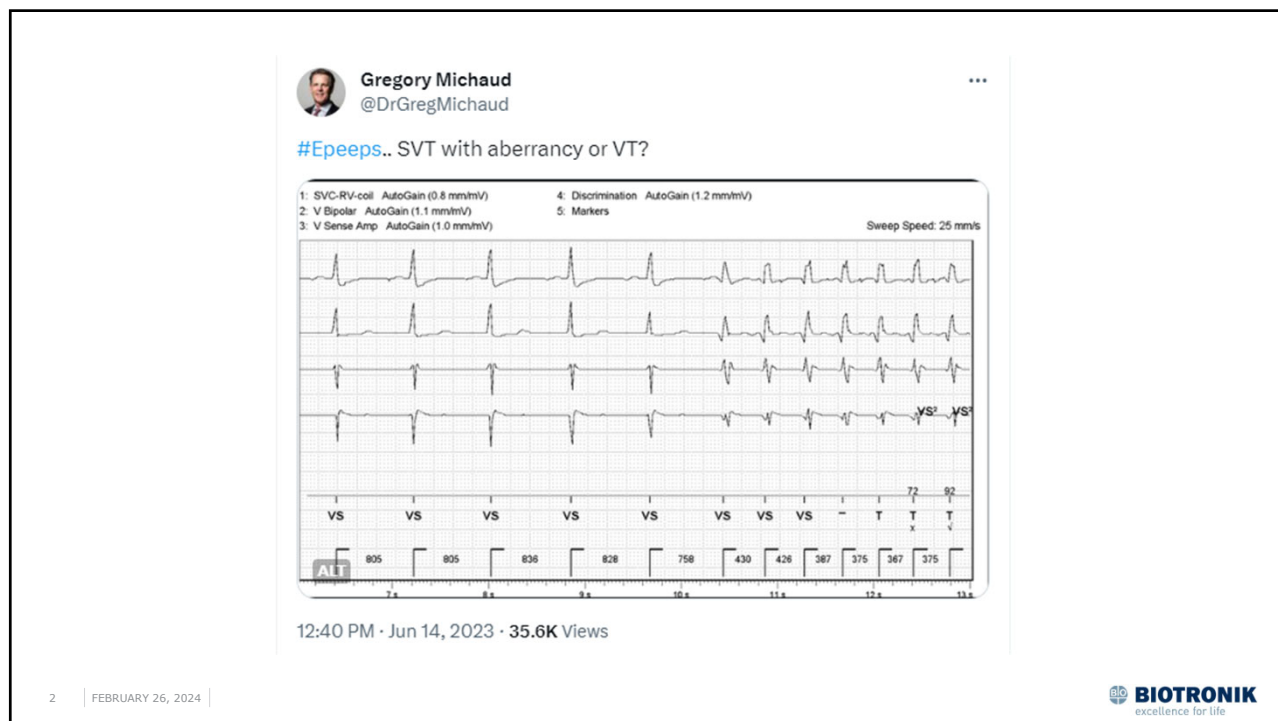


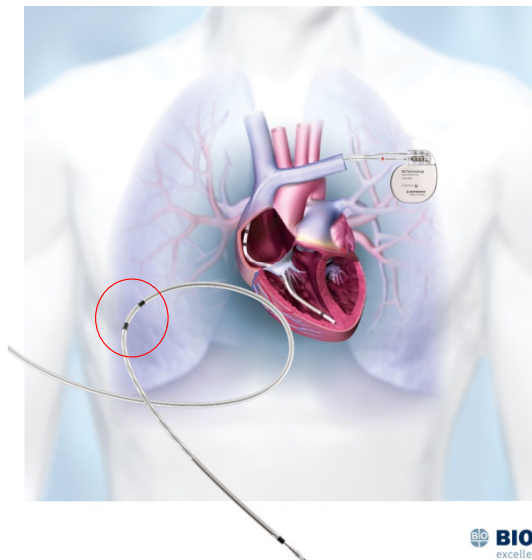
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2

