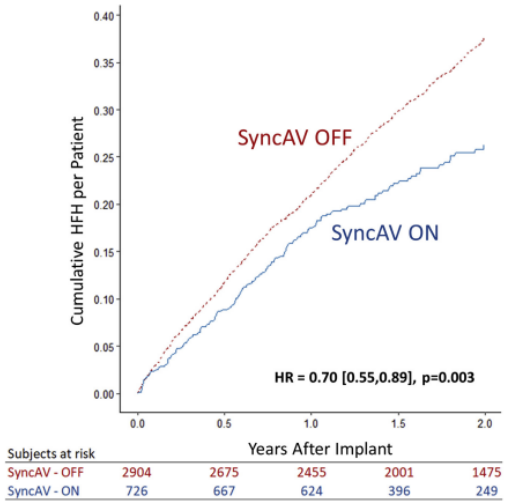
Primary Clinical Outcome:

- Cumulative rate of HFHs per patient-year
- Inclusion of preimplant HFH data in comparative analyses is a unique feature of the study's methodology

Observation Period:

- Cumulative rate of HFHs per patient-year at 2 years
- 30-day HFH readmissions
- 30-day all-cause hospital readmissions
- Total 2-year HFH-associated costs per patient

Results Summary



41% reduction in heart failure readmissions

34% reduction in all-cause hospitalization readmissions

30% reduction in cumulative heart failure hospitalizations

23% reduction ($1,135) in 2-year cost

$4,031 lifetime savings per CRT patient

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Results Summary (cont'd)

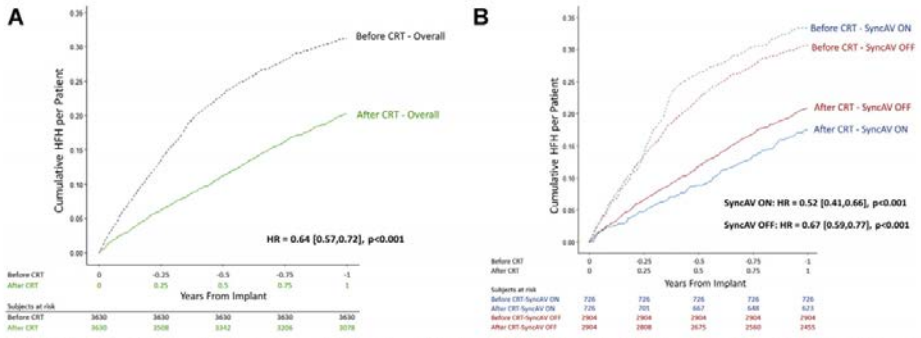

Figure 2 Effects of cardiac resynchronization therapy (CRT) on heart failure hospitalizations (HFHs): relative beneficial effects. Cumulative HFH rate in the year post-CRT compared with the year pre-CRT. **A:** Whole cohort. CRT reduced HFH rate dramatically. **B:** SyncAV OFF CRT maintains a reduction in HFH rate. SyncAV ON CRT demonstrated the strongest suppression of HFHs after treatment. The hazard ratio (HR), the corresponding 95% confidence interval, and the *P* value are presented on each graph. (The HR in panel A should be interpreted as average HR for the before and after CRT implant variable because of the evidence of mild violation of proportional hazards assumption for this variable).

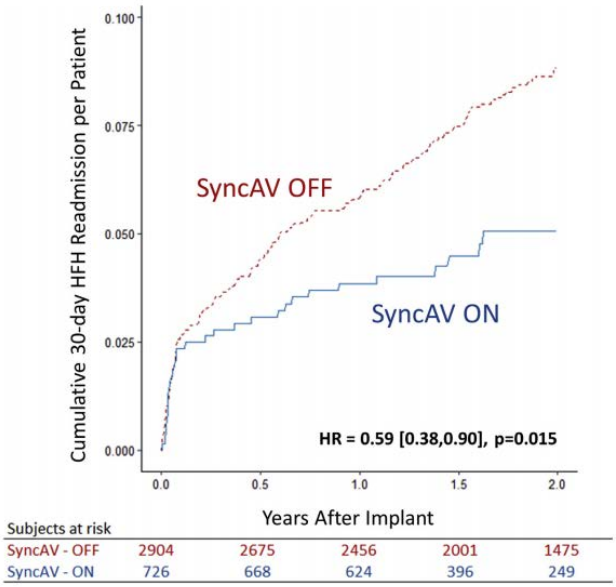

Figure 5 Thirty-day heart failure hospitalization (HFH) readmission was reduced in cardiac resynchronization therapy–treated patients with SyncAV ON vs SyncAV OFF. The graph shows cumulative 30-day HFH readmission rates from implant to 2 years post-implant in the 2 groups. The hazard ratio (HR), the corresponding 95% confidence interval, and the *P* value are presented.

Conclusions

This large, real-world study showed that HFHs were significantly reduced after CRT implant. This effect was more pronounced in patients receiving SyncAV™ CRT Technology compared to standard CRT. Furthermore, SyncAV CRT was associated with a significant reduction in the rate of 30-day readmission and overall HF-related costs. These data indicate the value of a device-based algorithm delivering dynamic electrical optimization.

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CRT Optimization Information Sources

3 Cardiac resynchronization therapy-induced acute shortening of QRS duration predicts long-term mortality only in patients with left bundle branch block

Link to publication

Citation: Jastrzębski, Marek, et al. "Cardiac resynchronization therapy-induced acute shortening of QRS duration predicts long-term mortality only in patients with left bundle branch block." *Ep Europace* 21.2 (2019): 281-289.

Background: QRS narrowing with initiation of biventricular pacing might be an acute electrocardiographic indicator of correction of left bundle branch block (LBBB)-induced depolarization delay and asynchrony. However, its impact on prognosis remains controversial, especially in non-LBBB patients. Our goal was to evaluate the impact of QRS narrowing on long-term mortality and morbidity in a large cohort of patients undergoing cardiac resynchronization therapy (CRT) with different pre-implantation QRS types: LBBB, non-LBBB, and permanent right ventricular pacing.

