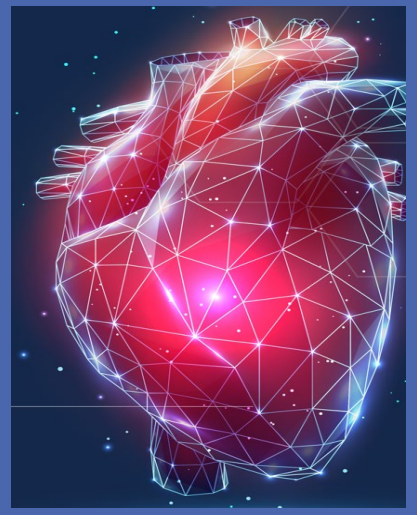
WHERE HF AND EP COLLIDE: ICDS, PHYSIOLOGIC PACING, AND REMOTE MONITORING FOR HF IN 2025



Heart Failure Symposium 2025

Kenneth Bilchick, MD, MS

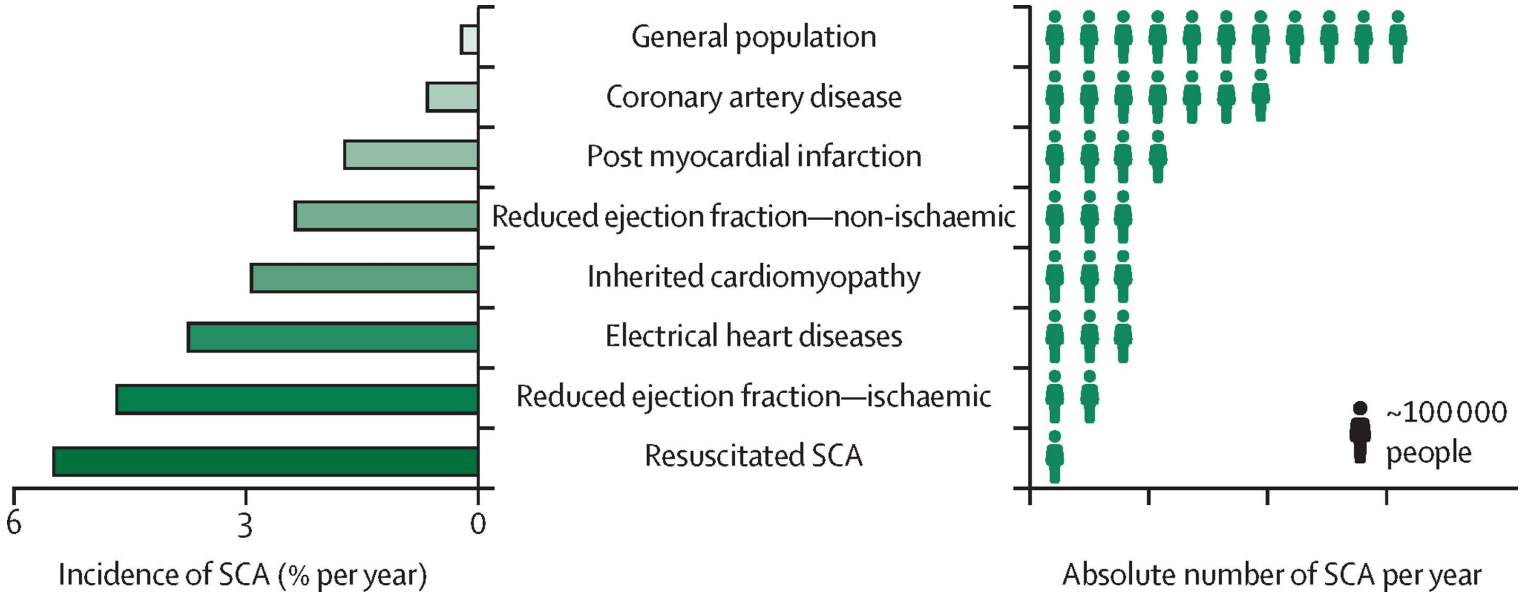
Learning Objectives

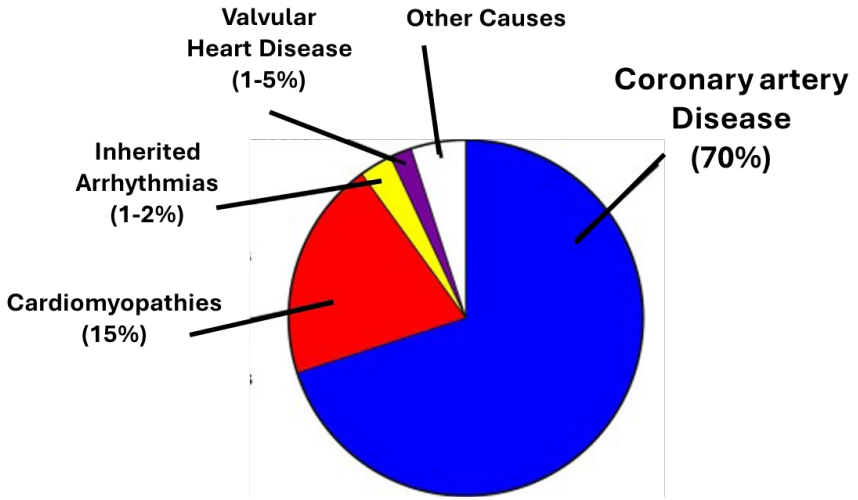
- Compare the roles of risk scores and cardiac magnetic resonance to predict ventricular arrhythmias in HF and the benefit from ICDs
- Identify the two main forms of cardiac physiology pacing, how cardiac magnetic resonance can personalize therapy, and options for implementation
- Recognize different approaches for monitoring of volume overload in heart failure
- Identify the key features of available algorithms on implantable cardioverter defibrillators to detect heart failure decompensation

RISK SCORES AND CMR TO PERSONALIZE ICD AND PACING THERAPIES IN HF

PART ONE

Who is At Risk for Sudden Cardiac Arrest?





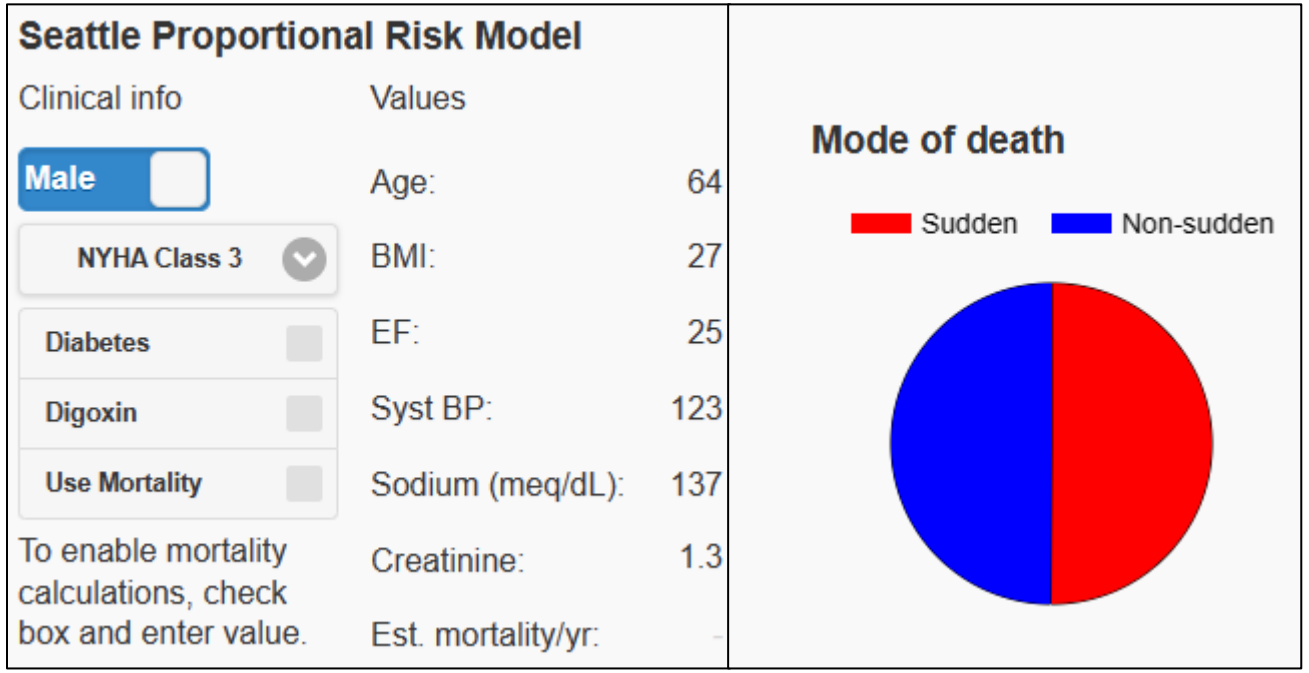
- The general population has the greatest absolute number with SCA
- Patients with structural heart disease have the greatest proportion with SCA
- Coronary artery disease (scar from MI) has the greatest association with SCA

Heart Lung Circ. 2019;28:6-14. *Lancet*. 2023;402:883-936. *Eur Heart J*. 2022;43:3997-4126.

Best Primary Prevention ICD Candidate: Good Expected Survival with High Risk of Arrhythmic Death

Seattle Heart Failure Model (SHFM): Overall Mortality in HF

Seattle Proportional Risk Model (SPRM): Proportional Risk of Arrhythmic Death

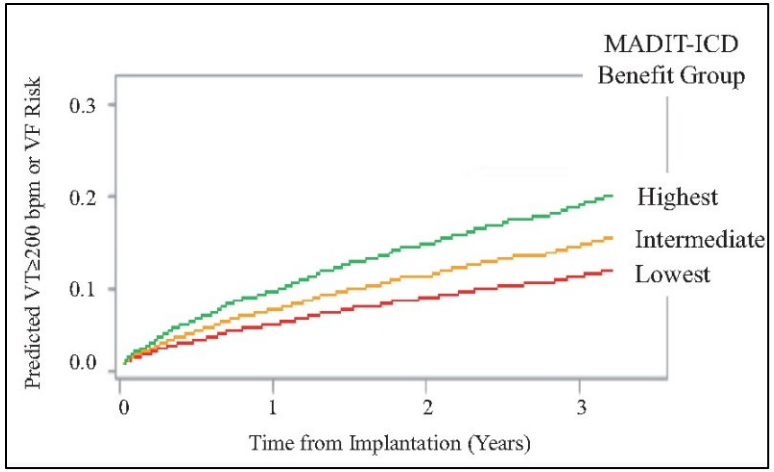


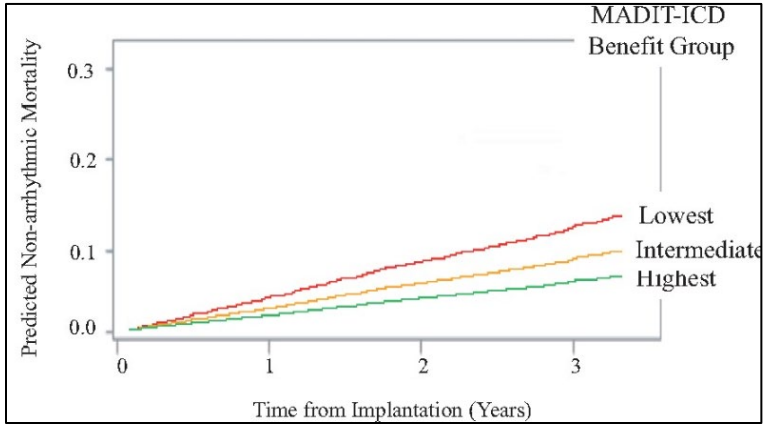
Levy et al., *Circulation* 2006;113:1424-33. Shadman et al., *Heart Rhythm* 2015;12:2069-77. Bilchick et al., *J Am Coll Cardiol* 2017;69:2606-2618. Bilchick et al., *Am Heart J* 2020;222:93-104.

CLINICAL RISK: MADIT ICD BENEFIT SCORE

- VTVF Score (0-13):
  - LVEF≤25% (1) +
  - atrial arrhythmias (1) +
  - HR>75bpm (1) +
  - SBP<140mmHg (2) +
  - MI (2) +
  - Age<75yrs (2) +
  - Male (2) +
  - NSVT (2)

- Non-arrhythmic Mort. Score (-1 to 10):
  - atrial arrhythmias (2) +
  - Diabetes (1) +
  - BMI<23kg/m2 (2) +
  - NYHA≥II (1) +
  - LVEF≤25% (2) +
  - Age≥75yrs (2) –
  - CRTD (1)





	Lowest ICD Benefit	Intermediate ICD Benefit		Highest ICD Benefit
VT/VF Score	**<7 (Low)**	**<7 (Low)**	**≥ 7 (High)**	**≥ 7 (High)**
Non-arrhythmic Mortality Score	**≥ 3 (High)**	**< 3 (Low)**	**≥ 3 (High)**	**< 3 (Low)**

Younis et al., Eur Heart J. 2021;42:1676-1684

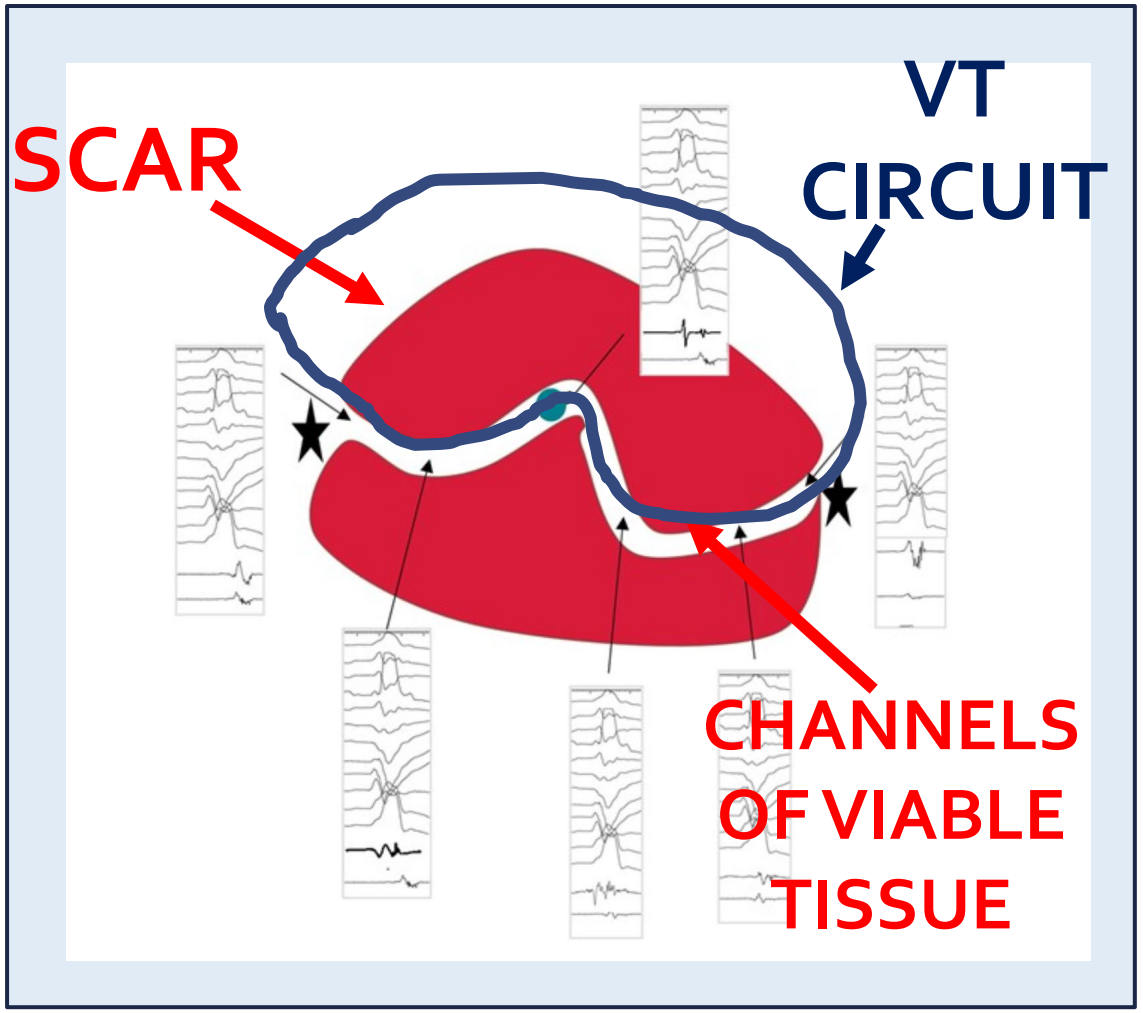
CONTEMP-ICD CLINICAL Trial

- Prospective, multicenter, open-label randomized-controlled study designed to evaluate the effectiveness of medical management without an implantable cardioverter defibrillator (ICD) versus with an ICD in patients with heart failure with reduced ejection fraction (HFrEF) who have a low (<50) MADIT ICD Benefit Score
- Participants with LVEF ≤ 35% and guideline-directed indication for an ICD will be randomly assigned to either guideline-directed medical therapy (GDMT) alone, or the ICD + GDMT

https://contemp-icd.org/

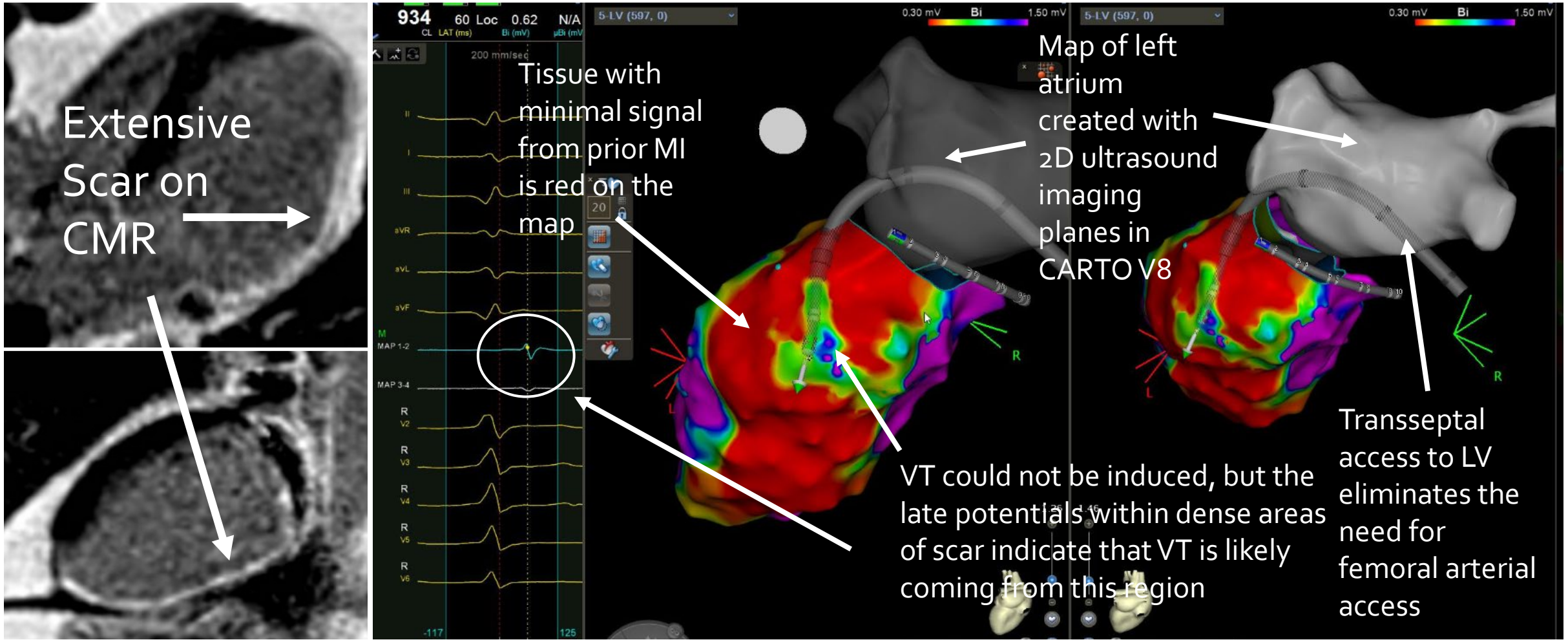
CMR LGE and Mechanism of VT

- Patients with heart failure are more like to have ventricular tachycardia and ventricular fibrillation
- Ventricular tachycardia reentry is facilitated by slower conduction speeds through channels in scar compared with faster conduction speeds in healthy tissue around scar
- Channels can be determined with cardiac magnetic resonance based on heterogenous area of scar with some interspersed healthy tissue
- Entrance sites, central channel sites, and exit sites can be identified
- CMR provides critical 3D characterization of scar