DX: Single-Chamber ICD with Atrial Sensing and AHRE Detection

- DX provides benefits of DC-ICDs by providing atrial diagnostics without an atrial lead
- Detection of AHRE with enhanced diagnostic accuracy
- Discrimination of VT vs SVT
- Avoiding unnecessary atrial lead placement means fewer complications
- Reduced procedure complexity
- Cost savings with a single lead

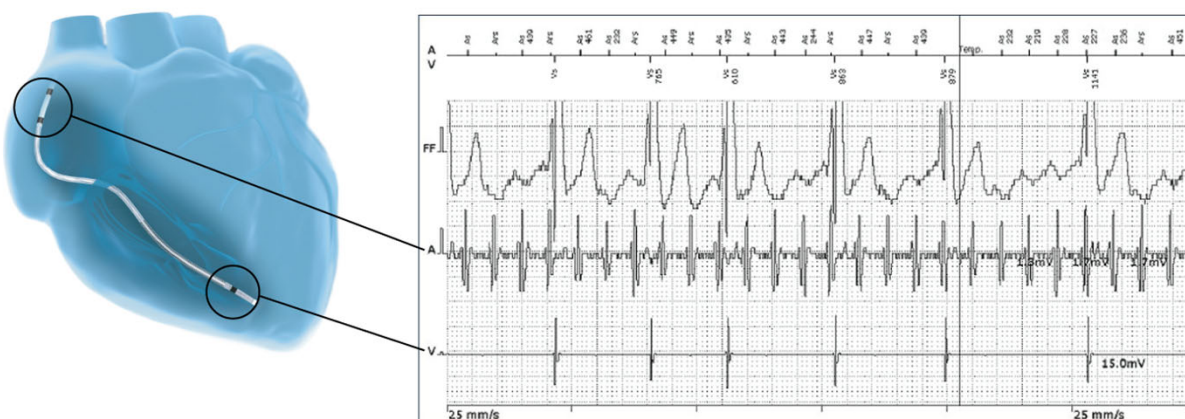


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Evolution of ICD Therapy: DX Technology



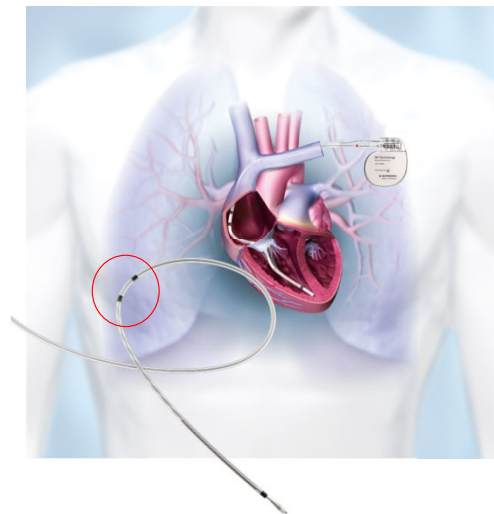
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BIOTRONIK DX System

- Single-chamber ICD [and 2 lead CRT system] that provides reliable atrial sensing by a floating atrial dipole.
- DX System expands the diagnostic capabilities of a standard single-chamber ICD by providing atrial sensing, which allows AHRE to be detected and burden of AT/AF to be quantified (*2-channel EGMs, and dual-chamber SVT discrimination, in a one-lead system*).
- This unique hardware and software combination has demonstrated atrial high-rate episode detection that is equivalent to a dual-chamber ICD system.³



3. Thomas G et al. J of Cardio Electrophysiology. 2019, 30(10)

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Expansive Body of Clinical Evidence Supporting DX