Methods and Results: This study included consecutive patients who underwent CRT device implantation. Study endpoints: death from any cause or urgent heart transplantation and death from any cause/urgent heart transplantation or hospital admission for heart failure. All pre- and post-implantation electrocardiograms were analyzed using digital calipers, high amplitude augmentation, 100 mm/s paper speed, and global QRS duration measurement method. A total of 552 CRT patients entered the survival analysis. During the 9 years observation period, 232 (42.0%) and 292 (52.9%) patients met primary and secondary endpoints, respectively. QRS narrowing predicted survival in the Kaplan–Meier analysis only in patients with LBBB. Multivariate Cox regression model showed that QRS narrowing was the major determinant of both study endpoints, with hazard ratios of 0.46 and 0.43, respectively. There was a strong relationship between mortality risk and shortening/widening of the QRS, albeit only in the LBBB group. Patients with non-LBBB morphologies had unfavorable prognosis similar to that in LBBB patients without QRS narrowing.

Conclusions: Acute QRS narrowing in patients with LBBB might be a desirable endpoint of CRT device implantation.

4 Programming Cardiac Resynchronization Therapy for Electrical Synchrony: Reaching Beyond Left Bundle Branch Block and Left Ventricular Activation Delay

Link to publication

Citation: Varma, N., O'Donnell, D., Bassiouny, M., Ritter, P., Pappone, C., Mangual, J., Cantillon, D., Badie, N., Thibault, B. and Wisnoskey, B., 2018. Programming cardiac resynchronization therapy for electrical synchrony: reaching beyond left bundle branch block and left ventricular activation delay. *Journal of the American Heart Association*, *7*(3), p.e007489.

Background: QRS narrowing following cardiac resynchronization therapy with biventricular (BiV) or left ventricular (LV) pacing is likely affected by patient-specific conduction characteristics (PR, qLV, LV-paced propagation interval), making a universal programming strategy likely ineffective. We tested these factors using a novel, device-based algorithm (SyncAV) that automatically adjusts paced atrioventricular delay (default or programmable offset) according to intrinsic atrioventricular conduction.

Methods and Results: Seventy-five patients undergoing cardiac resynchronization therapy (age 66±11 years; 65% male; 32% with ischemic cardiomyopathy; LV ejection fraction 28±8%; QRS duration 162±16 ms) with intact atrioventricular conduction (PR interval 194±34, range 128–300 ms), left bundle branch block, and optimized LV lead position were studied at implant. QRS duration (QRSd) reduction was compared for the following pacing configurations: nominal simultaneous BiV (Mode I: paced/sensed atrioventricular delay=140/110 ms), BiV+SyncAV with 50 ms offset (Mode II), BiV+SyncAV with offset that minimized QRSd (Mode III), or LV-only pacing+SyncAV with 50 ms offset (Mode IV). The intrinsic QRSd (162±16 ms) was reduced to 142±17 ms (−11.8%) by Mode I, 136±14 ms (−15.6%) by Mode IV, and 132±13 ms (−17.8%) by Mode II. Mode III yielded the shortest overall QRSd (123±12 ms, −23.9% [$P<0.001$ versus all modes]) and was the only configuration without QRSd prolongation in any patient. QRS narrowing occurred regardless of QRSd, PR, or LV-paced intervals, or underlying ischemic disease.

Conclusions: Post-implant electrical optimization in already well-selected patients with left bundle branch block and optimized LV lead position is facilitated by patient-tailored BiV pacing adjusted to intrinsic atrioventricular timing using an automatic device–based algorithm.

CRT Optimization Information Sources (cont'd)

5 Gain in real-world cardiac resynchronization therapy efficacy with SyncAV dynamic optimization: Heart failure hospitalizations and costs

Link to publication

Citation: Varma, Niraj, et al. "Gain in real-world cardiac resynchronization therapy efficacy with SyncAV dynamic optimization: Heart failure hospitalizations and costs." *Heart Rhythm* (2021).

Background: SyncAV, a device-based cardiac resynchronization therapy (CRT) algorithm, promotes electrical optimization by dynamically adjusting atrioventricular intervals.

Objective: The purpose of this study was to evaluate the impact of SyncAV on heart failure hospitalizations (HFHs) and related costs in a real-world CRT cohort.

Methods: Patients with SyncAV-capable CRT devices followed by remote monitoring and enrolled in Medicare fee-for-service for at least 1 year preimplant and up to 2 years postimplant were studied. Patients with SyncAV OFF were 4:1 matched to those with SyncAV ON on preimplant HFH rate, demographics, comorbidities, disease etiology, and left bundle branch block. HFHs were determined from the primary diagnosis of inpatient hospitalizations, and the cost for each event was the sum of Medicare, supplemental insurance, and patient payment.

Results: After 4:1 propensity score matching, 3630 patients were studied (mean age 75 6 8 years; 1386 [38%] female), including 726 (25%) patients with SyncAV ON. The pre-CRT HFH rate was 0.338 HFH events per patient-year. Overall, CRT diminished the HFH rate to 0.204 events per patient-year (P , .001). SyncAV elicited a larger reduction in HFH rate (SyncAV ON: hazard ratio [HR] 0.52; 95% confidence interval [CI] 0.41–0.66; P , .001 and SyncAV OFF: HR 0.68; 95% CI 0.59–0.77; P , .001). After 2 years, the HFH rate was lower in the SyncAV ON group than in the SyncAV OFF group (0.143 HFHs per patient-year vs 0.193 HFHs per patient-year; HR 0.70; 95% CI 0.55–0.89; P 5 .003) and fewer HFHs were followed by 30-day HFH readmissions (4.41% vs 7.68%; P 5 .003) and 30-day all-cause hospital readmissions (7.04% vs 10.01%; P 5 .010). The total 2-year HFH-associated costs per patient were lower with SyncAV ON (difference $1135; 90% CI $93–$2109; P 5 .038)

Conclusions: This large, real-world, propensity score–matched study demonstrates that SyncAV CRT is associated with significantly reduced HFHs and associated costs, incremental to standard CRT.