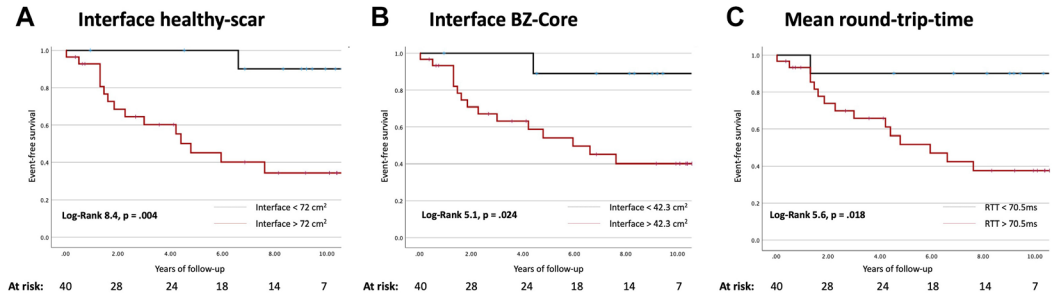
Roca-Luque, Europace 2020

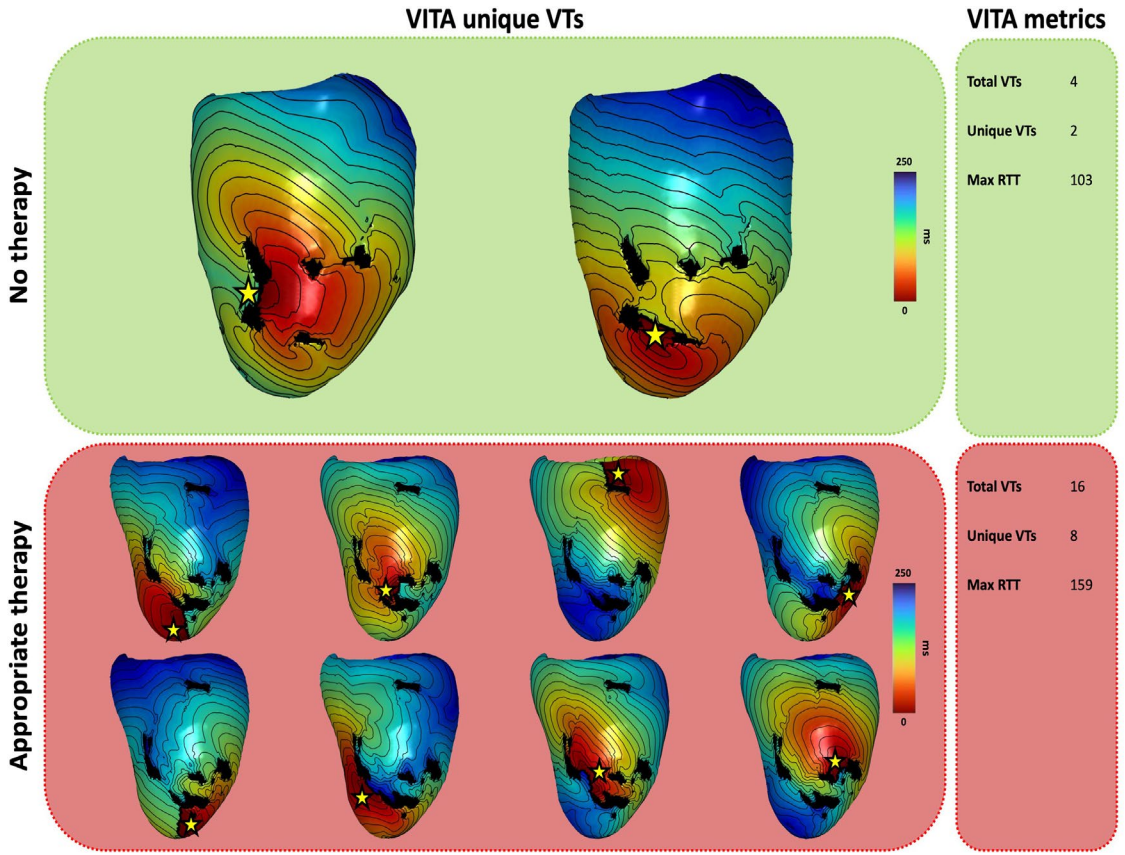
CMR Demonstrates VT Circuit in VT Ablation



ADAS Software Maps VT by Location and Extent of CMR Border Zone and Core Scar

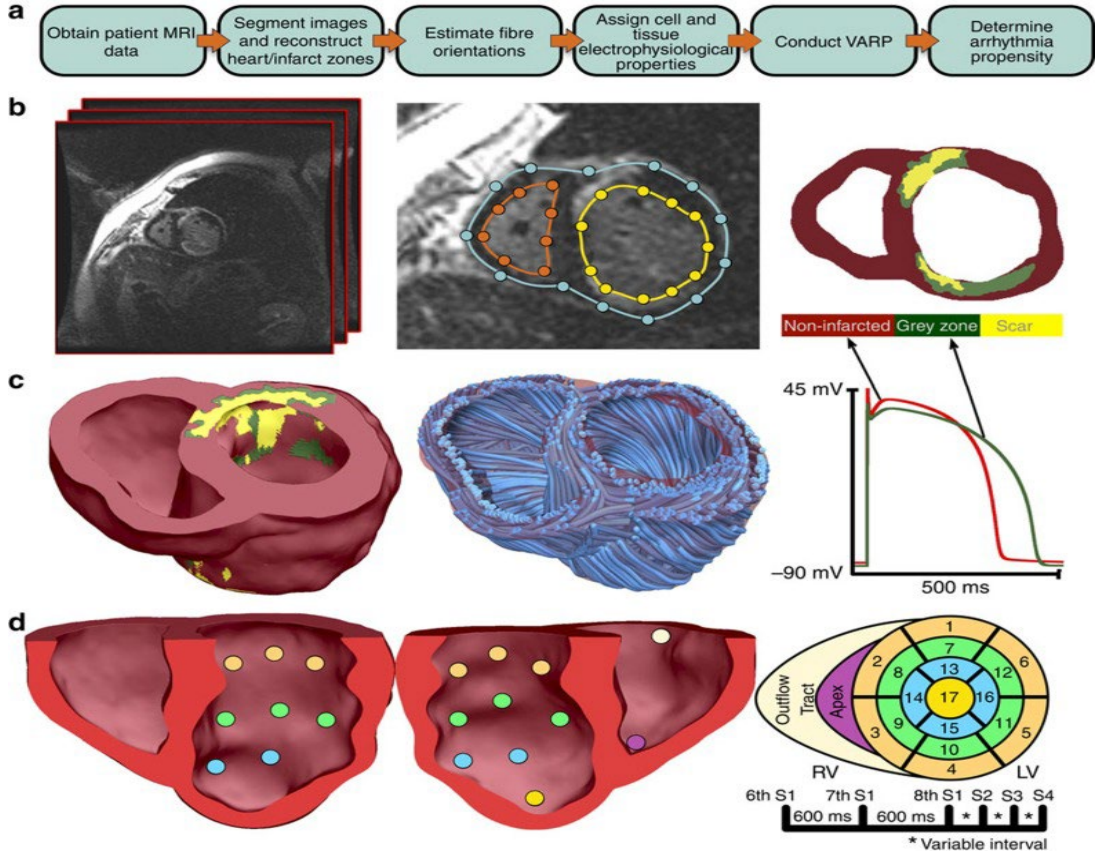
- Based on ADAS LV software analysis, only the interface areas between BZ and core (76 ± 26.7 vs 55.2 ± 27; *P* = .04) and between healthy myocardium and total enhancement (103.8 ± 34 vs 77.4 ± 33; *P* = .04) were significantly higher in patients with an event than in those without an event

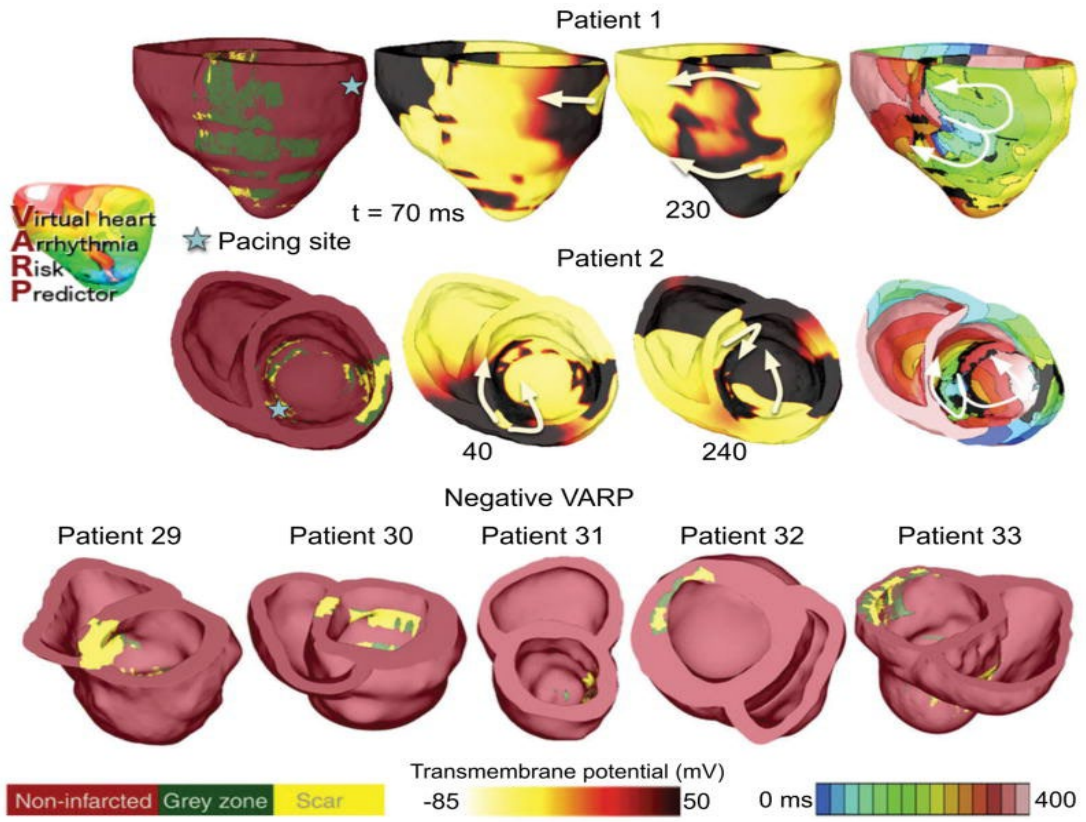




Bhagirath et al., *Heart Rhythm* 2024;1962 - 1969

Virtual EP Study for VT Based on CMR

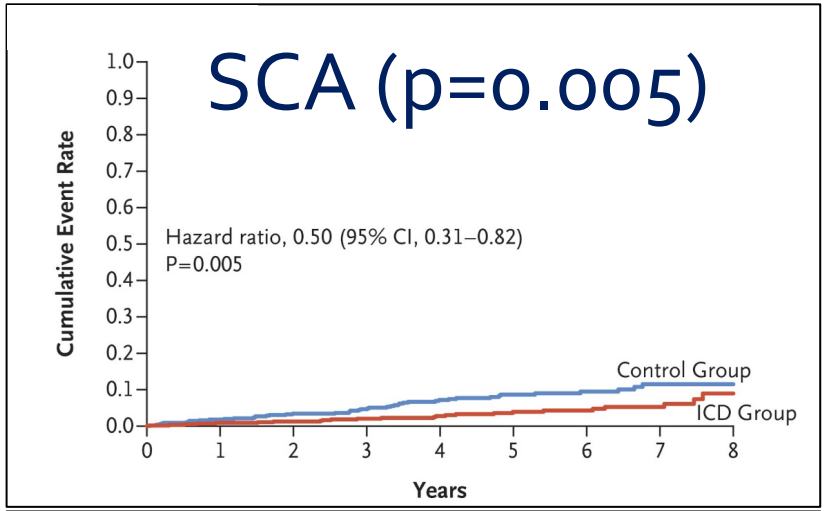


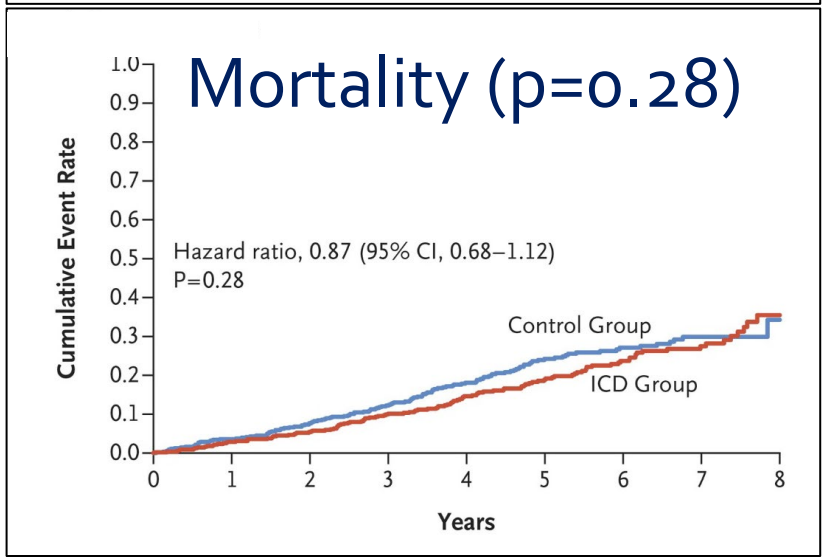


Arevalo et al., Nat Commun 2016; Trayanova et al., Heart Rhythm, 2017

ICDs in Nonischemic Cardiomyopathy (NICM): DANISH ICD Trial

- 556 patients with symptomatic systolic heart failure (left ventricular ejection fraction ≤35%) and NICM were assigned to receive an ICD, and 560 patients were assigned to receive usual clinical care (control group)
- Decreased SCA with ICDs but same survival
- As a result of this study, Netherlands no longer allows ICDs to be implanted for primary prevention in NICM
- Of note, in a substudy, NICM with a high predicted relative likelihood of SCD (higher SPRM score) had greater benefit from ICD implantation

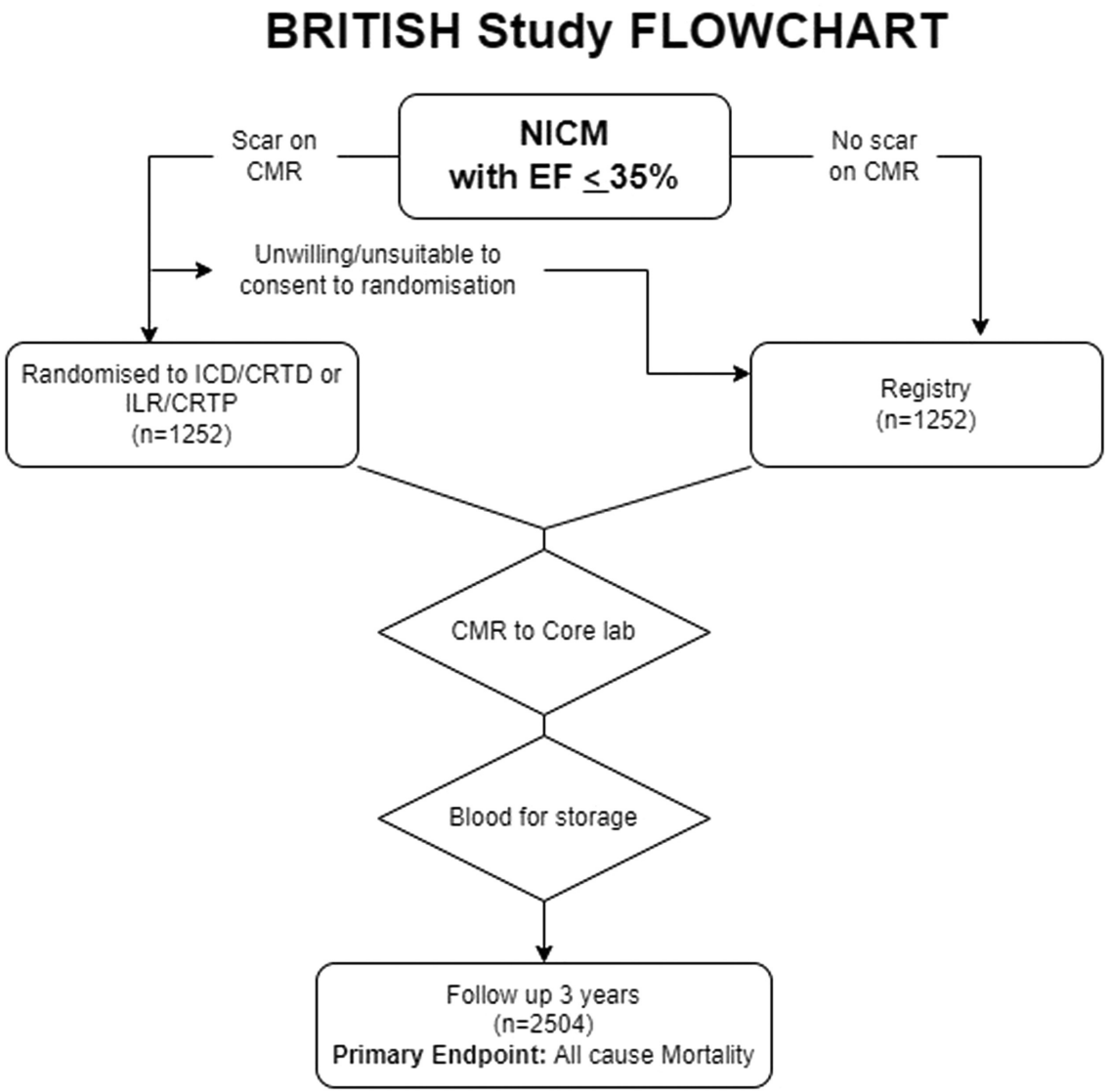




Køber et al., *N Engl J Med* 2016;375:1221-1230; Kristensen et al., *JACC Heart Fail* 2019;7:717-724