DX Publications

Study/Author	n	Follow-up Duration	Key Findings
Gwag, et al. ¹	86	24 months	P-waves stable at 24 months, atrial signal stabilizes greatly at 12-24 months
Mullane, et al.* ²	4,903	16 months	20% of CRT patients do not need an atrial lead
Pung, et al. ³	991**	24 months	Meta-analysis: DX superior to VR and equivalent to DR in AHRE detection
Shaik, et al. ⁴	240	6 months	CRT-DX patients fared better due to having fewer major complications and fewer inappropriate shocks
Biffi, et al. (2020) ⁵ THINGS	378	24 months	DX superior to VR in AHRE detection, OAC onset higher/earlier in DX group
Thomas, et al. ⁶ SENSE	150	12 months	DX superior to VR and equivalent to DR in AHRE detection
Kurt, et al. ⁷	212	24 months	Reduced inappropriate shocks
Biffi, et al. (2017) ⁸	37	36 months	Stable P-waves in CRT-DX
Safak, et al. ⁹	116	6 months	Appropriate atrial sensing in DX
Adria Investigators ¹⁰	249	12 months	DX can be implanted faster & is equal to DR in VT/SVT detection
Stazi, et al. ¹¹	43	12 months	Stable atrial sensing in DX, and amplification of P-wave effective
Niehaus, et al. ¹²	25	12 months	Stable detection of atrial & ventricular signals during all rhythms
Hindricks, et al. ¹³ MATRIX	2,054	24 months	High detection accuracy plus RM allows for effective subclinical AF monitoring
O'Connor, et al. ¹⁴ REACT-DX	234	16 months	Rapid intervention (within 24 days of detection) for high-risk group (81%), and >93% were not on OAC

* An analysis of atrial pacing percentage comparing CRT-DX (n = 387) to CRT-D (n = 4,516).

** A meta-analysis of SENSE, THINGS, and Statuto G, et al abstract

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SENSE Trial




Study Design

- Prospective, multi-site and cohort-controlled clinical trial
- 150 months follow-up
- Retrospective matched cohort analysis

Results:

Zero inappropriate therapies in DX Cohort

Subclinical atrial fibrillation detection with a floating atrial sensing dipole in single lead implantable cardioverter-defibrillator systems: Results of the SENSE trial

George Thomas MD¹  | Daniel Y. Choi MD¹ | Harish Doppalapudi MD, FHRS² | Mark Richards MD, PhD, FHRS³ | Sei Iwai MD, FHRS⁴ | Emile G. Daoud MD, FHRS⁵  | Mahmoud Houmsse MD, FHRS⁵ | Arvinth N. Kanagasundram MD, FHRS⁶ | Sumeet K. Mainigi MD, FHRS⁷ | Steven A. Lubitz MD, MPH⁸ | Jim W. Cheung MD, FHRS¹ 

Thomas G et al. JCE, 2019 Oct;30(10):1994-2001.

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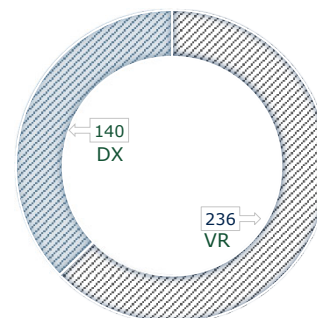
7

The THINGS Registry (The sINgle-lead reGiStry): Study Design

Prospective, observational and multicenter study comparing clinical outcomes of patients implanted with a conventional single-chamber ICD (ICD VR group) to those implanted with a DX ICD (ICD DX group)

561 subjects @ 15 participating Italian centers

- 236 (62.8%) subjects in ICD VR cohort
- 140 (37.2%) subjects in ICD DX cohort
- Followed for a median of 27 months
- Pts were excluded due to early study drop-out (n = 35) or history of AF (n = 148)