Detecting Life-Threating Arrhythmias

Undetected and Untreated VF Costs Lives

Failure to Treat Life-Threatening Ventricular Tachyarrhythmias in Contemporary Implantable Cardioverter–Defibrillators[6]

Thogersen, Anna Margrethe, et al. Circulation: Arrhythmia and Electrophysiology 10.9 (2017): e005305

Link to publication

This case series sought to determine the relationship between programmed parameters and failure of modern ICDs to treat ventricular fibrillation (VF). It showed that complex and unanticipated interaction between manufacturer-specific features and generic programming can prevent therapy for VF.

Methods Summary

Cases for 10 ambulatory patients, expected to live >1 year, and did not have an acute illness were reviewed at 4 institutions. Index events occurred from April 2015 to January 2017.

Inclusion criteria
- Failure to deliver timely therapy
- ICD system functioned normally
- VT/VF detection and therapies were programmed ON
- Amplitude of sinus-rhythm R waves exceeded 5 mV at implant and follow-up

No patients who met the inclusion criteria were excluded.

Results Summary

90% Patients whose VF event did not satisfy programmed detection criteria

56% Sudden deaths for which untreated VF was responsible despite recommended programming

5 Patients who died from untreated VF

Conclusions

Complex and unanticipated interactions between manufacturer-specific features and generic programming can prevent therapy for VF.

VF Therapy Assurance (VFTA)

VF Therapy Assurance allows for extended detection times while simultaneously speeding time to treatment for hemodynamically unstable arrhythmias that should be treated quickly. It is designed to deliver lifesaving HV therapy in a group of patients that may have not otherwise been treated.[7]

How VF Therapy Assurance Works:

- Uses the **Discrimination Channel** to check for far-field undersensing during a potential ventricular episode
- Once it is determined that far-field **Undersensing** is present, VF Therapy Assurance is triggered
- Programmed parameters are **Automatically Changed** for the remainder of the episode

VFTA Increases Detection Capabilities in Traditionally Challenging Arrhythmias

86% Patients who received HV therapy due to VFTA who would have been otherwise untreated for potentially life-threatening arrhythmias[8]

>800 Patients annually with challenging arrhythmias could have their lives saved because of VF Therapy Assurance[9]

VFTA Case Study

Gallant HF Alert of High Voltage Therapy with VFTA Activation
Ospedale P. Pederzoli, Peschiera del Garda, October 31, 2020

Description:
This case study presents a Merlin.net transmission of a Gallant HF with an alert of high voltage therapy delivered and VFTA activation. The report shows 2 therapy zones: VT monitor zone at 171 bpm and VF at 214 bpm.

Parametri				
Modalità	DDD	Configurazione Zona	VT	VF
Frequenza Base	80 min-1	Riconoscimento	171 min-1	214 min-1
MTR	130 min-1	Terapia **(ATTIVATA)**	Monitor	ATP x1
Ritardo AV Stimolato	200 ms			36,0 J
Ritardo AV Rilevato	150 ms			40,0 J
Stimolazione V.	Simul.			40,0 J x4

The episode showed that an arrhythmia of 2:52 minutes occurred. The episode was first detected as a VT (FC ≅ 207/min) in Monitor Zone, therapy was enabled only for FC > 214 bpm.

Episodi VT/VF				
Data / Ora	Tipo	Freq. (min-1)	Durata (M:S)	Terapia erogata
31 ott 2020 20:11	VF, Sicurezza terapia VF	214	02:52	36J

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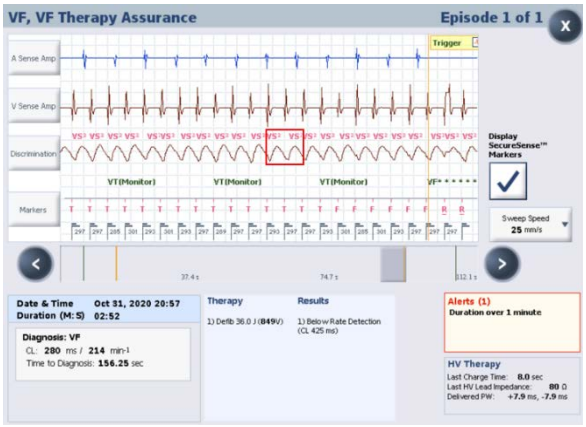
When VFTA Works

Reasons for VFTA triggering are that there is undersensing (sign amplitudes <0.3 mV) or two consecutive low amplitude sensing (signal amplitude 0.3 - 0.6 mV) on the discrimination channel.