BRITISH Study

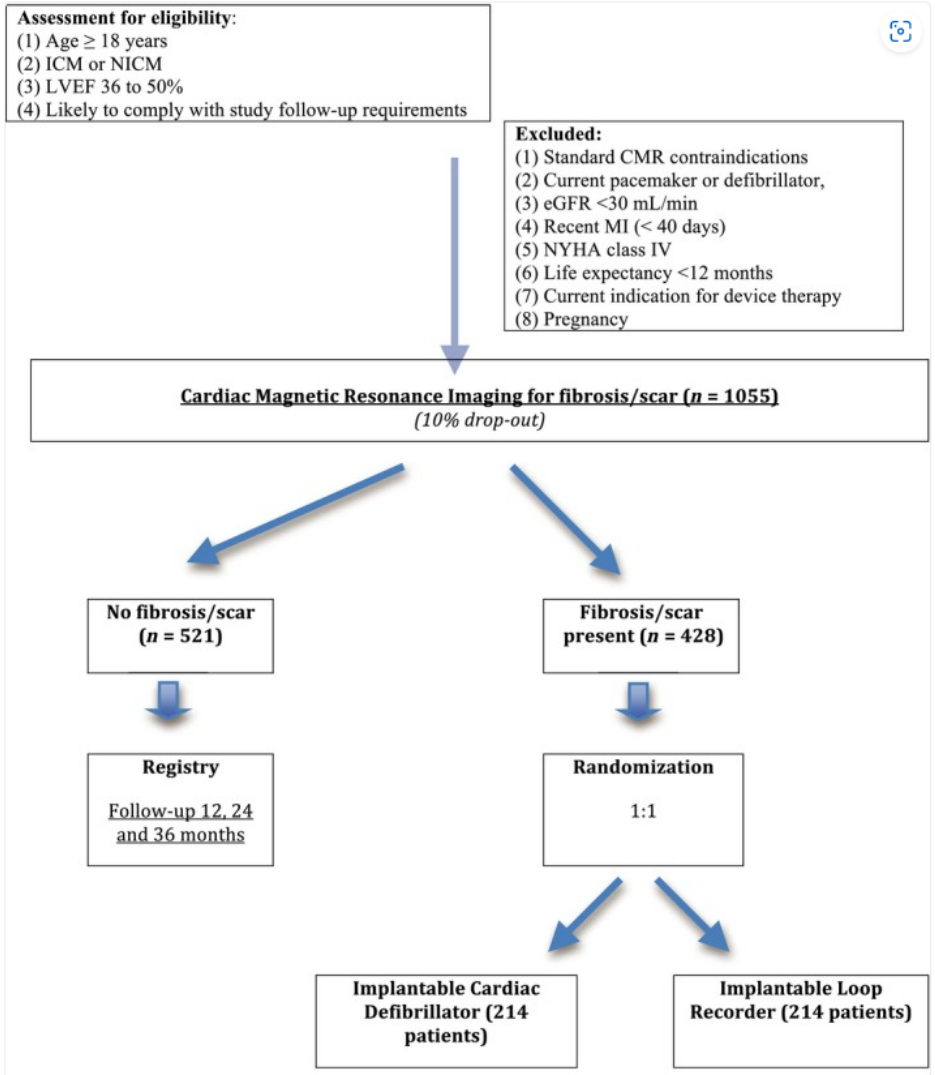
- A response to the DANISH study!
  - UK v. Netherlands
- Prospective, multicenter, randomized controlled trial aiming to enroll 1,252 patients with NICM (nonischemic scar on CMR) and an LVEF ≤35%m with randomization to:
  - ICD, with or without cardiac resynchronization (CRT-D)
  - Implantable loop recorder (ILR) or cardiac resynchronization (CRT-P)
- Primary endpoint is all-cause mortality at 3 years after the last randomization



Flett et al., *Am Heart J.* 2023;266:149-158

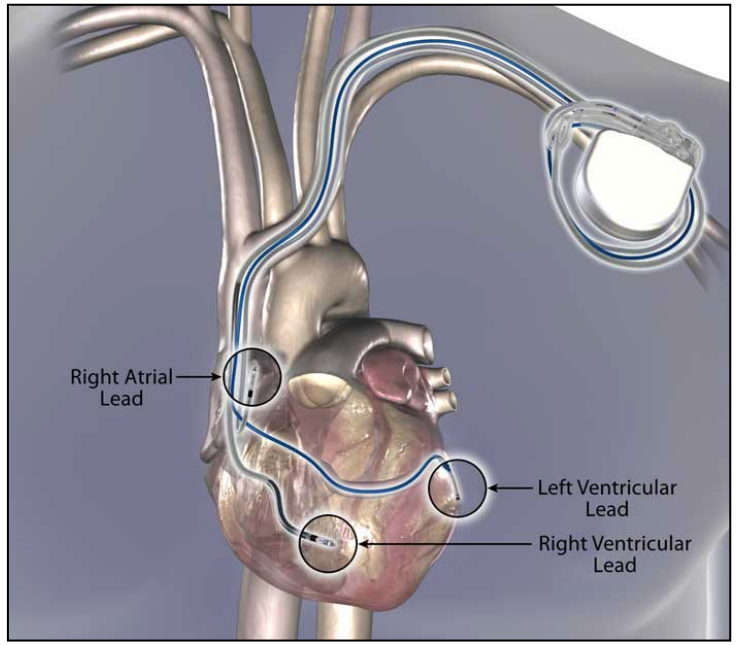
CMR Guide Trial (ICM AND NICM, EF 36-50%)

- CMR GUIDE is a prospective, multicenter randomized control trial enrolling patients with mild-moderate LV systolic dysfunction and CMR evidence of fibrosis on optimal HF therapy
- Randomized to primary prevention ICD or an implantable loop recorder (ILR)
- Primary endpoint is time to SCD or hemodynamically significant VA
- Enrollment is complete
- Results to be reported later this year

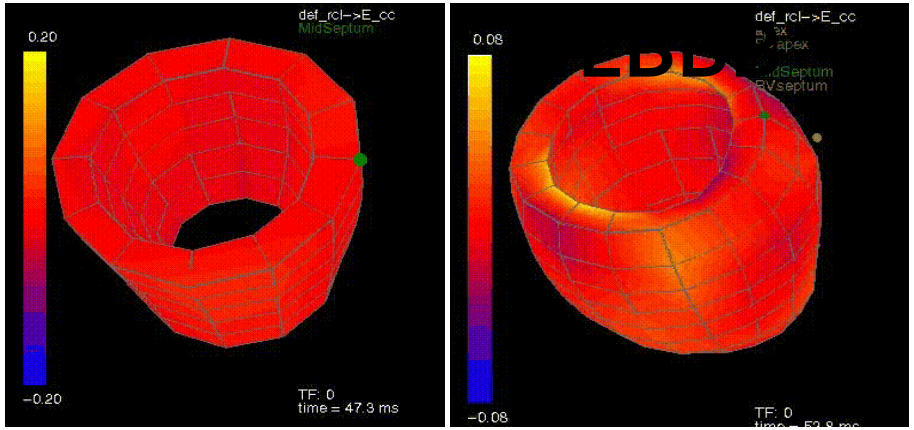


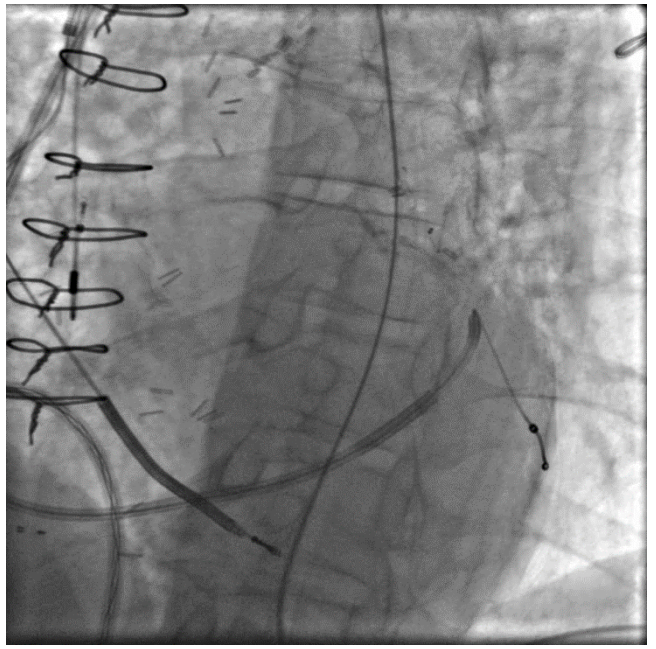
Selvanayagam et al., *Ann Noninvasive Electrocardiol*. 2017;22(4):e12420.

Pacing Therapy to Resynchronize Heart Failure



Normal **HF &**

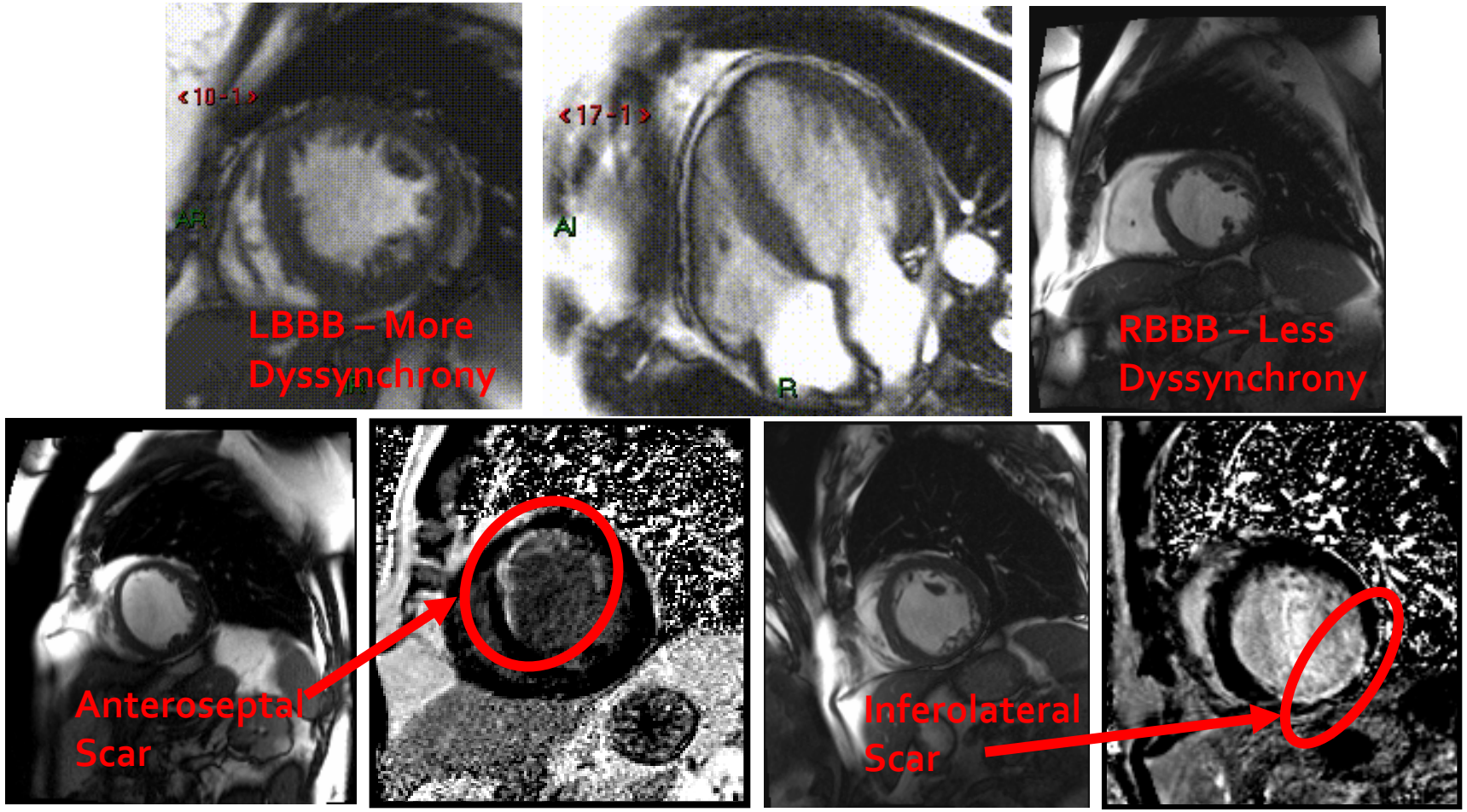




Stretch **Relaxed** **Contraction**

CRT is a cardiac pacing system that can improve heart function in patients with reduced left ventricular (LV) function, which is manifested as a decreased LV ejection fraction (LVEF), and electrical conduction delays such as left bundle branch block (LBBB) that result in asynchronous contraction of the LV

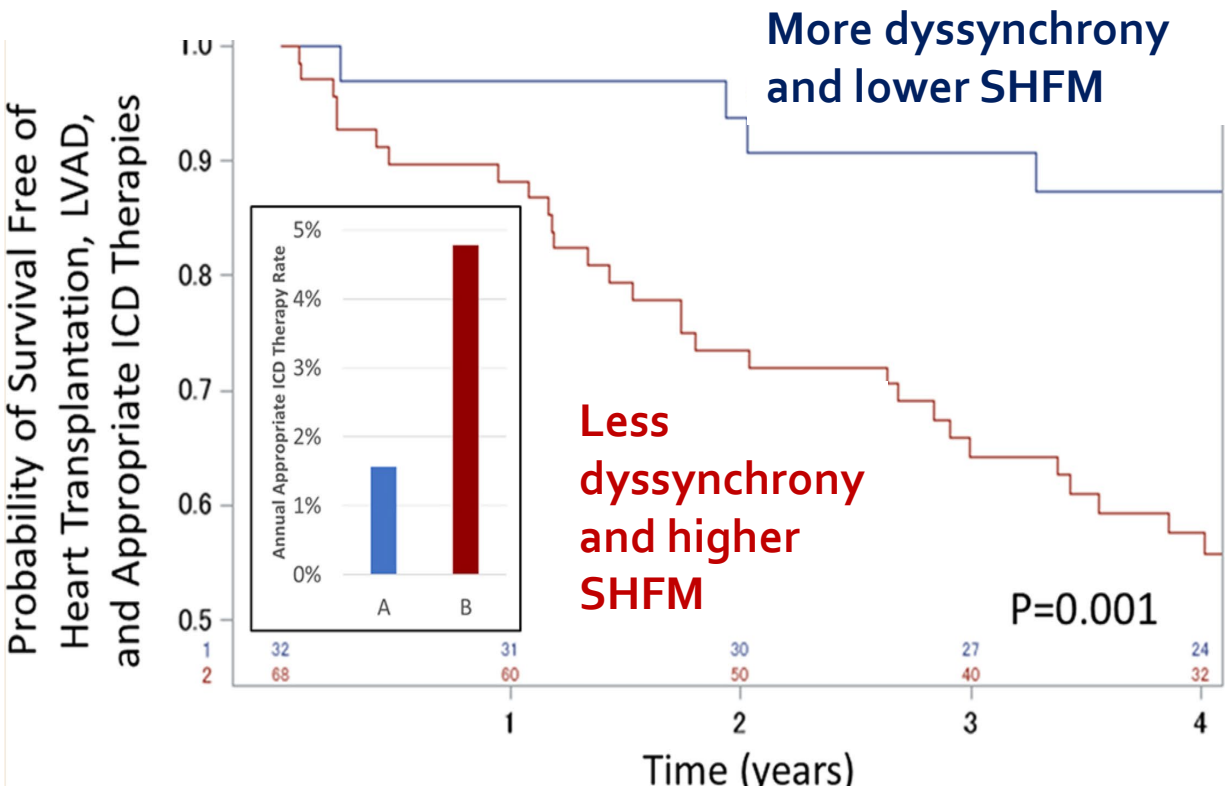
CMR Phenotyping of Cardiomyopathy



Pacing strategies for heart failure with biventricular pacing can be personalized based on the scar location and dyssynchrony