Biffi M, et al. J Cardiovasc Electrophysiol. 2020 Apr;31(4):846-853

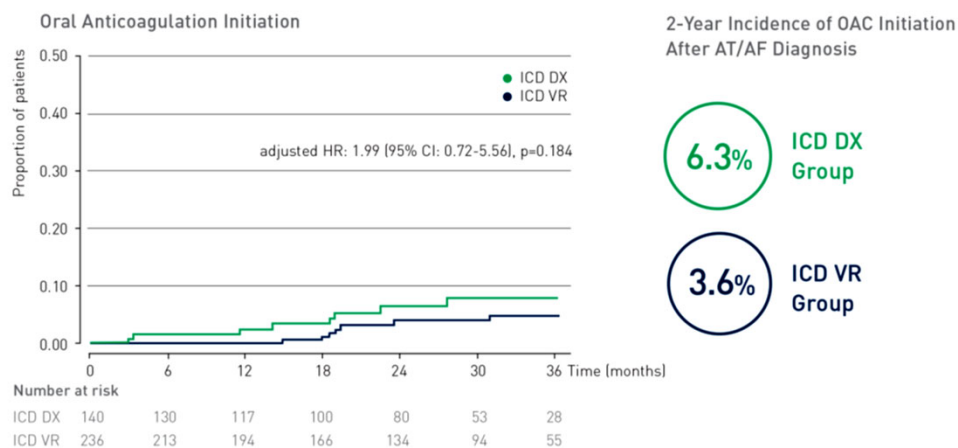
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8

THINGS Registry Results: New-onset OAC

Incidence of OAC Initiation: Trend for Higher Use with ICD DX



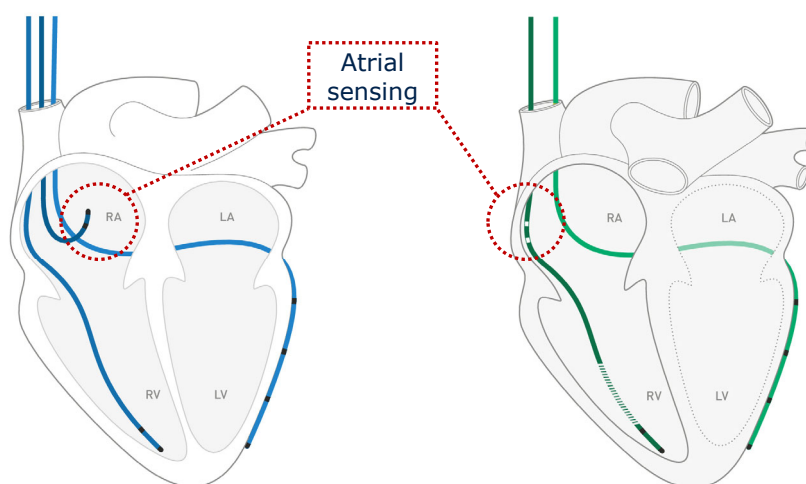
Biffi M, et al. J Cardiovasc Electrophysiol. 2020 Apr;31(4):846-853

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CRT-DX Offers 2-lead CRT



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QP ExCELS Lead Registry: 3-Lead CRT c/w DX CRT

Novel two-lead cardiac resynchronization therapy system provides equivalent CRT responses with less complications than a conventional three-lead system: Results from the QP ExCELS lead registry

Naushad A. Shaik MD¹ | Michael Drucker MD² | Christopher Pierce MD³ |
Gabor Z. Duray MD⁴ | Shane Gillett RN, BSN⁵ | Crystal Miller MS⁵ |
Camden Harrell MS⁵ | George Thomas MD⁶