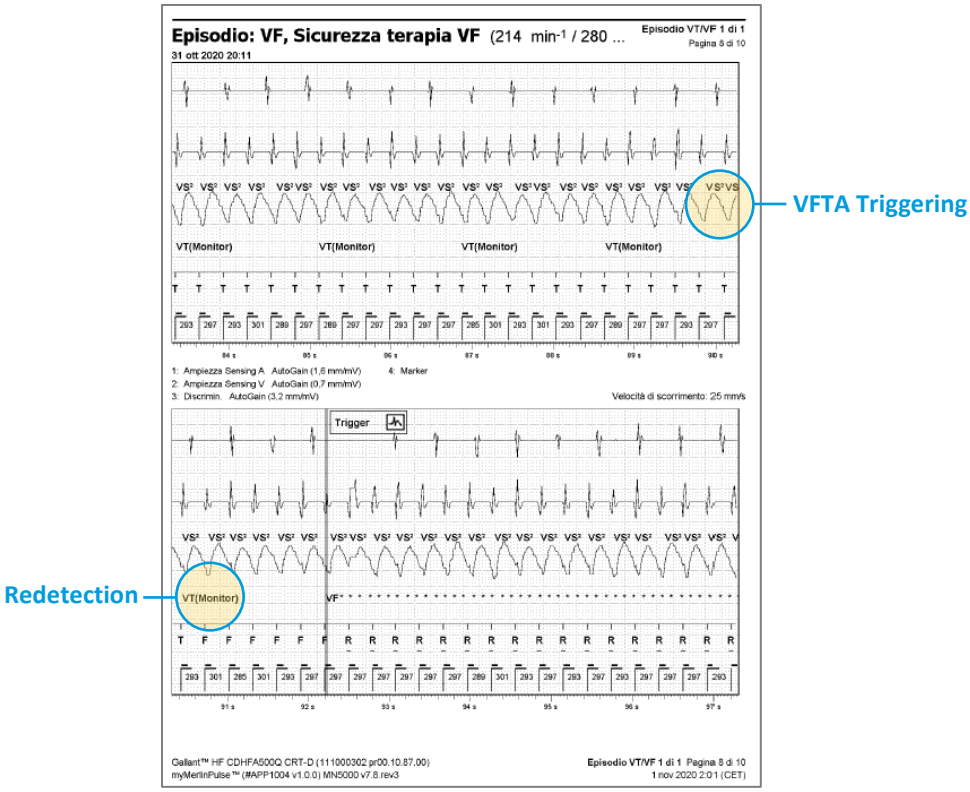
VFTA count is checked:

- Initial detection
- 45 cycles after first binned tachycardia interval (if detection has not been met)
- Redetection
- Within 15 cycles after ending an episode

There is no undersensing on the discrimination channel; therefore, VFTA must have been triggered because there are at least 2 consecutive low amplitude signals. Circled in red below are two consecutive events on the discrimination channel with amplitudes below 0.6 mV.



When VT is redetected thereafter, VFTA counter is checked and the algorithm starts to apply.



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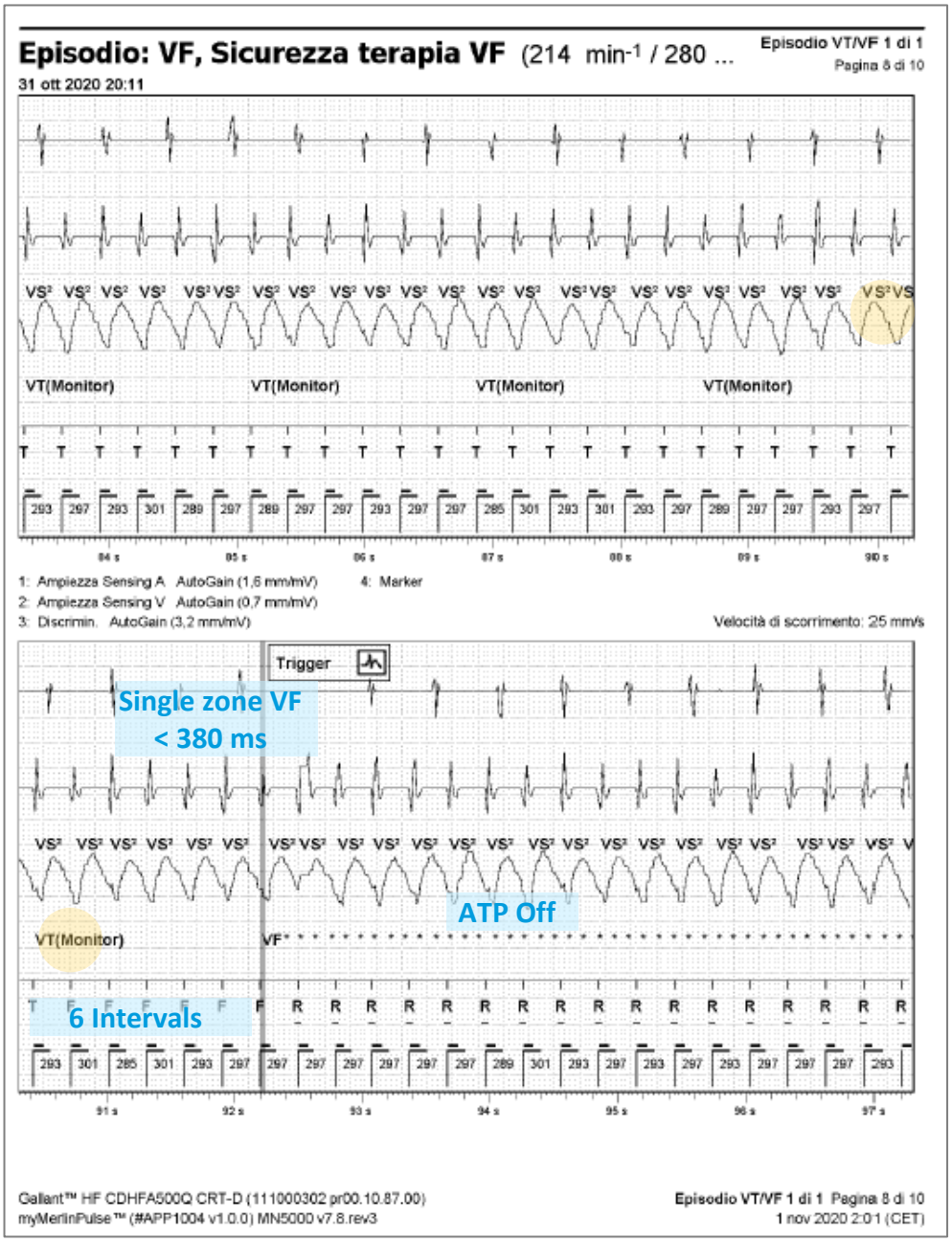
How VFTA Works

When VFTA is triggered, programmed parameters are automatically changed to encourage detection and treatment of the arrhythmia.