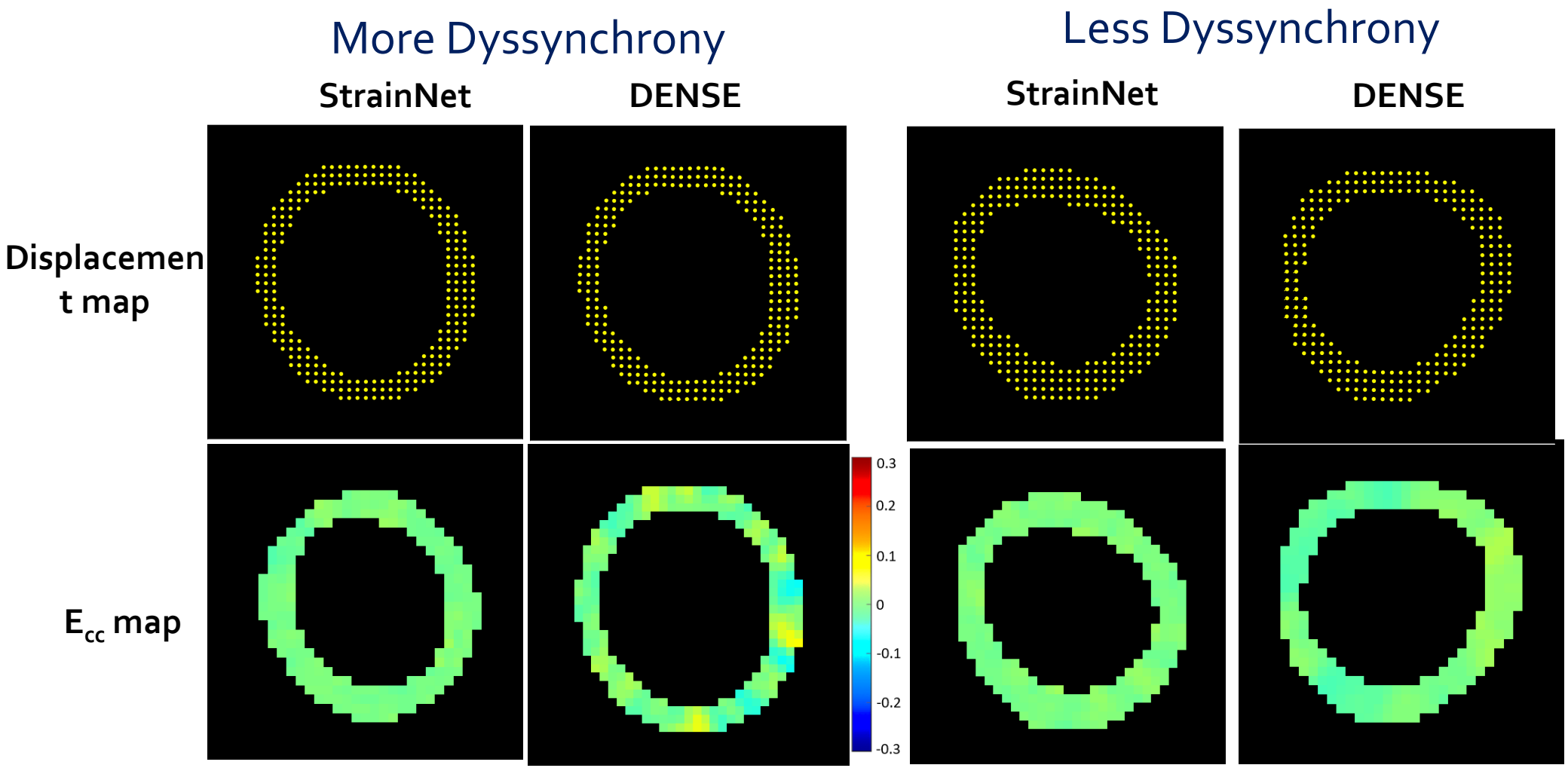
CMR Strain and Risk Score for CRT Candidate Selection

- Dyssynchrony was determined based on the CMR CURE-SVD with DENSE
- A favorable prognostic group (Group A, with CURE-SVD < 0.60 and SHFM-D < 0.70) had a very low rate of appropriate ICD therapies (1.5% per year) and a greater (90%) 4-year survival compared with Group B (CURE-SVD ≥ 0.60 and SHFM-D ≥ 0.70) patients (p=0.02).
- This approach can inform the need for a CRT pacemaker or CRT defibrillator based on ventricular arrhythmia (VA) risk post-implant



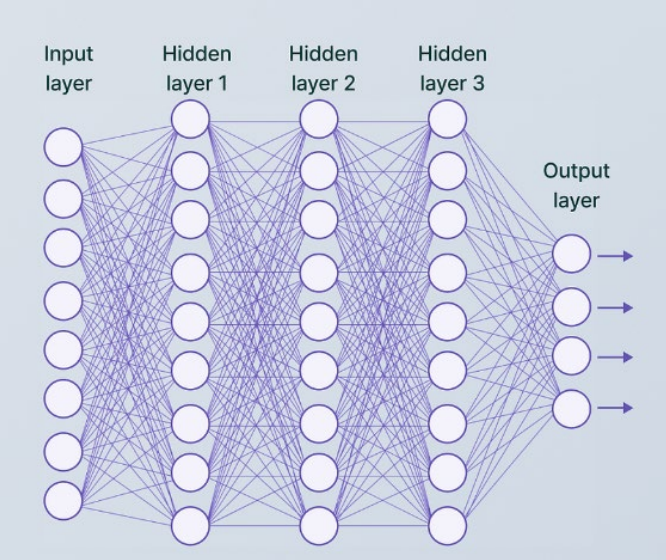
Bilchick, Epstein, Levy, et al., *JACC Cardiovasc Imaging*. 2020;13(4):924-936

AI (DNNs) Provide Strain for CRT from CMR Cine

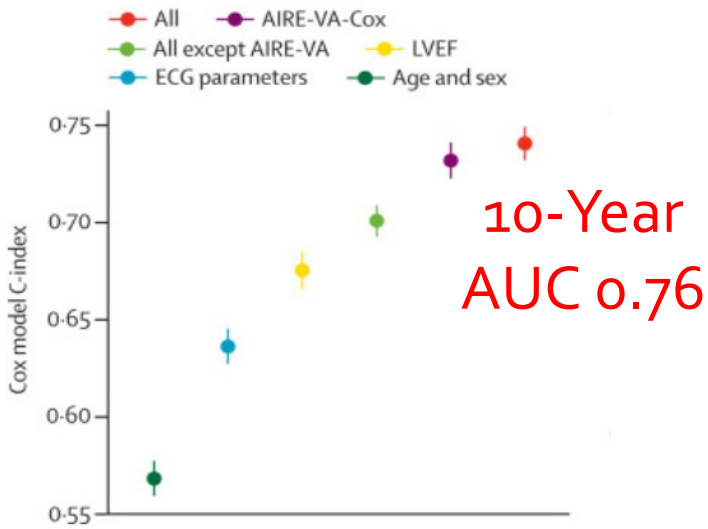


Wang, Bilchick, Epstein et al., *Radiol Cardiothorac Imaging*. 2023;e220196, doi: 10.1148/ryct.220196

AI-ECG (AIRE) to predict 10-Year VA and HF

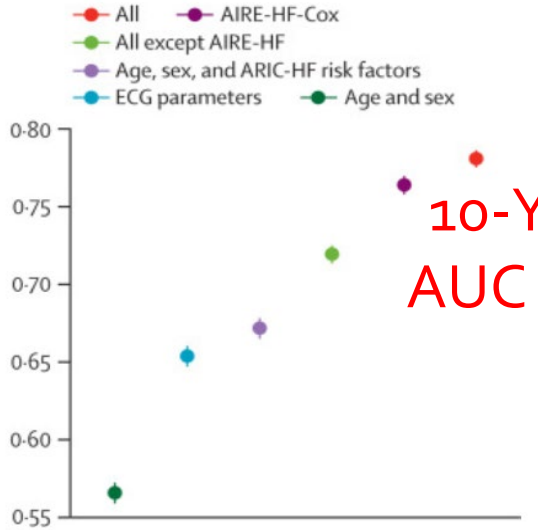


Ventricular Arrhythmia Prediction



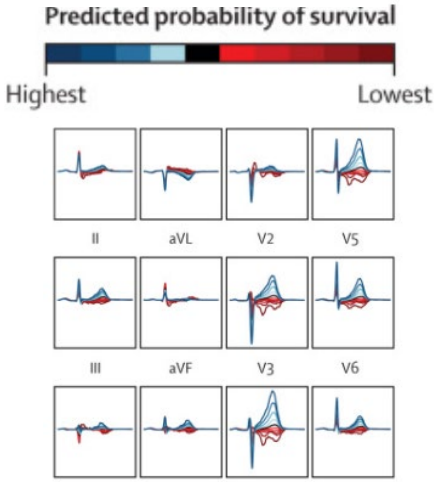
10-Year AUC 0.76

HF Prediction



10-Year AUC 0.79

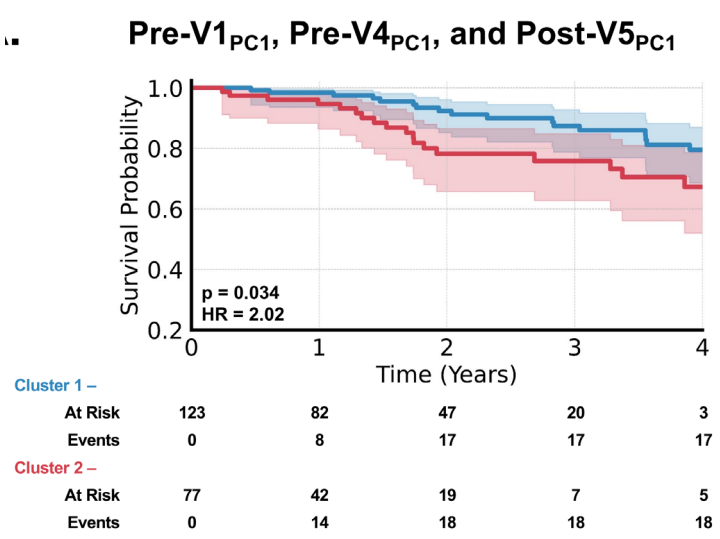
- Artificial intelligence (AI)-enabled electrocardiography (ECG) accurately predicts mortality, VA, and HF
- AIRE is currently being evaluated by the NHS for widespread implementation in the UK
- **<u>Potential to combine AI-ECG and AI-CMR</u>**

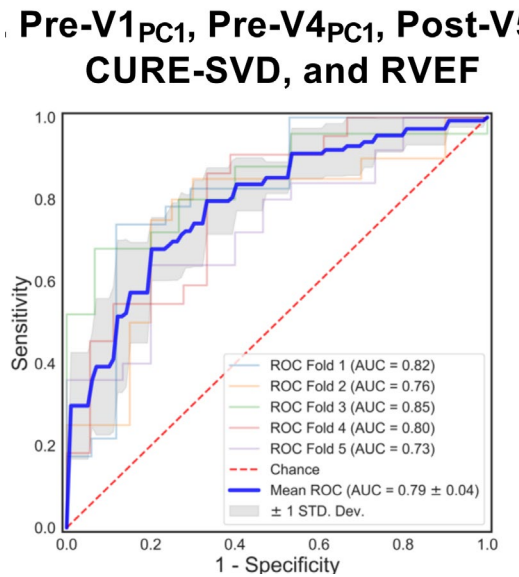


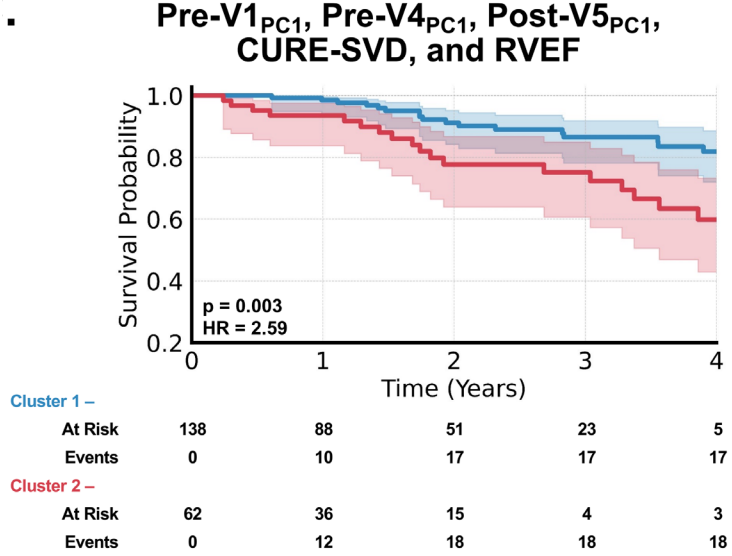
Ng et al., Lancet Digital Health 2024

ML/AI with ECG and CMR for CRT

- Functional Principal Component Decomposition (FPCD) defines orthogonal functions with most of the variance in the QRS voltage versus time functions
- FPCD weights were powerful predictors of CRT outcomes and independent of CMR predictors



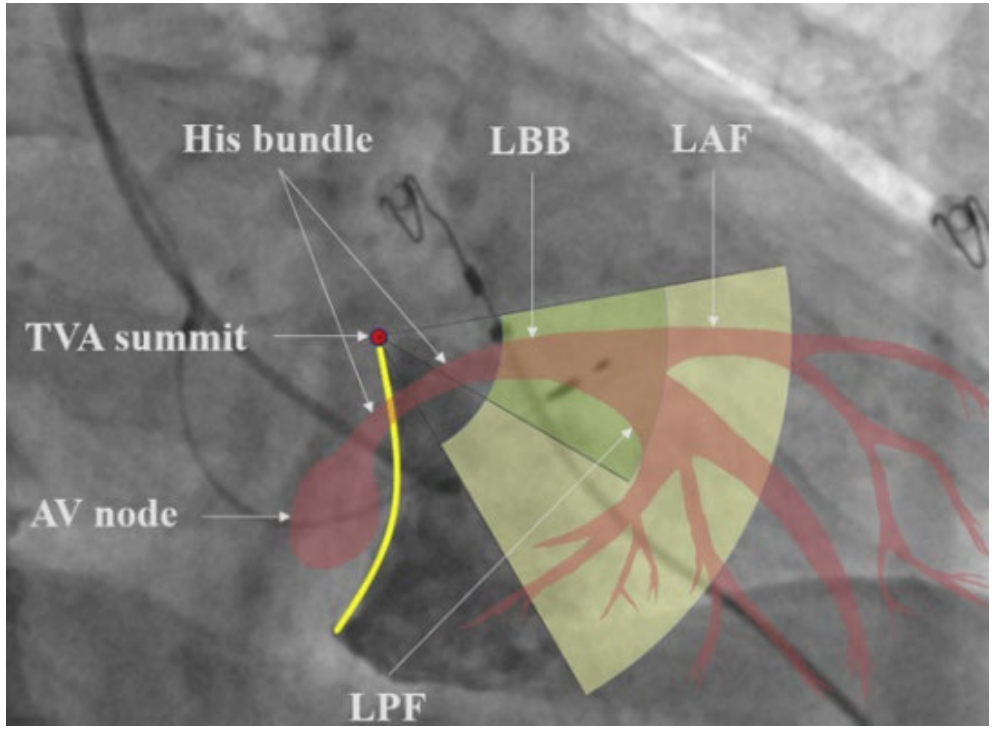


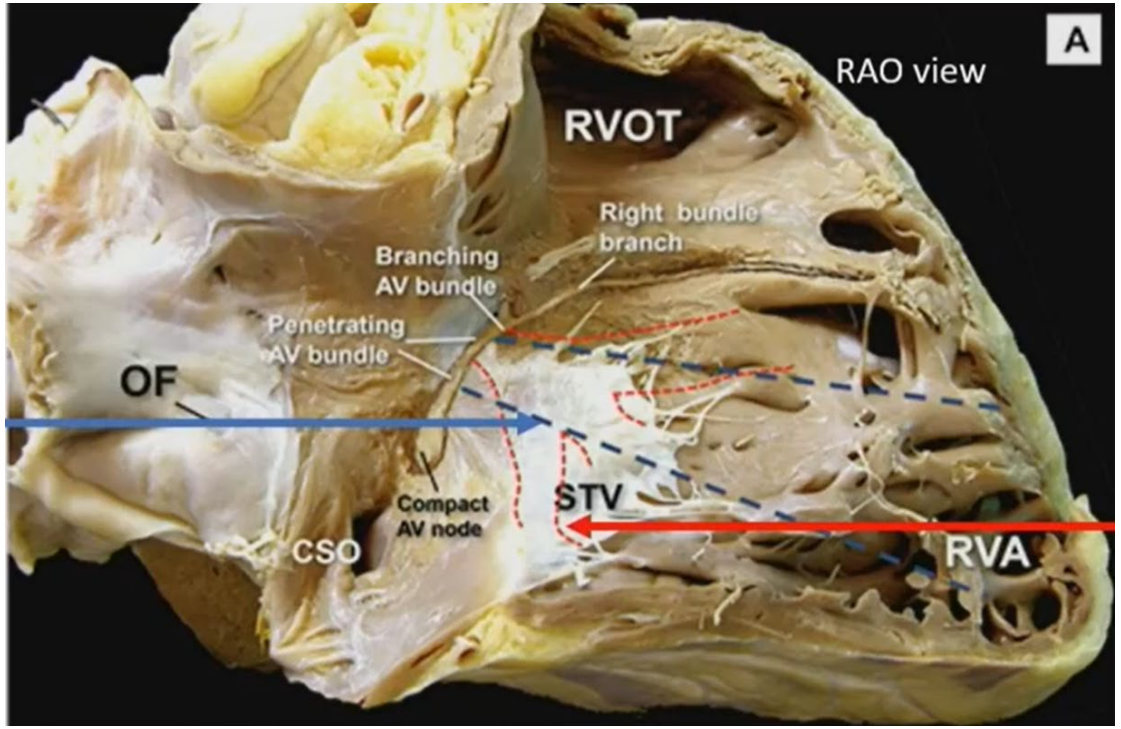


Bilchick et al., Comput Biol Med. 2024 May 22;178:108627. doi: 10.1016

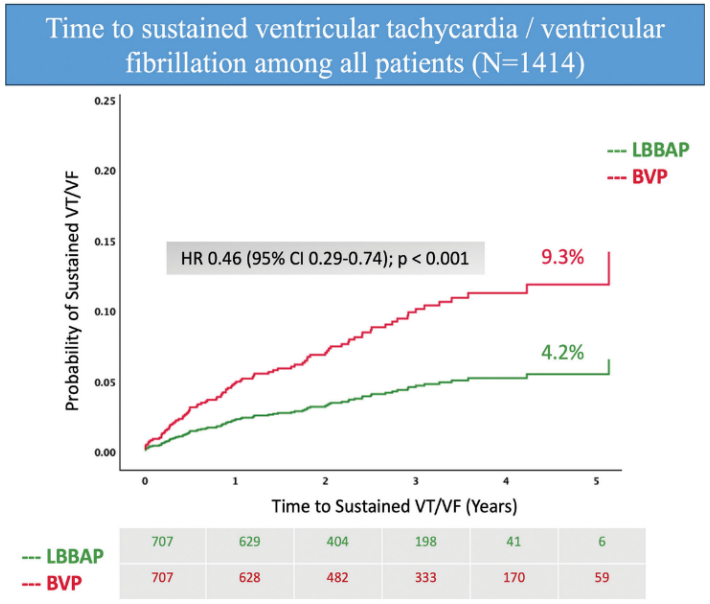
LBBAP

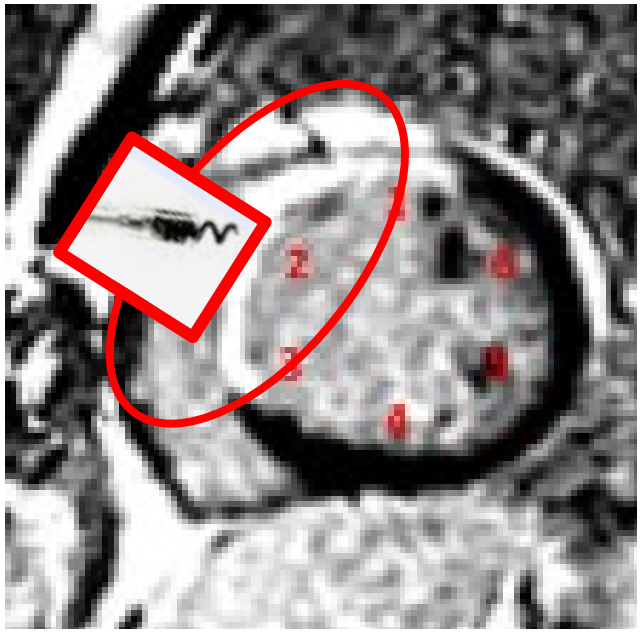
- Left bundle branch area pacing (LBBAP) – penetrates posterior RV septum to capture left bundle branch area and reproduce normal conduction in the heart
- His bundle pacing (HisBP) – captures His bundle directly