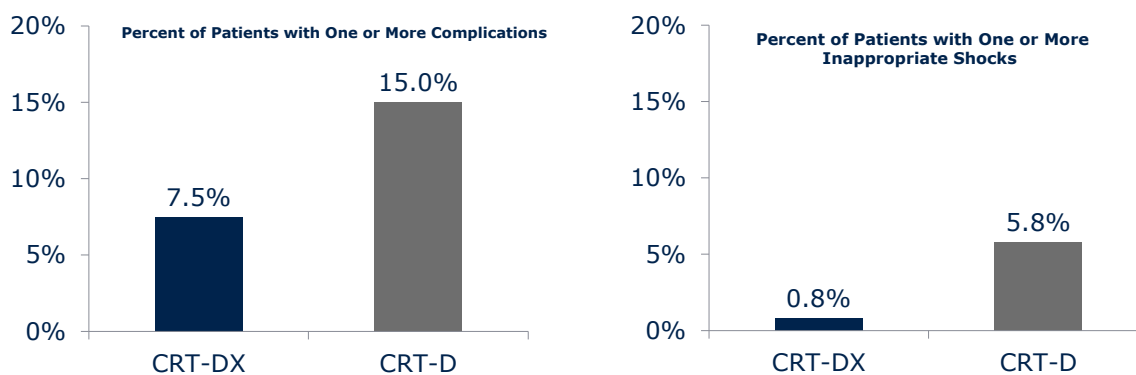
Shaik NA, et al. J Cardiovasc Electrophysiol. 2020 Jul;31(7):1784-1792.

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CRT-DX Patients Had Fewer Complications, and Fewer Shocks



Complication-free survival favored the CRT-DX group with 92.5% of patients without a major complication compared to 85.0% in the CRT-D cohort ($P=0.0495$; 95% CI 0.1%–14.9%) over a mean follow-up of 1.3 and 1.4 years, respectively.

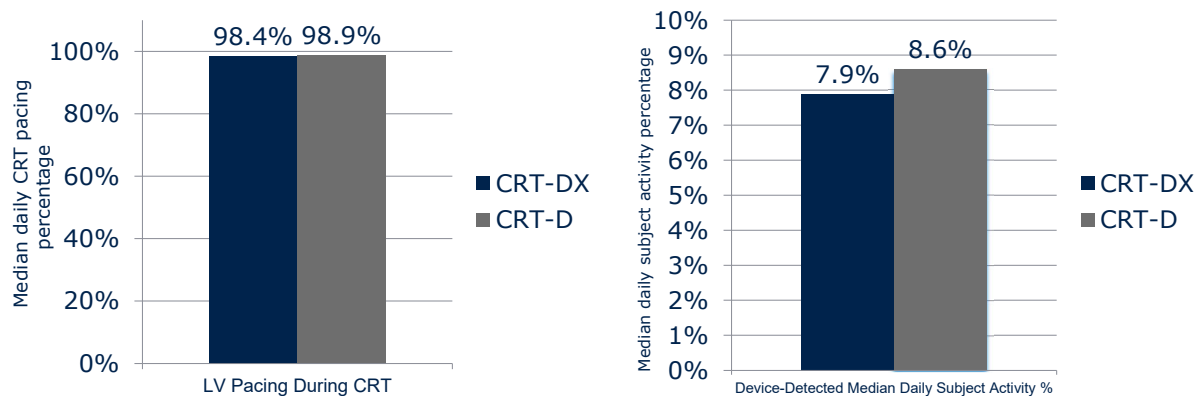
Shaik NA, et al. J Cardiovasc Electrophysiol. 2020 Jul;31(7):1784-1792.

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No Meaningful Difference in LV Pacing Percentage During CRT or Patient Activity



Over the follow-up period, the device-detected median (IQR) LV pacing during CRT was similar for both cohorts at 98.4% (Q1 95.4%, Q3 99.8%) and 98.9% (Q1 97.6%, Q3 99.8%), in the CRT-DX and CRT-D cohorts, respectively ($P=0.2025$; 95% CI -0.6%—0.2%). Device-detected median daily subject activity % in the CRT-DX cohort was 7.9% (Q1 5.5%, Q3 11.2%) compared with 8.6% (Q1 5.7%, Q3 12.1%) in the CRT-D cohort ($P=0.1647$; 95% CI -2.0%—0.9%).