- Number of intervals for detection is 6
- Single zone – VF only
- Decreased VF Detection Rate: It will be set to lowest VT Therapy Zone + 100ms (to a max of 400ms). In this case, there's only a Monitor VT zone, and VF zone programmed to 280 ms. The VFTA detection rate would then be 280 + 100 ms = 380 ms
- ATP Off



VFTA Triggering

Redetection

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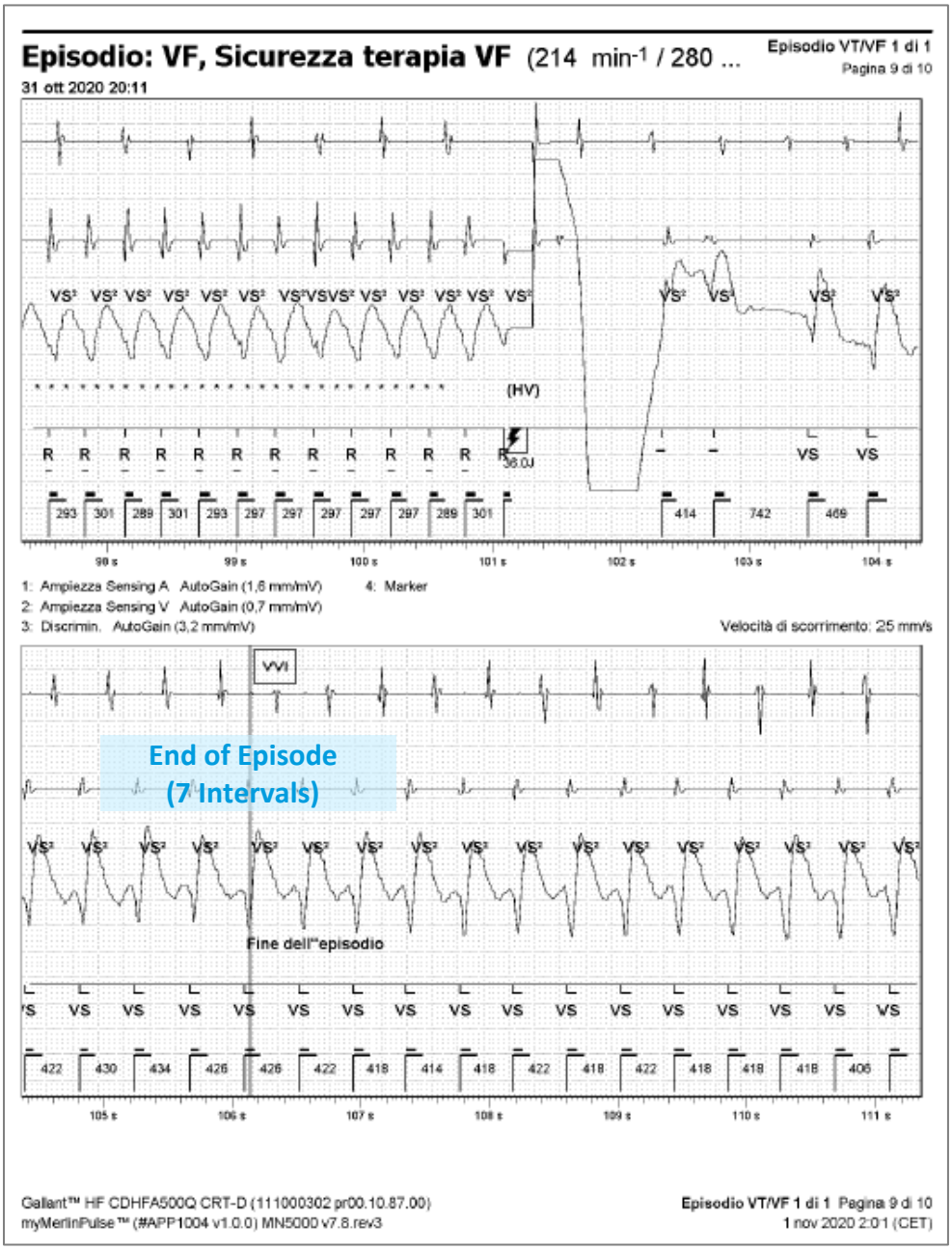
How VFTA Works (cont'd)

- End of Episode increased to 7 intervals



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VFTA Information Sources

6 Failure to Treat Life-Threatening Ventricular Tachyarrhythmias in Contemporary Implantable Cardioverter–Defibrillators

Link to publication

Citation: Thøgersen, Anna Margrethe, et al. "Failure to treat life-threatening ventricular tachyarrhythmias in contemporary implantable cardioverter–defibrillators: implications for strategic programming." Circulation: Arrhythmia and Electrophysiology 10.9 (2017): e005305.

Background: In clinical trials, manufacturer-specific, strategic programming of implantable cardioverter–defibrillators (ICDs), including faster detection rates, reduces unnecessary therapy but permits therapy for ventricular tachycardia/ventricular fibrillation (VF). Present consensus recommends a generic rate threshold between 185 and 200 beats per minute, which exceeds the rate tested in clinical trials for some manufacturers. In a case series, we sought to determine the relationship between programmed parameters and failure of modern ICDs to treat VF.

Methods and Results: We reviewed cases in which normally functioning ICDs failed to deliver timely therapy for VF from April 2015 to January 2017 at 4 institutions. Of 10 ambulatory patients, 5 died from untreated VF, 4 had cardiac arrests requiring external shocks, and 1 was rescued by a delayed ICD shock. VF did not satisfy programmed detection criteria in 9 patients (90%). Seven of these patients had slowest detection rates that were consistent with generic recommendations but not tested in a peer-reviewed trial for their manufacturer's ICDs. Manufacturer-specific factors interacted with fast detection rates to withhold therapy, including strict VF episode termination rules, enhancements to minimize T-wave oversensing, and features that restrict therapy to regular rhythms in ventricular tachycardia zones. Untreated VF despite recommended programming accounted for 56% of sudden deaths and 11% of all deaths during the study period.