CMR Can Help Identify the Best Candidates for LBBAP versus BIVP

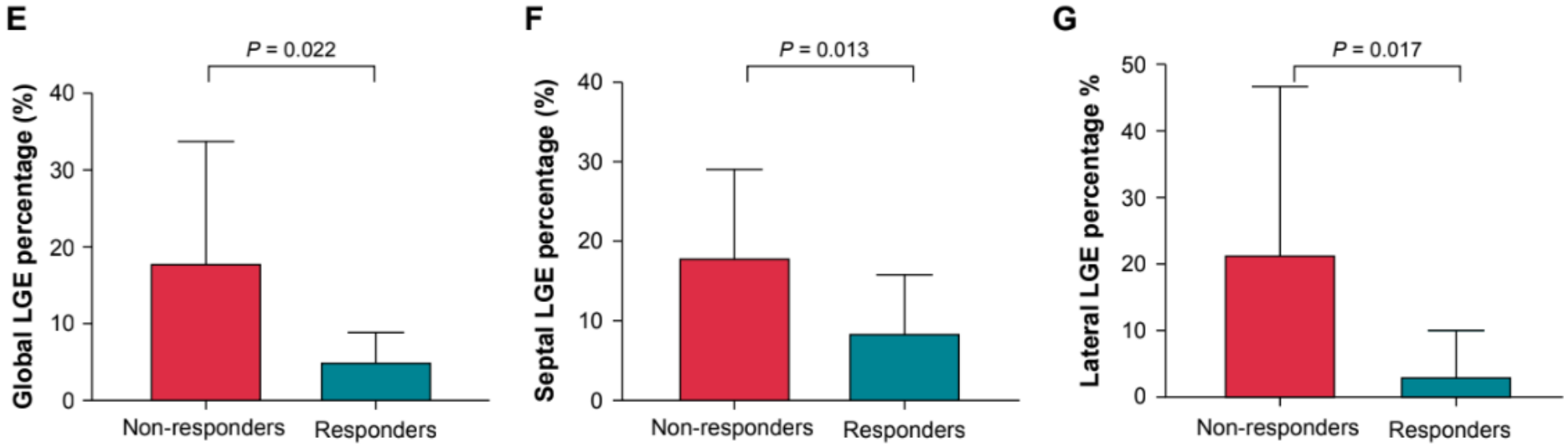




- LGE (scar) in the LBB pacing area is a negative predictor of successful LBBAP because this is where the conduction system pacing leads are placed

Vijayaraman et al., Circulation. 2024 Jan 30;149(5):379-390

LGE Predicts Response to LBBAP

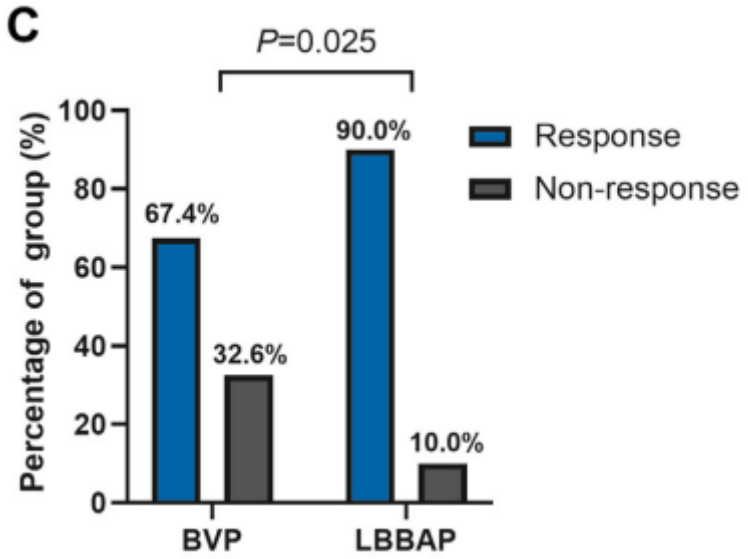


- Global, septal, and lateral scar percentage all predicted echocardiographic response with areas under the curve (AUCs) of 0.857, 0.864, and 0.822, respectively
- CMR LGE was superior to QRS morphology criteria for response (Strauss left bundle branch abnormality, AUC = 0.696)

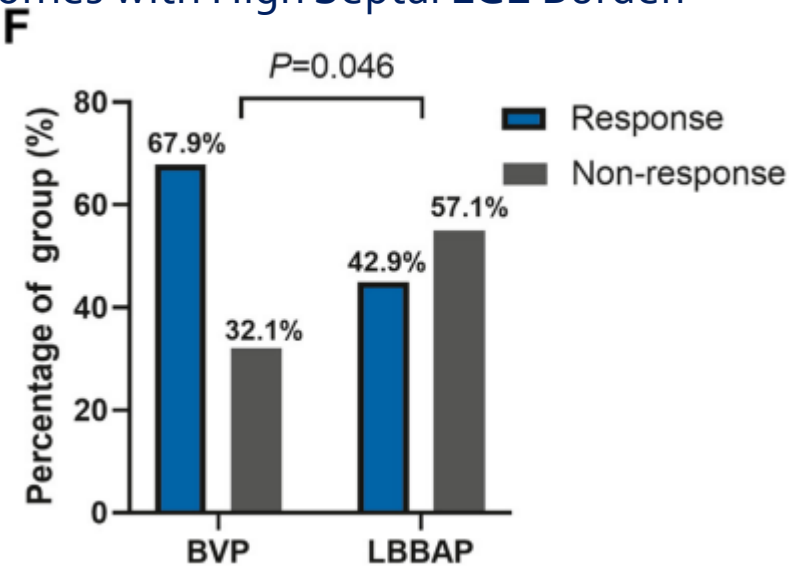
Chen et al., Europace. 2023;25(11):euad326

LGE can Personalize LBBAP/BIVP in NICM

Outcomes with Low Septal LGE Burden



Outcomes with High Septal LGE Burden



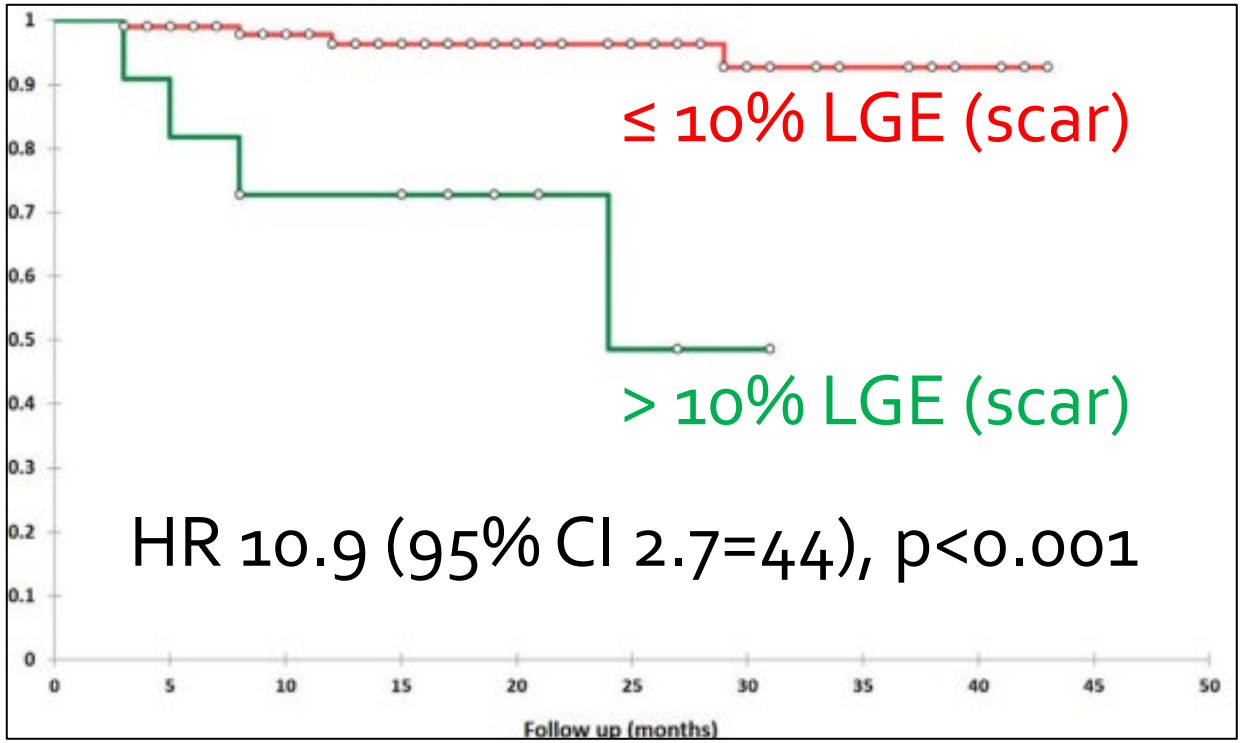
- Remodeling response to LBBAP and BVP among nonischemic cardiomyopathy patients is modified by septal scar burden
- Worse prognosis with high septal scar burden

Chen et al, *J Am Coll Cardiol EP*. 2024 Jul, 10 (7_Part_1) 1439–1451

MADURAI LBBP Study

- Patients with LB-NICM, LVEF 35%, and HF were prospectively enrolled from 2019 to 2022
- If CMR LGE ≤ 10% by CMR, they were assigned LBBAP only (group I)
- If CMR LGE > 10%, they were assigned to receive LBBAP + ICD (group II)
- The CMR-guided approach to identify the need for an ICD with LBBAP is safe and feasible in
- There is potential to reduce health care costs and benefits for patients

Death, HF Hosp, or VT/VF

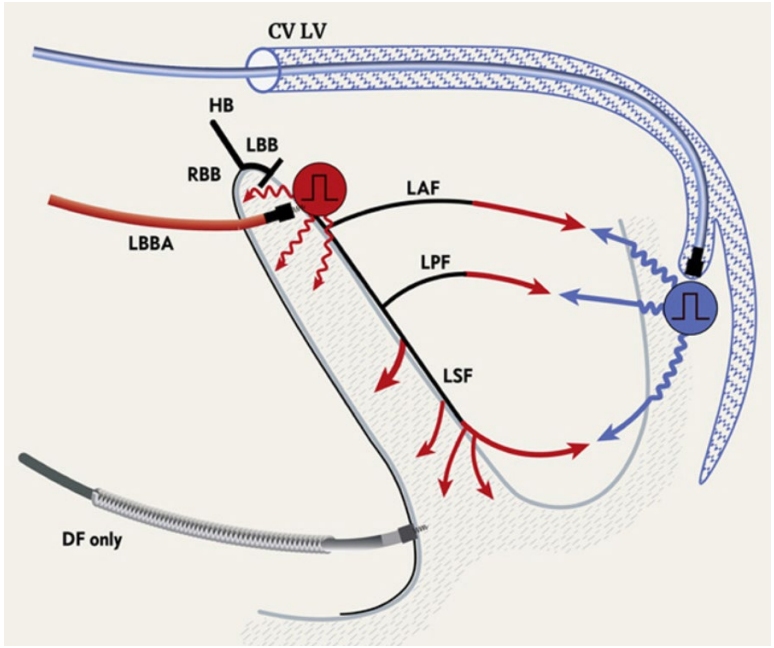


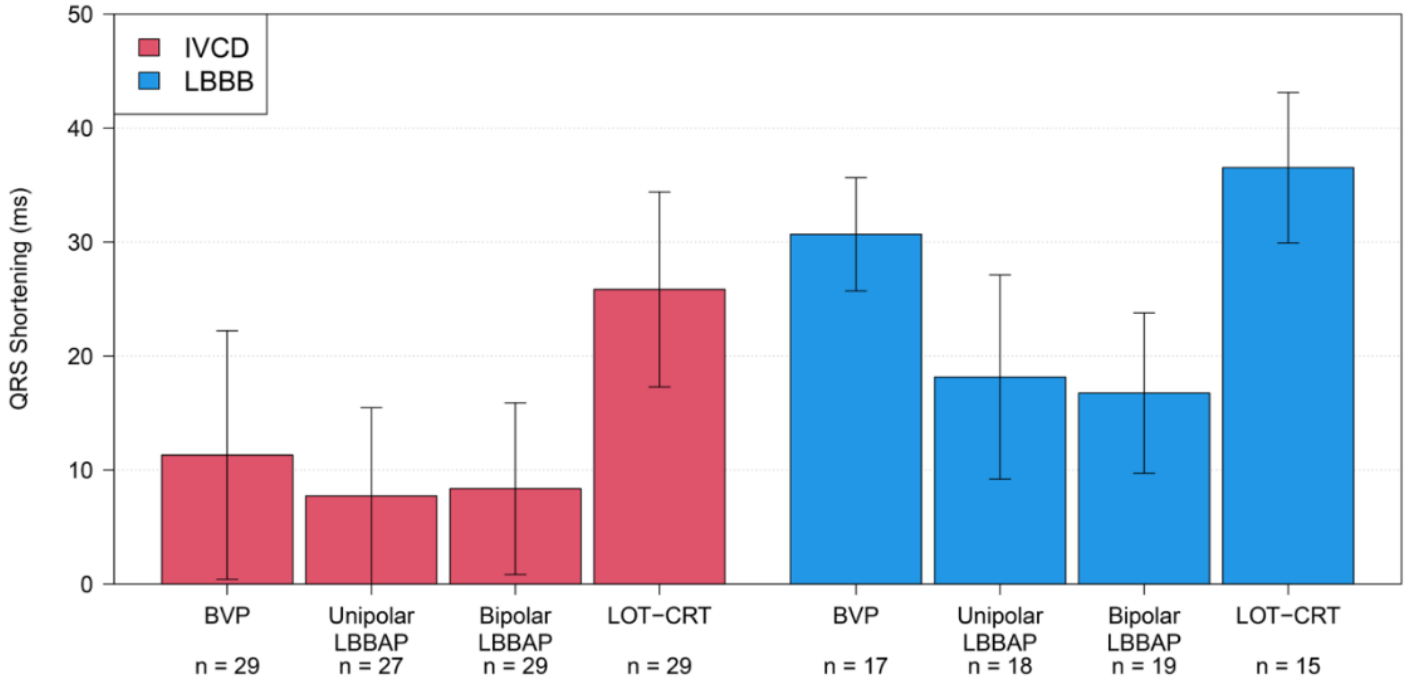
Ponnusamy, Heart Rhythm 2023

Left Versus Left Randomized Clinical Trial

- This PCORI-funded trial evaluates the effects of His or left bundle branch pacing (LBBP) comparative to biventricular pacing on quality of life, exercise capacity, hospitalization for heart failure, and mortality in patients with heart failure and conduction system disease
- Inclusion Criteria:
  - Men and women 18 years of age or older.
  - A LVEF ≤ 50% within 6 months prior to enrollment.
  - Resting QRS duration ≥ 130 ms on ECG.
  - Anticipated right ventricular pacing > 40% OR Device in place with right ventricular pacing > 40%.
  - Optimized on heart failure guideline directed medical therapy.
- Planned enrollment is 2,136 patients at 65 centers in the US and Canada
- Substudy with AI-ECG and AI-CMR promises to lead to informative analyses with respect to personalization of therapy

Left-Bundle Optimized CRT (LOT-CRT)