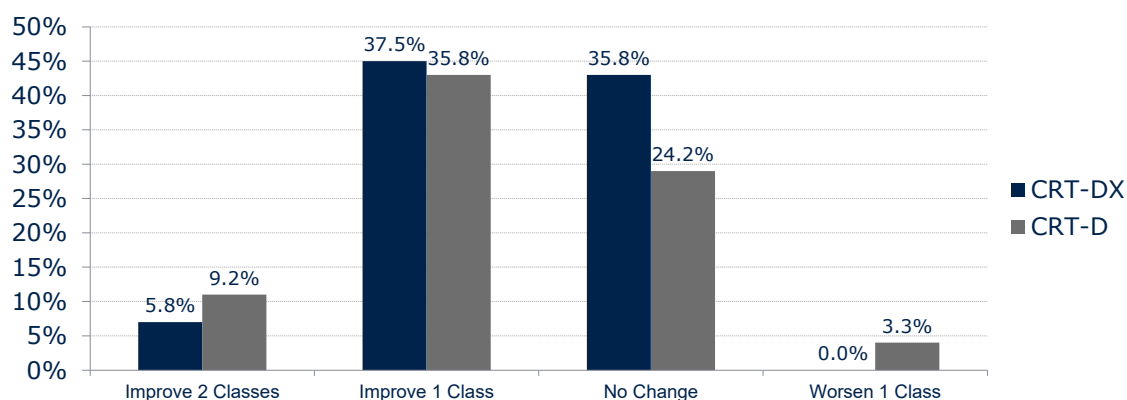
Shaik NA, et al. J Cardiovasc Electrophysiol. 2020 Jul;31(7):1784-1792.

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Similar NYHA Class Improvement at 6 Months



NYHA changes at 6 months follow-up. NYHA was not obtained at baseline and/or 6 months for 25 and 33 subjects in the CRT-DX and CRT-D cohorts, respectively. All percentages are displayed as absolute percentages (out of 120 subjects).

Shaik NA, et al. J Cardiovasc Electrophysiol. 2020 Jul;31(7):1784-1792.

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MATRIX

Using DX + HM to Remotely Monitor for Subclinical AF

- International, multicenter registry at **119 sites** in **24 countries**
- **Enrolled 2,054 DX-ICD patients and followed for 24 months**
- Key Takeaways
 - **99.6% detection accuracy** for AHRE lasting ≥ 1 hour
 - **92.5% Home Monitoring®** transmission performance
 - AF found in 8.2% of patients with no known history of AF, and these patients were often at high-risk of stroke (**80% high CHA₂DS₂-VASc scores of which 69.5% no OAC**)

"A 99.7% detection accuracy for AHRE lasting for ≥ 1 h, and 97.5% accuracy for AF ≥ 6 min, in combination with a 92.5% Home Monitoring® transmission performance allows a reliable guideline-recommended remote monitoring of subclinical AF in the vast majority of patients treated with a single-chamber ICD with atrial sensing capabilities (DX ICD)."

Highly Accurate AHRE Detection

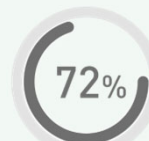


Progression is common

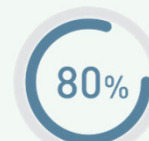


31.1%

of patients with new-onset AF showed progression. (AHRE durations ≥ 1 h)



Patients with new-onset AHRE who were not on OAC therapy at baseline (86/119)



Patients with new-onset AHRE with a high CHA₂DS₂-VASc score (95/119)

Hindricks G et al. EP Europace, 2023 Apr 11; euad061; doi: 10.1093/europace/euad061

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Journal of the American Heart Association

ORIGINAL RESEARCH

Single- Versus Dual-Chamber Implantable Cardioverter-Defibrillator for Primary Prevention of Sudden Cardiac Death in the United States