Conclusions: Complex and unanticipated interactions between manufacturer-specific features and generic programming can prevent therapy for VF. More data are needed to assess the risks and benefits of translating evidence-based detection parameters from one manufacturer to another.

[7] VF Therapy Assurance. Data on file.

[8] Based on over 560,000 episodes (20,0000 patients). Performance of VF Therapy Assurance Feature. Abbott Clinical Summary.

[9] Data on file. 60101422 Internal Validation Report. Total 2019 global high-voltage implants, all manufacturers, estimated to be 440,434 units (Source: Abbott Market Research).

Clinicians Still Face Challenges of High DFTs in Some Patients

Optimized Defibrillation Waveforms Have Been Shown to Lower DFTs

Stepped defibrillation waveform is substantially more efficient than the 50/50% tilt biphasic[10]
Seidl, Karlheinz, et al. Heart Rhythm 3.12 (2006): 1406-1411

Link to publication

The purpose of this dual-site study was to assess the clinical utility of improved defibrillation waveforms. Even with biphasic waveforms, patients with high DFTs still are seen. It showed the stepped waveform reduced the DFT compared to 50/50% tilt.

Methods Summary

- 20 patients completed this dual-site study
- Delivered energy DFT was measured using the stepped waveform and a 50/50% tilt biphasic truncated exponential as the control
- Patients must have been approved to receive a de novo ICD or an ICD replacement, be stable, and provide written informed consent

Results Summary

95% Patients whose peak voltage was reduced with the stepped waveform

33% Median energy DFT was reduced from 11.7 to 7.8 Joules (P = .008)

Conclusion

The stepped waveform reduced the DFT compared to the 50/50% tilt waveform in this preliminary study.

"Tuned" Defibrillation Waveforms Outperform 50/50% Tilt Defibrillation Waveforms: A Randomized Multi-Center Study[11]

Natarajan, Senthil, et al. Pacing and Clinical Electrophysiology 30 (2007): S139-S142

Link to publication

This multi-center, randomized, paired-sample study measured DFTs for tuned versus 50/50% tilt waveforms in a random order by using the optimized binary search method. It showed that energy and voltage are lowered with an ICD that uses tuned waveform compared to a standard 50% tilt biphasic waveform.

Methods Summary

- Study population consisted of 34 patients
- DFT was measured during implantation of commercially available ICDs
- Two DFT tests were performed and patients were randomized to begin DFT testing with either 50/50% tilt waveform or tuned waveform based on a 3.5ms membrane model time constant
- A paired Student's *t*-test was used to compare DFTs for tuned and 50/50% tilt waveforms

Results Summary

16% Reduction in delivered energy for the tuned waveform cohort compared to the 50/50% waveform cohort

16% Reduction in stored energy for the tuned waveform cohort compared to the 50/50% waveform cohort

9% Reduction in delivered voltage for the tuned waveform cohort compared to the 50/50% waveform

Table I.

Defibrillation Threshold Metrics for Tuned Versus 50/50% Tilt-Based Waveforms

	Tuned (n = 34)	50/50% Tilt (n = 34)	P
Delivered energy (J)	7.3 ± 4.6	8.7 ± 5.3	0.01
Stored energy (J)	8.2 ± 5.1	9.7 ± 5.6	0.01
Delivered voltage (V)	406 ± 122	445 ± 123	0.008
Shock impedance (Ω)	41.4 ± 7.3	40.9 ± 7.9	0.44
HVLI (Ω)	37.2 ± 5.2		–

Values are means ± SD.
HVLI = high voltage lead impedance.

Conclusion

Biphasic waveforms tuned to an assumed cardiac membrane time constant of 3.5ms significantly reduced the delivered and stored energy and voltage DFT compared to a 50/50% tilt waveform.

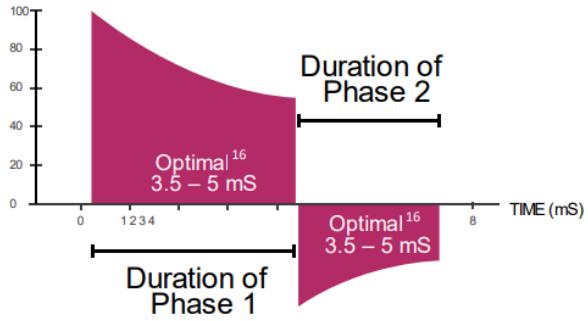
DeFT Response™ Technology

DeFT Response™ Technology allows fixed pulse width programmability, or the ability to control the length of each phase of shock waveform. It provides non-invasive programming options to rapidly optimize therapy performance to each patient's unique needs, exclusively from Abbott.

Shock optimization has never been more important.

DeFT Response™ Technology allows you to customize matching of the shock waveform to patients' cellular response time to lower DFTs.

- DFT testing is less common
- More implanters are choosing single coil leads which may lead to higher impedances and longer, sub-optimal shock durations[12]



Safer Management of Care

Defibrillation waveform duration adjustment increases the proportion of acceptable defibrillation thresholds in patients implanted with single-coil defibrillation leads[13]

Gabriels, James, Adam S. Budzikowski, and John T. Kassotis. Cardiology 124.2 (2013): 71-75

Link to publication

100% Success in preserving a 10J safety margin with DeFT Response technology vs. 83% achievement of 10J safety margin in fixed-tilt group of patients with competitive devices.[13]

DeFT Response™ Technology Case Study

Non-invasive Management of a High DFT Post-Implant

Dr. Nicholas J. Mandalakas
Cardiac Consultants, P.C.

Presentation:

During routine follow-up, diagnostics acquired from the ICD of a 71-year old man revealed that a 36-joule shock from the device had failed to convert an episode of rapid VT that fell into the VF rate zone. Fortunately, the arrhythmia terminated spontaneously. Diagnostics at this time also revealed seven episodes of non-sustained VT, with three episodes in the VF zone where therapy was aborted because of spontaneous termination of the tachycardia. The device is an Atlas®+ DR ICD (42 joules stored, 36 joules delivered), and had been implanted about four months previously; the lead was an SPL™ dual-coil defibrillator lead that had been implanted earlier.