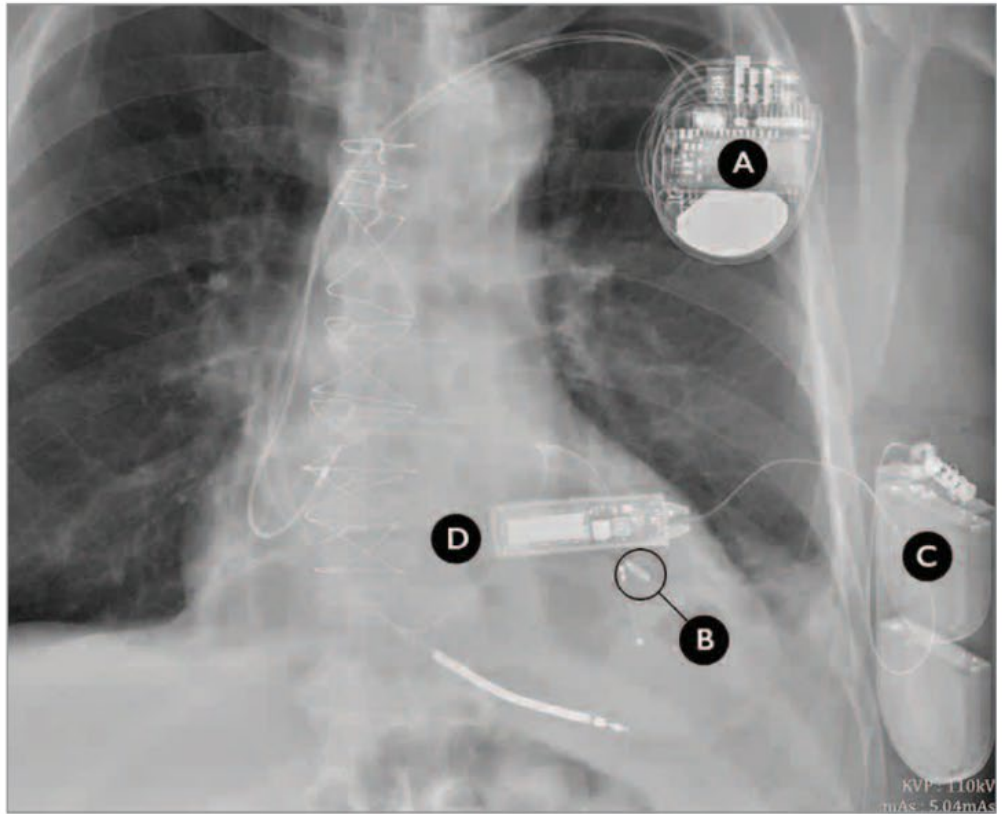


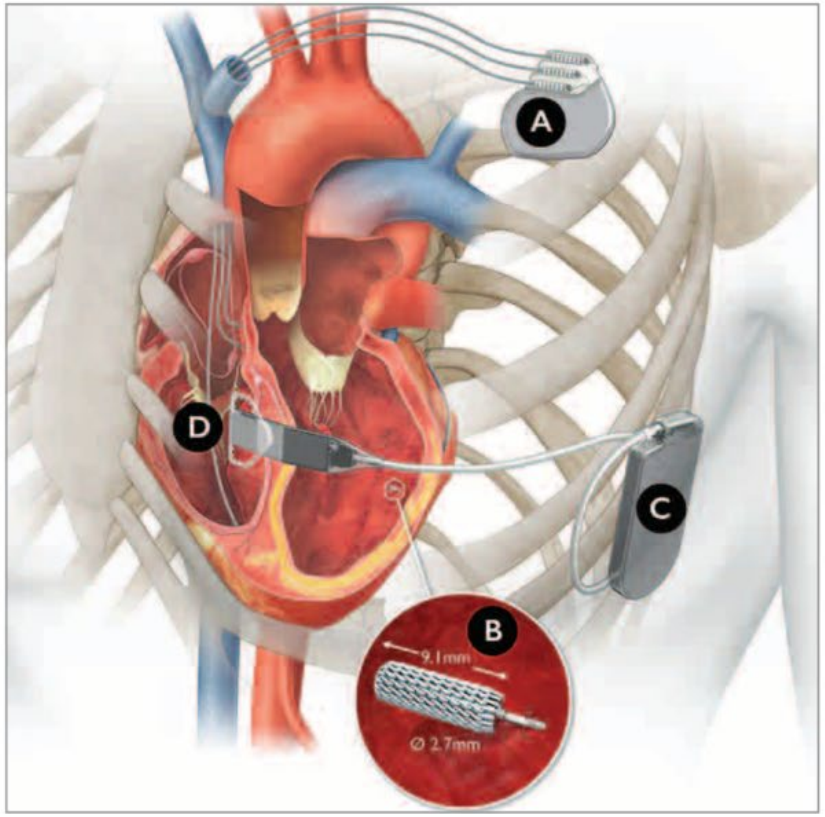


- Patients with IVCD may do better with the combination of LV pacing from the coronary sinus and also LBBAP (opportunity for personalization)
- CSPOT Study: Participants with a wider QRS or deep septal pacing are more likely to benefit from the addition of a left ventricular coronary vein lead to LBBAP

Circ Arrhythm Electrophysiol. 2024;17:e013059. DOI: 10.1161/CIRCEP.124.013059

WISE-CRT Leadless LV Pacing (SOLVE-CRT)

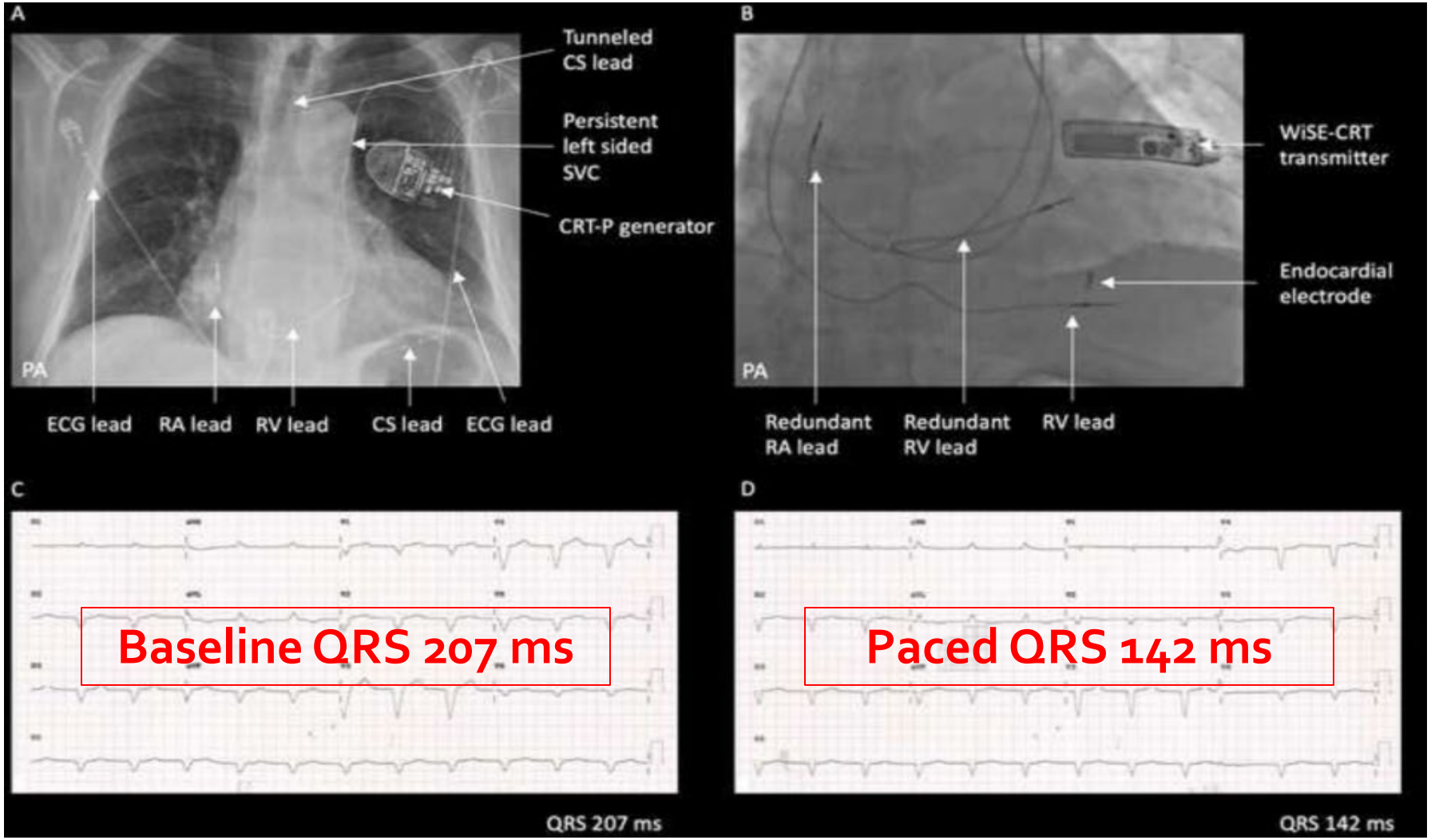




- SOLVE-CRT: Primary efficacy end point was met with 16.4% (95% CI, −21.0% to −11.7%) reduction in mean LVESV (P = .003), and the primary safety endpoint was also met
- FDA approved in February 2025; commercial implants are expected next quarter

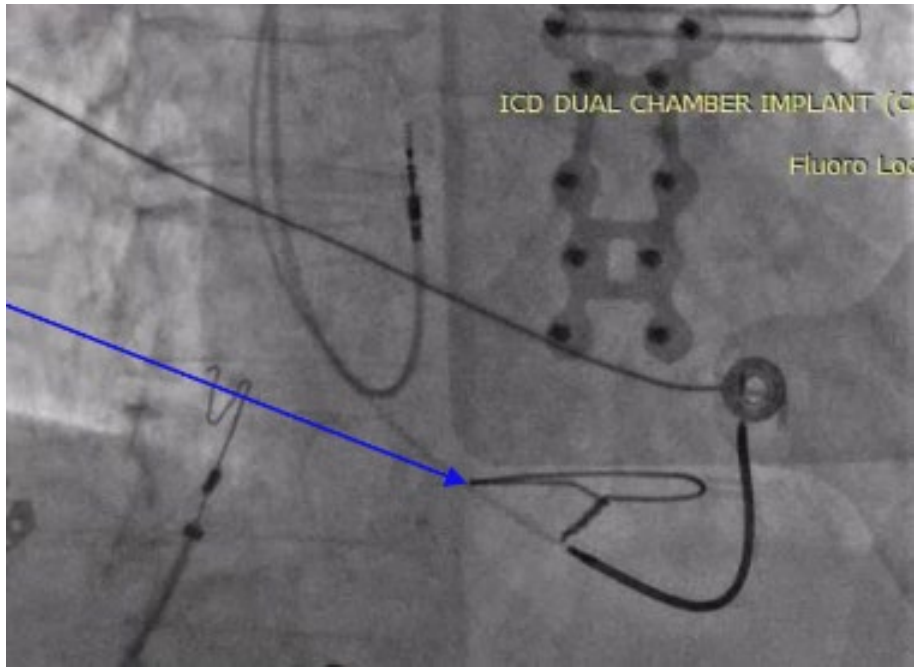
JAMA Cardiol. 2024;9(10):871-879. doi:10.1001/jamacardio.2024.2050

Leadless LBBAP with Wise CRT



Elliott, Rinaldi, et al. European Heart Journal - Case Reports (2021) 5(11), 1–7

LEADR-LBBAP (a "two-lead" LBBAP ICD solution)

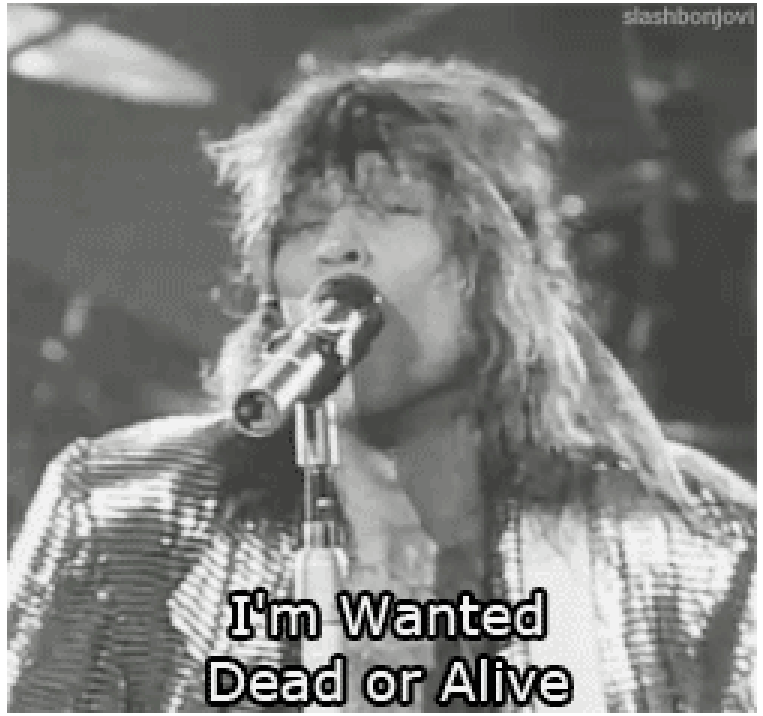


- Medtronic 093000 lead has a small diameter than standard ICD leads and can be used to accomplish LBBAP as an alternative to the 3830 LBBAP pacing lead
- In HF patients who need LBBAP and defibrillation, a two-lead system is possible as opposed to a standard three-lead system (RA pacing, RV high-voltage, LBBAP)

Conclusions – Personalization for ICDs and Cardiac Physiologic Pacing

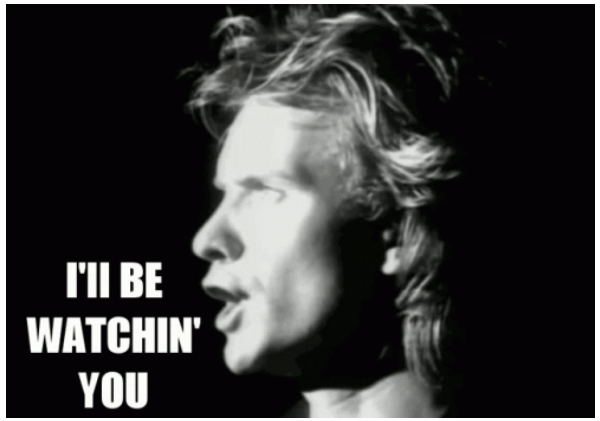
- Clinical scores weigh the risk of ventricular arrhythmia (VA) with the risk of non-arrhythmic death
- CMR LGE > 10% is associated with more VA and potentially greater ICD benefit, particular in NICM
- Cardiac dyssynchrony/strain from CMR using deep neural networks and LGE predict benefit from cardiac physiologic pacing and VA risk
- New lead technologies and configurations give us more options for cardiac physiologic pacing

Ready for Part Two?
Which image best describes how you are feeling about the content so far?



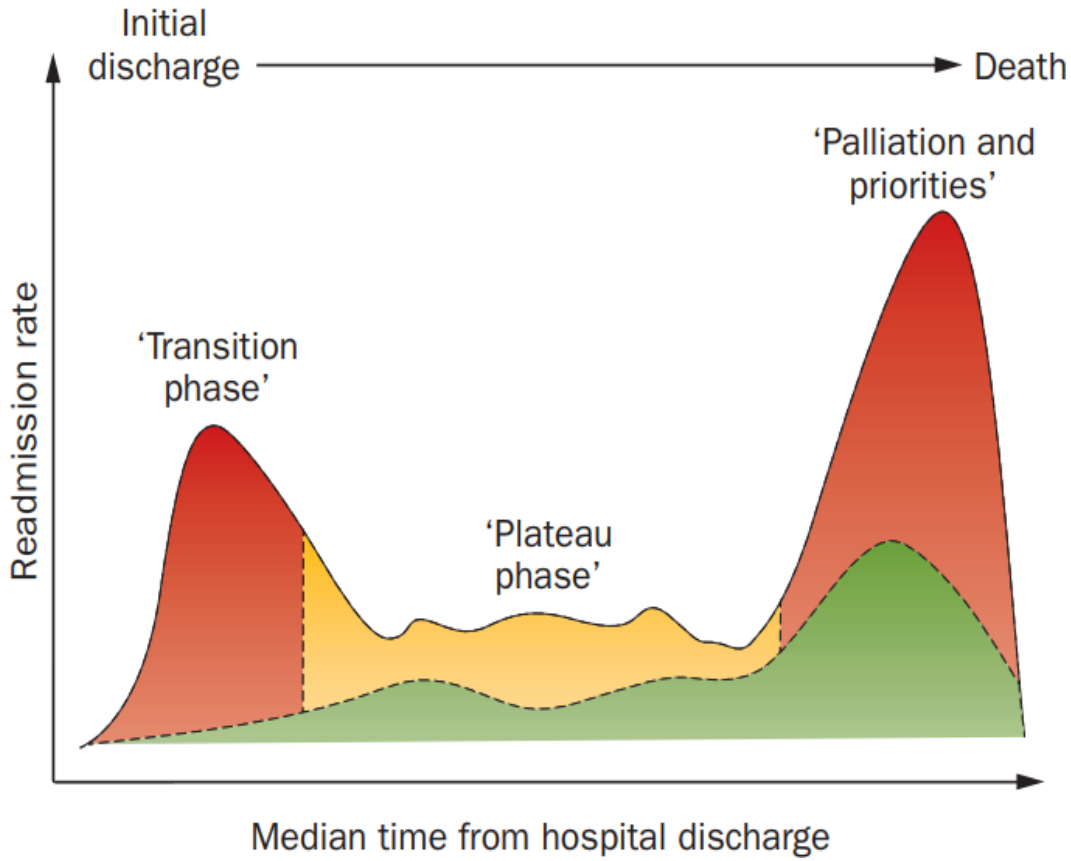
ICDS FOR REMOTE MONITORING OF CONGESTION AND ARRHYTHMIAS IN HF

PART TWO



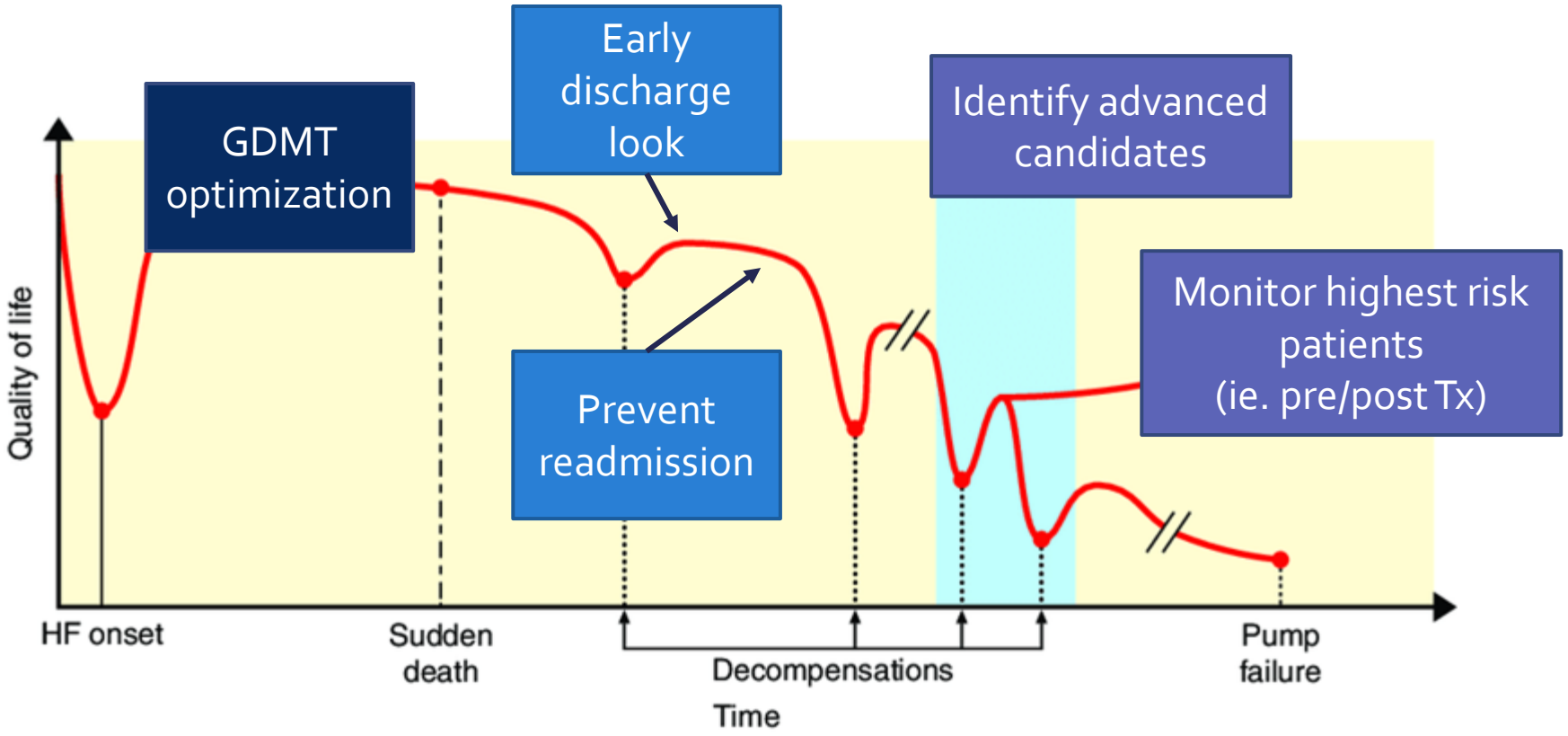
Why Do HF Hospitalizations Matter?