Gilad Margolis, MD; Nashed Hamuda, MD; Ofer Kobo, MD, MHA; Gabby Elbaz Greener, MD, MHA; Offer Amir, MD; Munther Homoud, MD; Christopher Madias, MD; Edwin Kevin Heist, MD, PhD; Jeremy N. Ruskin , MD; Mark Kazatsker, MD; Ariel Roguin , MD, PhD; Eran Leshem , MD, MHA; Guy Rozen , MD, MHA

Margolis, et al. JAHA 2023;12

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Single-Chamber vs Dual-Chamber ICD for Primary Prevention

- Dual-chamber ICD complication rate = 12.8%
- Single-chamber ICD complication rate = 10.7% ($p < 0.001$)
- Complication difference driven by:
 - \uparrow hemothorax in DC-ICD (4.6% v 3.4%, $p < 0.001$)
 - \uparrow lead dislodgement in DC-ICD (3.6% v 2.3%, $p < 0.001$)
- Atrial lead addition was an independent predictor for any complication, pneumo/hemothorax and atrial lead dislodgement

monitoring unjustifiable.¹⁹ In the subset of patients who may benefit from long-term atrial rhythm monitoring such as those with a markedly elevated stroke risk, the option of implanting a single ventricular implantable cardioverter-defibrillator lead with a floating atrial dipole was shown to be comparable to dICD in detecting atrial high-rate episodes.³³

As an sICD system does not provide atrial backup pacing, patients who are anticipated to meet a pacing

Margolis, et al. JAHA 2023;12 - Highlighted text summarized from Thomas G, et al., 2019

33. Thomas G, Choi DY, Doppalapudi H, Richards M, Iwai S, Daoud EG, Houmsse M, Kanagasundram AN, Mainigi SK, Lubitz SA, et al. Subclinical atrial fibrillation detection with a floating atrial sensing dipole in single lead implantable cardioverter-defibrillator systems: results of the SENSE trial. J Cardiovasc Electrophysiol. 2019; 30:1994-2001

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Interpreting Multiple Ventricular Rhythms in a Patient with a Single-Lead ICD



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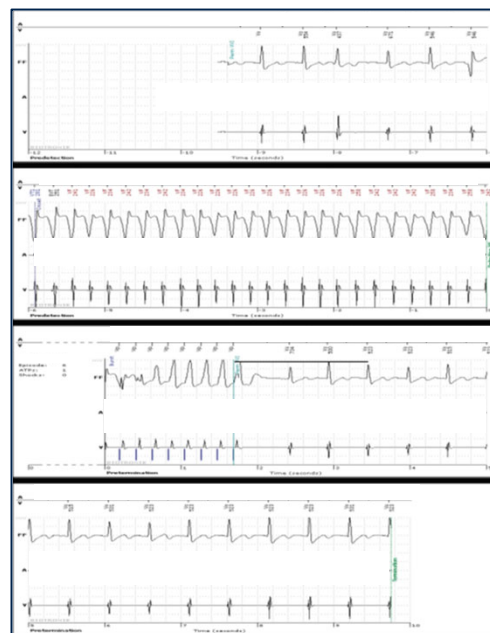
Case Study: What Are the Various Rhythms?

- 72 year old male with history of a previous MI and LVEF= 30% implanted with an ICD utilizing DX technology
- Clinic staff reviewing and interpreting multiple Home Monitoring transmissions
- Does DX allow accurate recognition and analysis of the various rhythms?

What Is the Rhythm?

Device:	Intica 7 VR-T DX
Implantation:	04/2018
Episode:	VF from 04/2018
Description:	Fast VT at 248 bpm detected in the VF Zone. ATP One Shot delivered after 24 cycles, successfully terminating rhythm. Device begins charging, but aborts a full charge after confirmation of VT termination.