This patient has a long history of documented recurrent episodes of symptomatic VT, and this is the third ICD he has received. His other cardiac conditions include non-ischemic cardiomyopathy and atrial fibrillation (leading to His bundle ablation). His most recent measured ejection fraction was 28%. The patient also has a history of hypertension and diabetes, and was taking the following medications: bumetanide; digoxin; atenolol; metformin; glipizide; coumadin; magnesium with zinc; potassium, and vitamins C and E. At implant, the patient's defibrillation threshold (DFT) had been 25 joules, and so the device was programmed to deliver a maximum-energy shock to maintain a 10-joule safety margin. Its failure to convert his episode of VF therefore dictated the need for intervention.

Resolution:

Our initial plan was to implant another defibrillator lead with the coil positioned in the inferior vena cava (IVC) in an attempt to improve the shocking vector and lower the DFT. Favale et al. have reported that the addition of an IVC lead significantly reduced the DFT of a single-lead, active-can, pectoral ICD.1 However, this would have required the use of a Y-adapter to connect the new lead to the ICD. Rather than attempting further surgery, we elected to try to reduce the DFT by adjusting the pulse widths of the defibrillating waveform (it had originally been programmed with a fixed tilt of 65%, yielding pulse widths of 6.1 ms for each phase). The testing sequence and results are outlined below. With the programmed settings used in the last attempt, and based on a measured impedance of 49Ω, the device's maximum deliverable energy was 33.5 joules.

Attempt	Tilt	Pulse widths	Cycle length	Shock	Result
1	65%	6.1/6.1 ms	190 ms	25 J	Successful
2	NA	4.0/3.0 ms	235 ms	16.6 J	Successful
3	NA	4.0/3.0 ms	215 ms	11.3 J	Successful

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Discussion:

In this case, using only three inductions, we succeeded in reducing the patient's DFT to approximately half of what it had been at implant, while increasing the safety margin by 50%. Since the first shock of our test essentially replicated the 25-joule DFT measured at implant, we attribute the reduction entirely to abandoning fixed tilt in favor of pulse width adjustment. Much has been written about the tilt and pulse width of the biphasic waveform; see, for example Mouchawar et al.,[2] Irnich,[3] Merkely et al.,[4] etc. Tilt describes the percentage difference between leading and trailing-edge voltages at the point where the phase shifts. Pulse width refers to the duration of each phase of the waveform.

Unfortunately, a conclusive understanding of the impact of these variables on clinical defibrillation is hampered by the lack of certainty surrounding the fundamental mechanisms of defibrillation. While adjustment of tilt would have been possible in this case, optimal tilts have not been defined. Furthermore, in a recent animal study reported by Nanthakumar et al., tilt was not found to affect defibrillation voltage requirements.[5] Current thinking suggests that pulse width adjustment may be a better approach to providing low DFTs because it enables a better correspondence between the durations of each phase and their functions as postulated in the "charge burping" theory describing biphasic defibrillation.[6] Briefly, this theory suggests that the optimal role of the first phase is to depolarize or extend the refractory periods of essentially all ventricular muscle cells, and the second phase serves to remove excess charge on cells that were not "captured" by the first phase. This theoretically removes electrical potentials that otherwise would retain the capacity to sustain (or reinitiate) the fibrillatory pattern. This strategy (i.e., pulse width adjustment) has been reported to reduce DFTs in the clinical setting.[2,7]

Conclusion:

The ability to adjust the pulse widths of each phase of the defibrillation waveform in the Atlas+ DR ICD reduced our patient's DFT by approximately 50%, significantly increased the safety margin, and avoided additional surgery to ensure that the ICD could reliably terminate the patient's VF

Case Study References:

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DFT and DeFT Response™ Technology Information Sources

10 Stepped defibrillation waveform is substantially more efficient than the 50/50% tilt biphasic

Link to publication

Citation: Seidl, Karlheinz, et al. "Stepped defibrillation waveform is substantially more efficient than the 50/50% tilt biphasic." Heart Rhythm 3.12 (2006): 1406-1411.

Background: Even with biphasic waveforms, patients with high defibrillation thresholds (DFTs) still are seen; thus, improved defibrillation waveforms may be of clinical utility. The stepped waveform has three parts: the first portion is positive with two capacitors in parallel, the second is positive with the capacitors in series, and the last portion is negative, also with the capacitors in series.

Methods and Results: We measured the delivered energy DFT in 20 patients in a dual-site study using the stepped waveform and a 50/50% tilt biphasic truncated exponential as the control. All shocks were delivered using an arbitrary waveform defibrillator, which was programmed to mimic two 220-μF capacitors (110 μF in series and 440 μF in parallel). The peak voltage at DFT was reduced in 19 of the 20 patients. The median peak voltage was reduced by 32.0%, from 472 V to 321 V (P <.001). The median energy DFT was reduced by 33%, from 11.7 J to 7.8 J (P = .008). The mean voltage and energy were reduced by 25.3% and 20.2%, respectively. On average, the stepped waveform was able to defibrillate as well as the 50/50% tilt biphasic, with 33% more energy. The benefit was more pronounced in patients with either a lower ejection fraction or a superior vena cava coil. The benefit of the stepped waveform had an inverse quadratic correlation with the resistance (r2 = 0.47), suggesting that the capacitance values chosen for the stepped waveform were close to optimal for a 35-Ω resistance.

Conclusions: The stepped waveform reduced the DFT compared to the 50/50% tilt waveform in this preliminary study.

11 "Tuned" Defibrillation Waveforms Outperform 50/50% Tilt Defibrillation Waveforms: A Randomized Multi-Center Study

Link to publication

Citation: Natarajan, Senthil, et al. ""Tuned" defibrillation waveforms outperform 50/50% tilt defibrillation waveforms: a randomized multi-center study." Pacing and Clinical Electrophysiology 30 (2007): S139-S142.