- HFH is associated a poor outcome
- Most expensive single diagnosis in US healthcare ($40-60 billion/year)
  - HFH account for half of costs
- Many re-admissions are "preventable"
  - 9/10 patients with HFH are "warm and wet"



What are the Goals of Remote Monitoring?

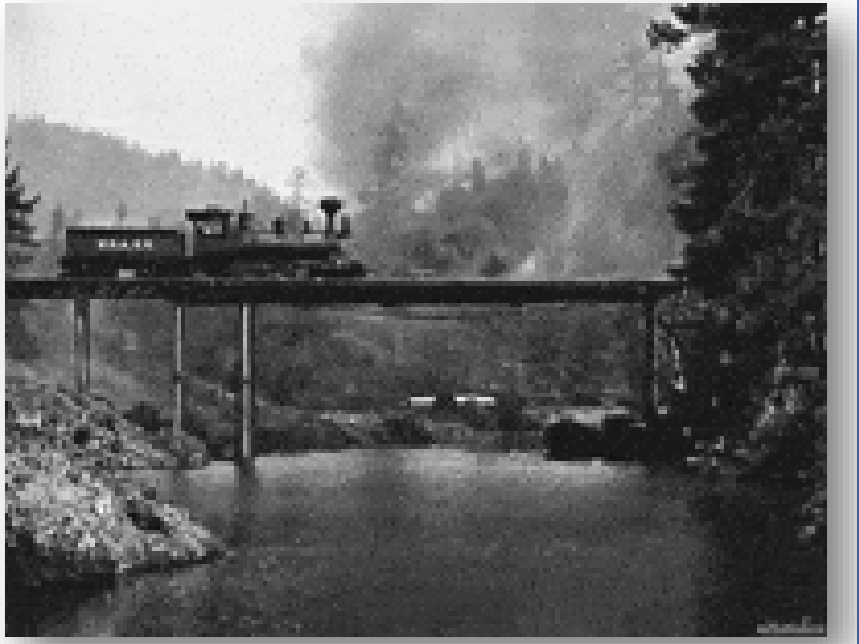
Prevention?



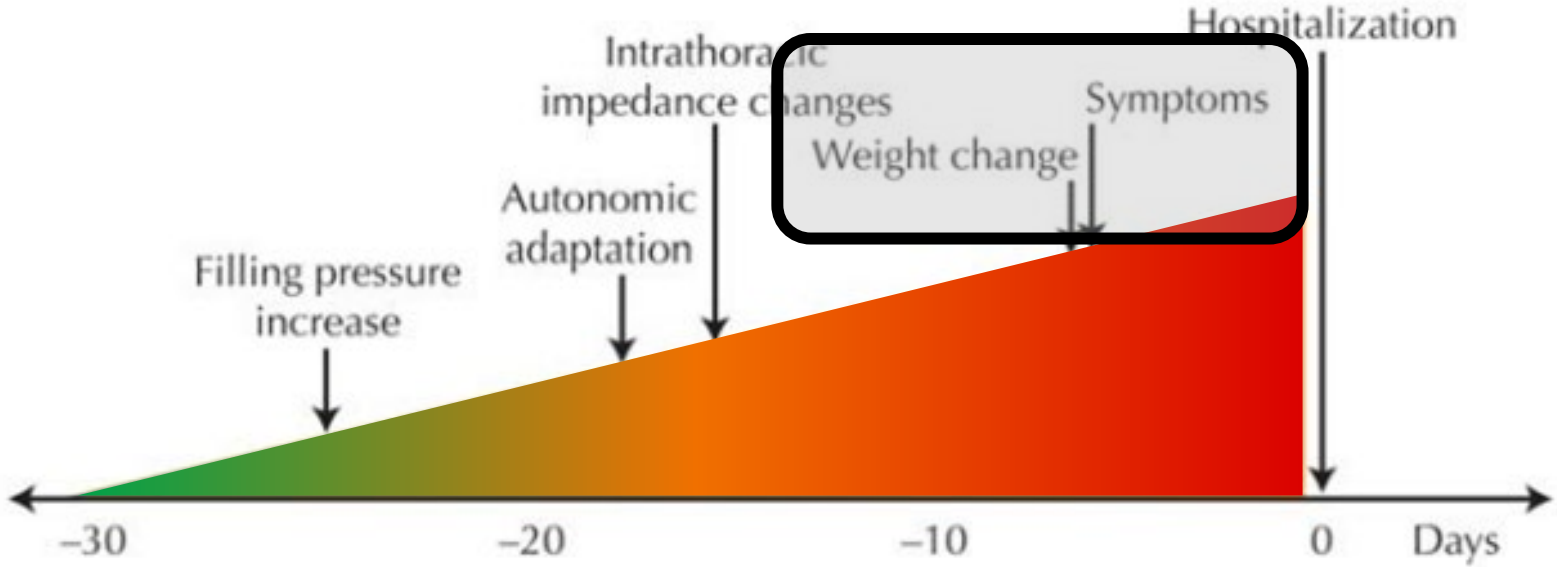
Klein et. Al. Arch Card Dis 2024

Characteristics of Good Remote Monitoring Tools: Change the Course of the Train Before the Crash

- **Sensitive:** Recognize HF physiologic changes
- **Specific:** Avoid false positives
- **Timely:** Enough lead time for intervention
- **Multi-parameter:** Reflect complexity of HF
- **Easy to interpret:** Allows wide implementation
- **Actionable:** Available therapy to respond to signal



Traditional Telemonitoring Does Not Reduce HFH



Trial	Impact on Heart Failure Hospitalization
TELE-HF 2010	No Benefit
BEAT-HF 2016	No Benefit (small increase in QOL)
TIM-HF I 2010	No Benefit
TIM-HF II 2018	Small mortality benefit with 24/7 emergency phone access

Adapted from Curr HF Rep 2009

Implantable Hemodynamic Sensors: Effective But Also Invasive and Expensive

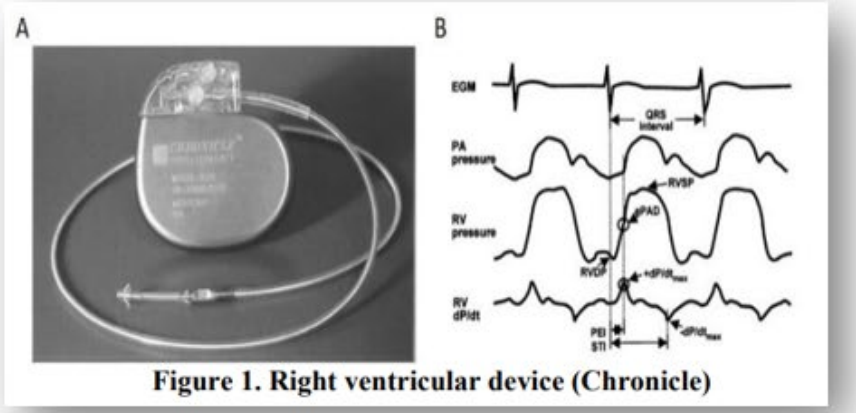


Figure 1. Right ventricular device (Chronicle)

RV Pressure Sensors
(COMPASS-HF)

LA Pressure Sensors
(LAPTOP, V-LAP)

PA Pressure Sensors
(CHAMPION)

UVA Health

Pressure-guided Management Reduces HFH in CHAMPION Trial

1° Outcome: HFH

2° Outcome: Mortality + HFH

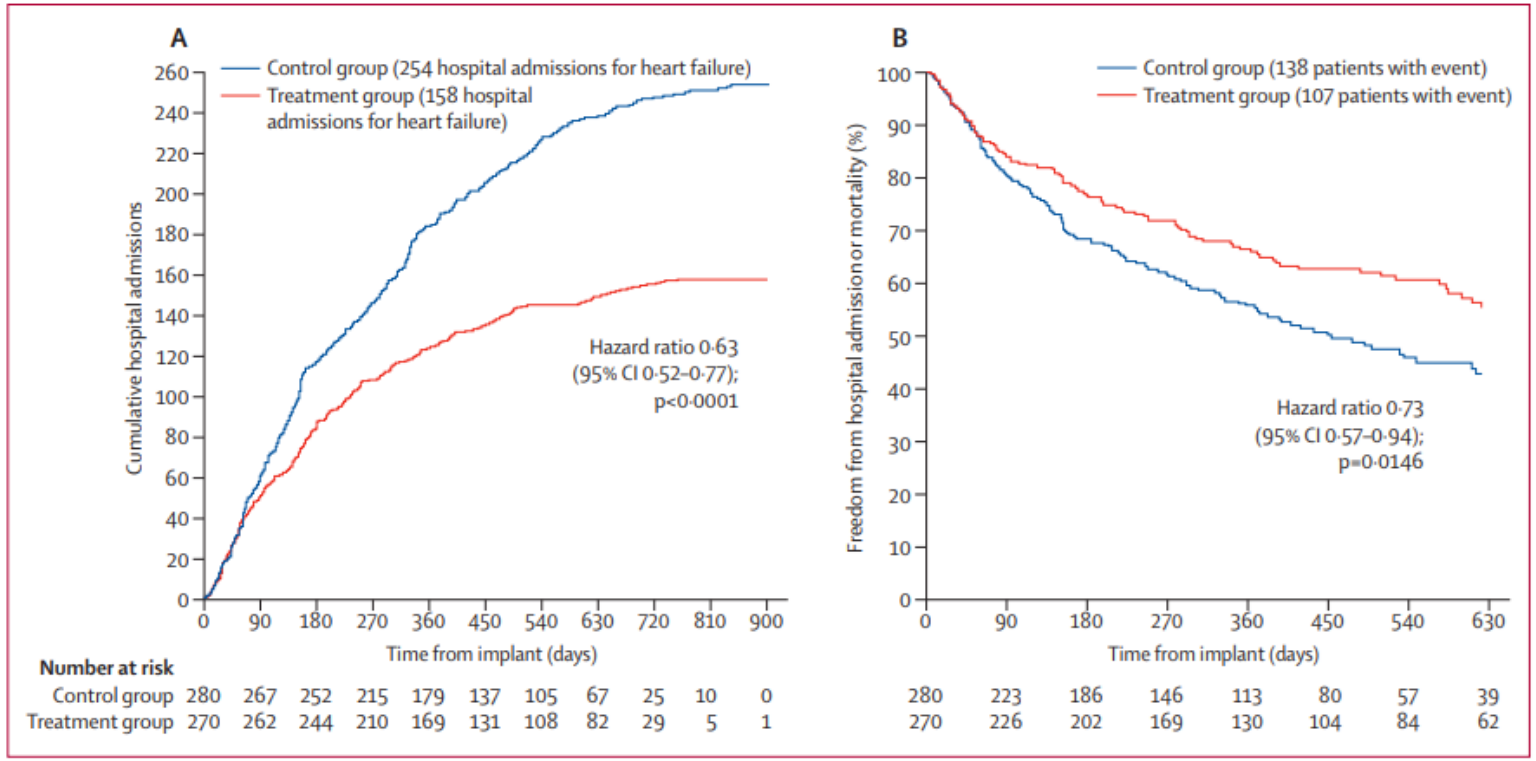
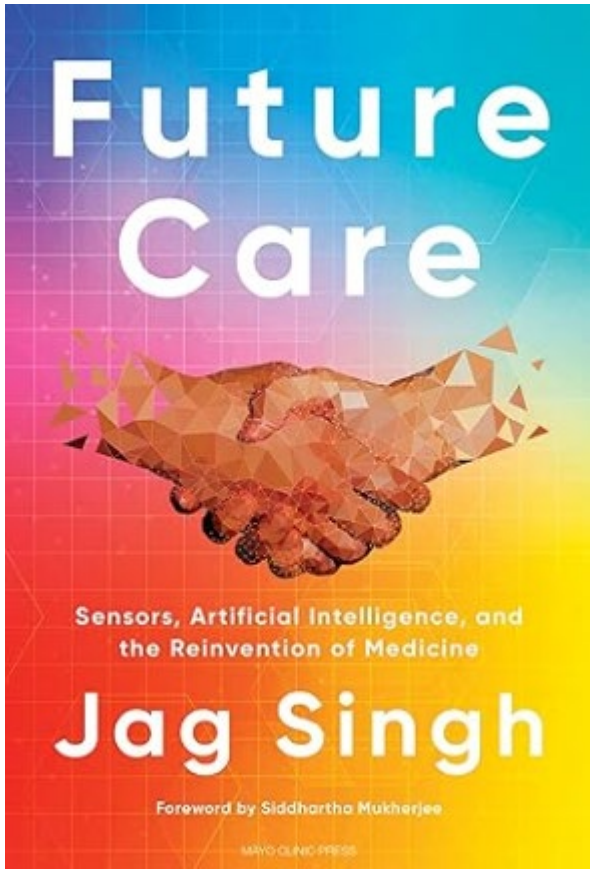


***Figure 3*: Cumulative heart-failure-related hospitalisations during entire period of randomised single-blind follow-up (A), and freedom from first heart-failure-related hospitalisation or mortality during the entire period of randomised follow-up (B)**

Abraham Lancet 2011

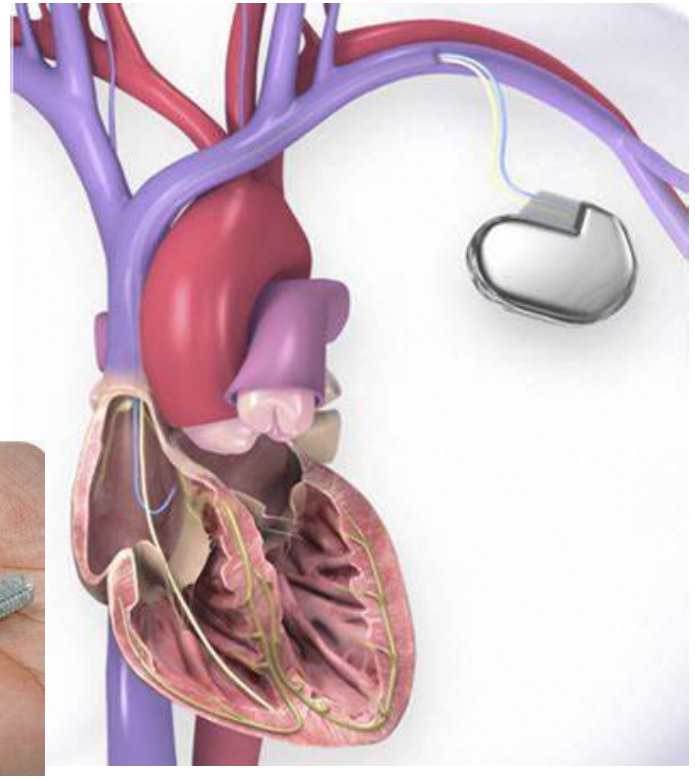
Future Care: Sensors, Artificial Intelligence, and the Reinvention of Medicine

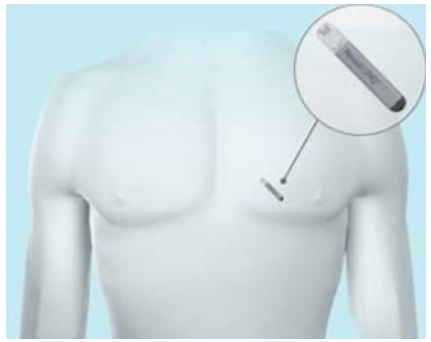


Future care if heart failure will likely be based on the following foundations:

- Virtual
- Sensor-aided
- Powered by AI
- Sustainable workflows
- Improves clinical outcomes

Wearable and Implantable Sensors for Atrial Arrhythmias and Association with HF Episodes

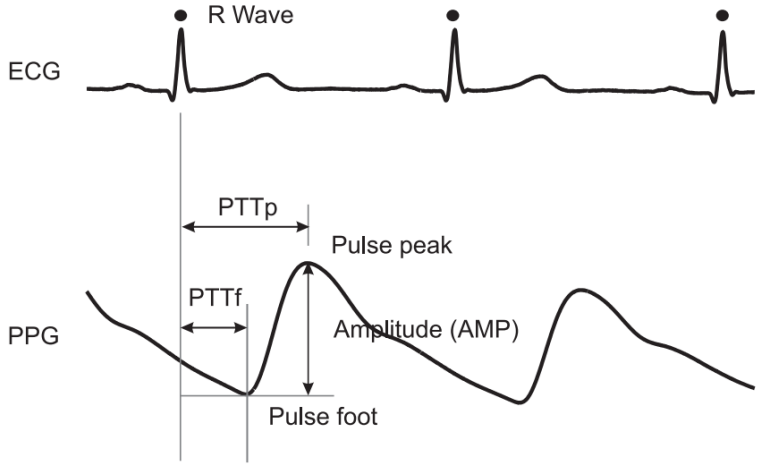


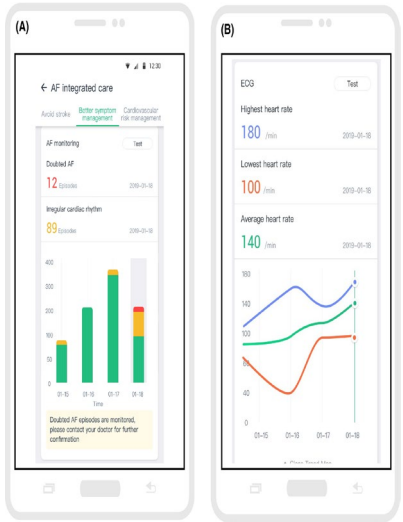


- There is great interest in the use of both wearable and implantable devices for AF detection
- We will discuss the connection between atrial arrhythmias and HF events