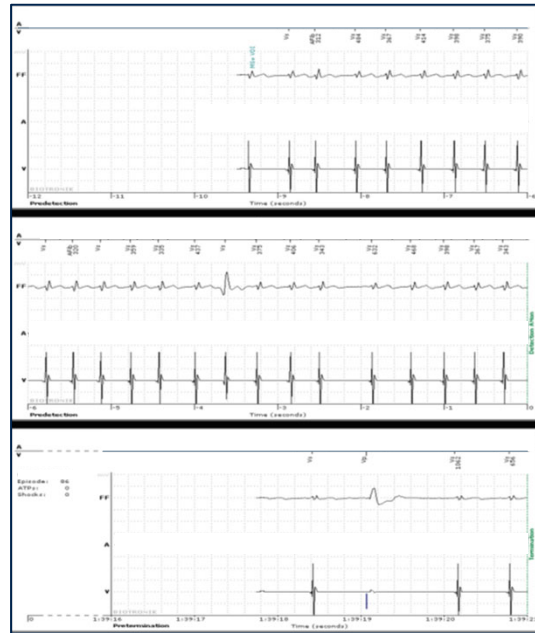
- Analyze the ventricular channel
- Assess morphology of far-field channel
- Now analyze with visualizing the atrium
 1. What is the V to A ratio?
 2. Are the V-V and A-A intervals stable?
 3. Are the A and V associated?



What Is the Rhythm?

Device:	Intica 7 VR-T DX
Implantation:	01/2019
Episode:	Atrial monitoring episode from 03/2020
Description:	Afib with rapid ventricular rate at 152 bpm

- Analyze the ventricular channel
- Assess morphology of far-field channel
- Now analyze with visualizing the atrium
 - What is the V to A ratio?
 - Are the V-V and A-A intervals stable?
 - Are the A and V associated?



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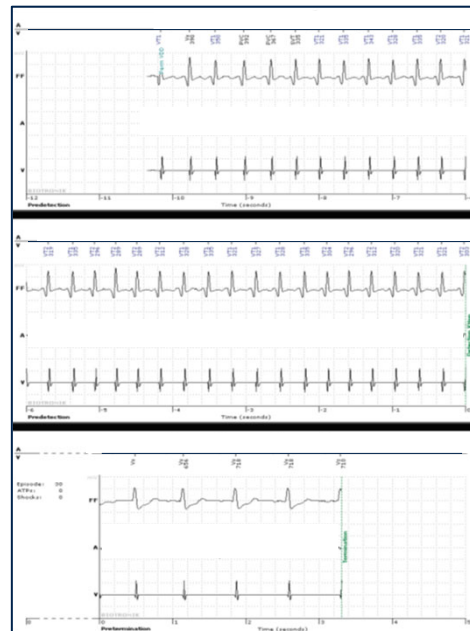
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What Is the Rhythm?

Device:	Intica 7 VR-T DX
Implantation:	12/2018
Episode:	VT from 08/2019
Description:	VT in monitoring zone with narrow morphology that is almost indistinguishable from sinus. The atrial channel indicates that this rhythm is ventricular driven.

- Analyze the ventricular channel
- Assess morphology of far-field channel
- Now analyze with visualizing the atrium
 - What is the V to A ratio?
 - Are the V-V and A-A intervals stable?
 - Are the A and V associated?



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Summary

- Large and expanding evidence base supporting clinical advantages of DX to SC-ICD and advantages to DC-ICD when atrial pacing not indicated
- Margolis, et al, demonstrated significantly higher complication rate in patients receiving atrial pacing leads when no clinical need for atrial support
- Higher detection of AHRE and faster clinical response, e.g. initiation of OAC, with DX compared to SC-ICD
- Fewer inappropriate shocks in multiple studies



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Thank you!

If you have questions or would like to provide feedback regarding today's session, please contact the BIOTRONIK Training & Education Department:

Education.us@biotronik.com

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