Background: A superior performance of a tuned waveform based on duration using an assumed cardiac membrane time constant of 3.5 ms and of a 50/50% tilt waveform over a standard 65/65% tilt waveform has been documented before. However, there has been no direct comparison of the tuned versus the 50/50% tilt waveforms.

Methods and Results: In 34 patients, defibrillation thresholds (DFTs) for tuned versus 50/50% tilt waveforms in a random order were measured by using the optimized binary search method. High voltage lead impedance was measured and used to select the pulse widths for tuned and 50/50% tilt defibrillation waveforms. Delivered energy (7.3 ± 4.6 J vs 8.7 ± 5.3 J, P = 0.01), stored energy (8.2 ± 5.1 J vs 9.7 ± 5.6 J, P = 0.01), and delivered voltage (405.9 ± 121.7 V vs 445.0 ± 122.6 V, P = 0.008) were significantly lower for the tuned than for the 50/50% tilt waveform. In four patients with DFT ≥15 J, the tuned waveform lowered the mean energy DFT by 2.8 J and mean voltage DFT by 45 V. For all patients, the mean peak delivered energy DFT was reduced from 29 J to 22 J (24% decrease). Multiple regression analysis showed that a left ventricular ejection fraction <20% is a significant predictor of this advantage.

Conclusions: Energy and voltage DFTs are lowered with an implantable cardioverter defibrillator that uses a tuned waveform compared to a standard 50% tilt biphasic waveform.

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Rx Only

Intended Use:
The Implantable Cardioverter Defibrillator (ICD) and Cardiac Resynchronization Therapy Defibrillator (CRT-D) devices are intended to provide ventricular anti-tachycardia pacing and ventricular cardioversion/defibrillation. The CRT-D devices are also intended to resynchronize the right and left ventricles. The myMerlinPulse™ mobile application is intended for use by people who have an Abbott Medical implanted heart device and access to a mobile device. The app provides remote monitoring capability of the implanted heart device by transmitting information from the patient's implanted heart device to the patient's healthcare provider.

Indications:
The ICD and CRT-D devices are indicated for automated treatment of life-threatening ventricular arrhythmias. CRT-D devices are also indicated to treat symptoms in patients who have congestive heart failure with ventricular dyssynchrony. In addition, dual chamber ICD and CRT-D devices with the AT/AF detection algorithm are indicated in patients with atrial tachyarrhythmias or those patients who are at significant risk of developing atrial tachyarrhythmias. MR Conditional ICDs and CRT-Ds are conditionally safe for use in the MRI environment when used in a complete MR Conditional system and according to instructions in the MRI-Ready Systems manual. Scanning under different conditions may result in severe patient injury, death, or device malfunction. The myMerlinPulse™ mobile application is indicated for use by patients with supported Abbott Medical implanted heart devices.

Contraindications:
Contraindications for use of the pulse generator system include ventricular tachyarrhythmias resulting from transient or correctable factors such as drug toxicity, electrolyte imbalance, or acute myocardial infarction. The myMerlinPulse™ mobile application is contraindicated for use with any implanted medical device other than supported Abbott Medical implanted heart devices.

Adverse Events: Possible adverse events associated with the implantation of the pulse generator system include the following: Arrhythmia (for example, accelerated or induced), Bradycardia, Cardiac or venous perforation, Cardiac tamponade, Cardiogenic shock, Death, Discomfort, Embolism, Endocarditis, Erosion, Exacerbation of heart failure, Excessive fibrotic tissue growth, Extracardiac stimulation (phrenic nerve, diaphragm, pectoral muscle), Extrusion, Fluid accumulation within the device pocket, Formation of hematomas, cysts, or seromas, Heart block, Hemorrhage, Hemothorax, Hypersensitivity, including local tissue reaction or allergic reaction, Infection, Keloid formation, Myocardial damage, Nerve damage, Occlusion/Thrombus, Pericardial effusion, Pericarditis, Pneumothorax, Pulmonary edema, Syncope, Thrombosis, Valve damage. Complications reported with direct subclavian venipuncture include pneumothorax, hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage and rarely, death. Among the psychological effects of device implantation are imagined pulsing, depression, dependency, fear of premature battery depletion, device malfunction, inappropriate pulsing, shocking while conscious, or losing pulse capability. Possible adverse device effects include complications due to the following: , Abnormal battery depletion, Conductor fracture, Device-programmer communication failure, Elevated or rise in defibrillation/cardioversion threshold, Inability to defibrillate or pace, Inability to interrogate or program due to programmer or device malfunction, Incomplete lead connection with pulse generator, Inhibited therapy including defibrillation and pacing, Inappropriate therapy (for example, shocks and anti-tachycardia pacing [ATP] where applicable, pacing), Interruption of function due to electrical or magnetic interference, Intolerance to high rate pacing (for example dyspnea or discomfort), Lead abrasion, Lead fracture, Lead insulation damage, Lead migration or lead dislodgement, Loss of device functionality due to component failure, Pulse generator migration, Rise in DFT threshold, Rise in pacing threshold and exit. block, Shunting of energy from defibrillation paddles, System failure due to ionizing radiation. Additionally, potential adverse events associated with the implantation of a coronary venous lead system include the following: Allergic reaction to contrast media, Breakage or failure of implant instruments, Prolonged exposure to fluoroscopic radiation, Renal failure from contrast media used to visualize coronary veins.

Refer to the User's Manual for detailed intended use, indications, contraindications, warnings, precautions, and potential adverse events. No potential adverse events have been identified with use of the myMerlinPulse™ mobile application. * For additional information about specific MR Conditional ICDs and leads, including scan parameters, warnings, precautions, adverse conditions to MRI scanning, and potential adverse events, please refer to the Abbott MRI Ready Systems Manual at medical.abbott/manuals.

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