Wearables Use Photoplethysmography (PPG)

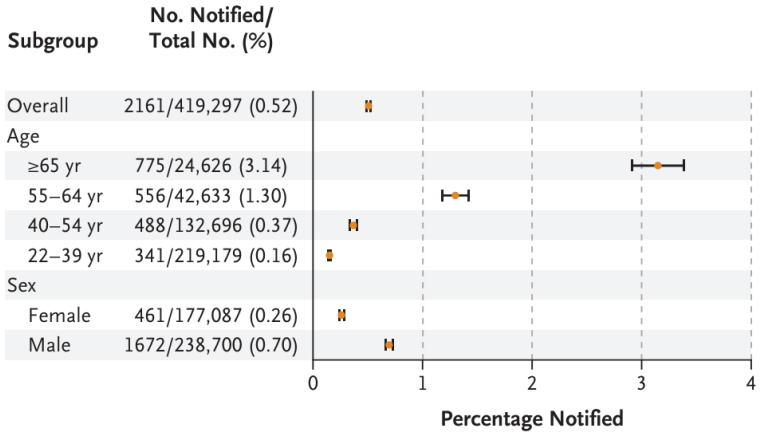
- PPG detects blood volume changes in the microvascular bed of tissue based on measurements at the skin surface
- The waveform comprises a pulsatile physiological waveform attributed to cardiac synchronous changes in the blood volume with each heartbeat
- The desired heartbeat signal is superimposed on a slowly varying DC baseline with various lower frequency components attributed to respiration, sympathetic nervous system activity, and thermoregulation

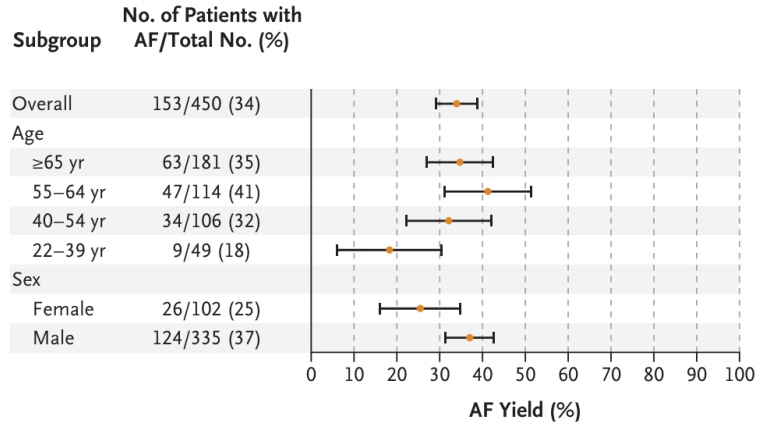




Apple Heart Study: Model for Population AF Screening with Wearable Devices

- 419,297 participants recruited over 8 months
- Over a median of 117 days, 2161 participants (0.52%) received notifications of an irregular pulse
- Among participants who received notifications, 34% had atrial fibrillation on subsequent ECG patch readings
- There were limitations that could be potentially improved with AI

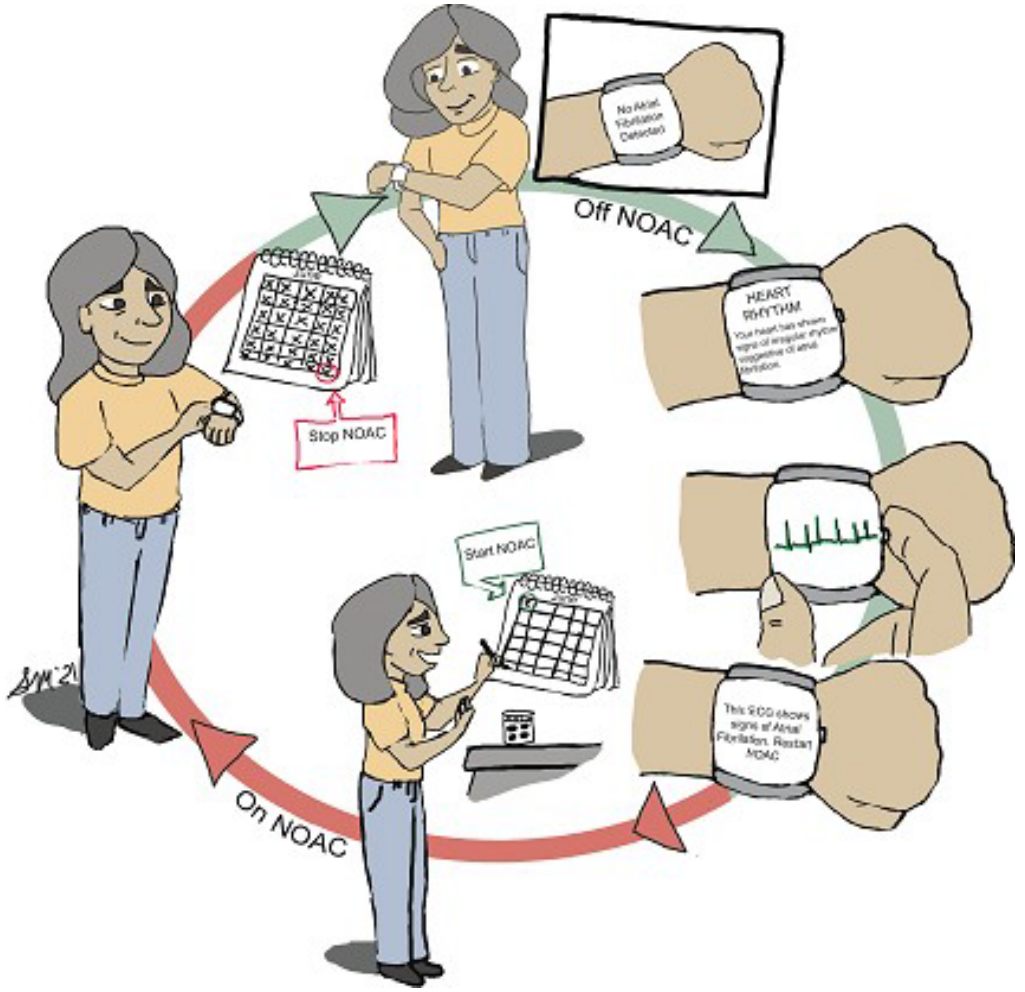




Perez MV et al. Apple Heart Study Investigators. Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation. N Engl J Med. 2019 Nov 14;381(20):1909-1917

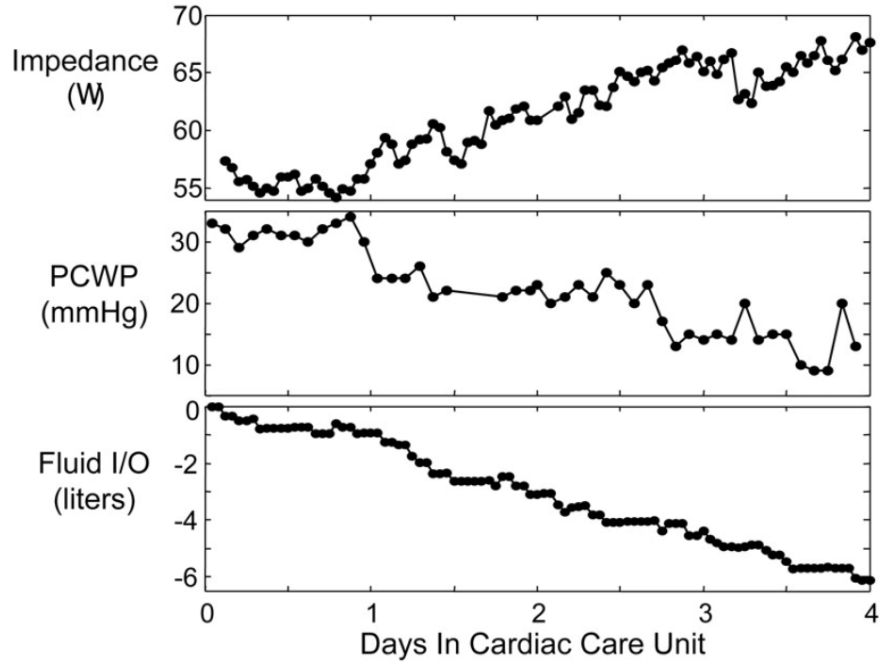
Sequel to Apple Heart Study – REACT-AF

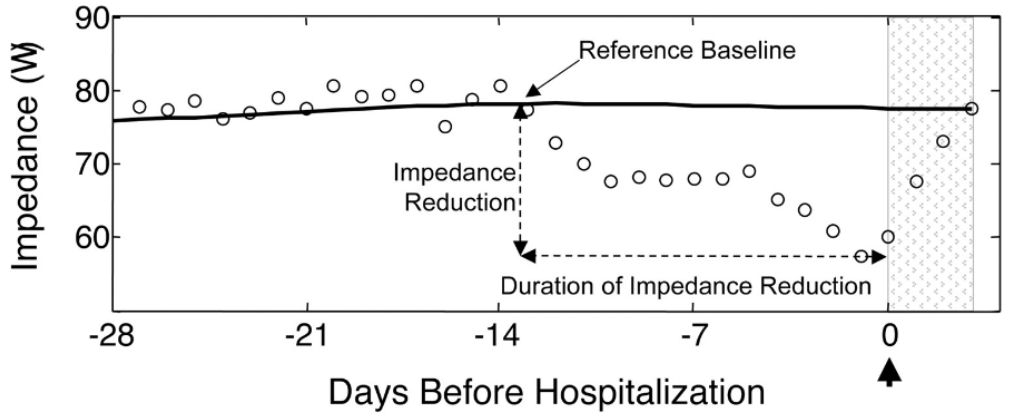
- *R*HYTHM *E*VALUATION FOR *A*NTI*C*OAGULATION *T*HERAPY FOR *A*TRIAL *F*IBRILLATION
- Focus on guiding anticoagulation decisions rather than population screening
- How can we reduce morbidity from unnecessary anticoagulation?
- Which catheter ablation patients can stop their anticoagulants post-procedure?



Intrathoracic Impedance: Core of HF Monitoring

- Intrathoracic impedance:
  - declines with increased ventricular volumes and pressures
  - is inversely correlated with PCWP, fluid balance and NT-pro BNP
  - precedes patient's symptoms and heart failure hospitalizations by two weeks
  - decreases as fluid retention increase

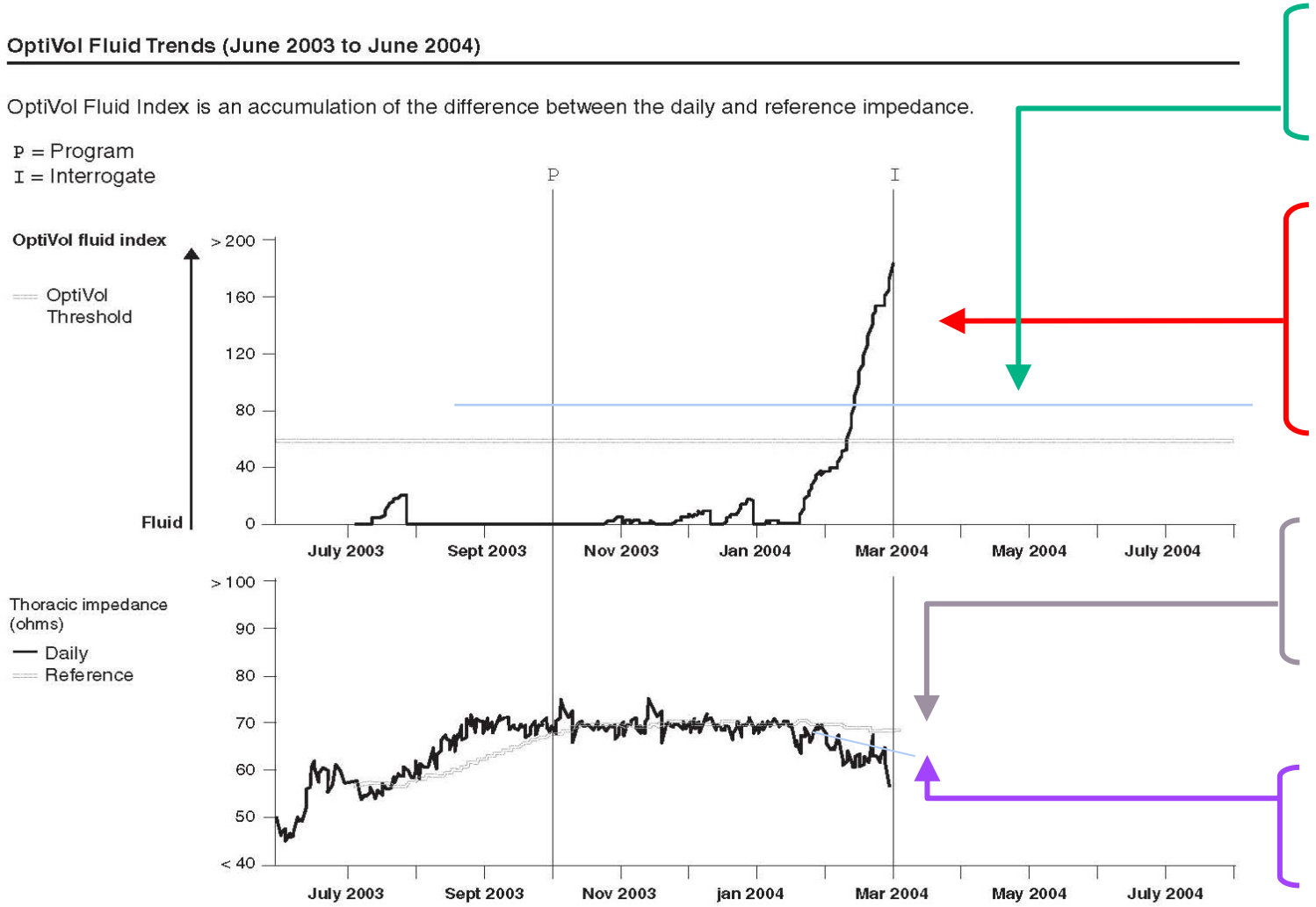




Yu CM, et al. *Circulation*. 2005;112:841-848
Wang L, et al. *Pacing Clin Electrophysiol.* 2005;28:404-411.
Lüthje L, et al. *Eur J Heart Fail*. 2007;9:716-722.

How the OptiVol and the Fluid Index Work

- Patients with fluid crossings are twice as likely to have a heart failure adverse event.
- Frequent or sustained events identified patients at risk for acute decompensated heart failure hospitalizations.



Observation Threshold

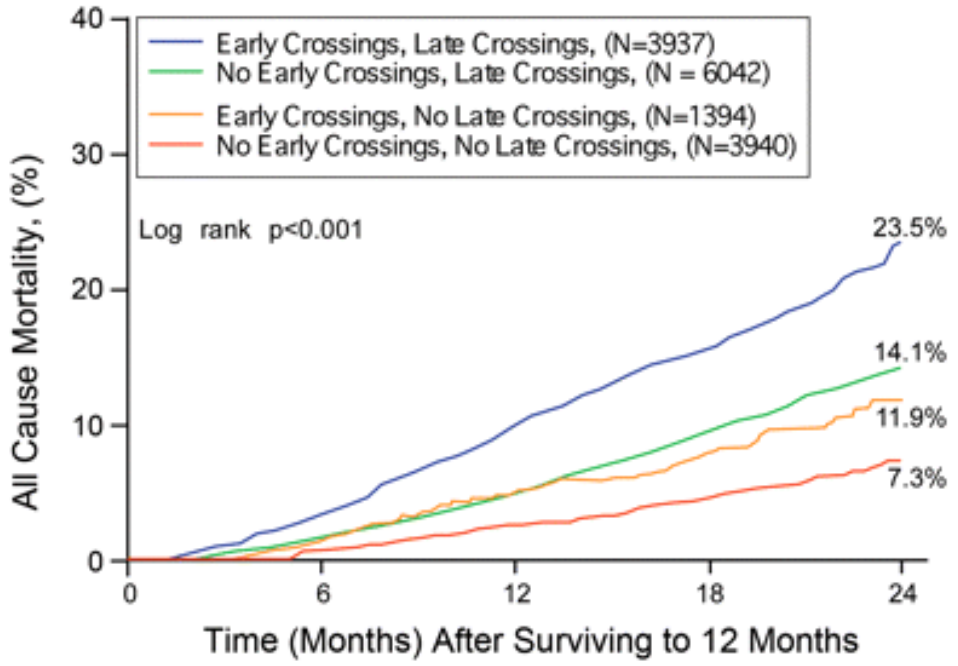
Accumulation of the difference between the daily and reference impedance

Reference impedance slowly adapts to daily impedance

Daily impedance is the average of each day's measurements

Early and Late OptiVol Fluid Crossings Predict Mortality

- **Weight monitoring, 6-MHW, BNP marker**
  - OptiVol detects 3 times more heart failure events than weight monitoring alone
  - OptiVol Fluid Index increases are associated with worsening 6-MHW and BNP
- **Heart failure readmissions**
  - Device-derived heart failure diagnostic criteria identified patients at significantly higher risk of a heart failure event within 30 days post discharge
- **Mortality risk**
  - Patients who experienced threshold crossings within the initial 6 months of remote monitoring had a 2.15-fold increased long-term mortality risk (Figure)



No. at Risk					
Early Crossings, Late Crossings	3937	2698	1548	826	248
No Early Crossings, Late Crossings	6042	4320	2621	1438	468
Early Crossings, No Late Crossings	1394	1005	618	340	105
No Early Crossings, No Late Crossings	3940	2823	1866	1019	349

Whellan DJ, et al. *J Am Coll Cardiol*. 2010;55:1803-1810.
Small RS, et al. *J Card Fail*. 2009;15:475-481.
Abraham WT, et al. *Congest Heart Fail*. 2011;17:51-55.
Gulati SK, et al. *J Card Fail.* 2010;16(suppl):S65.
Tang WH, et al. *Eur Heart J.* 2012;33:2189-2196.

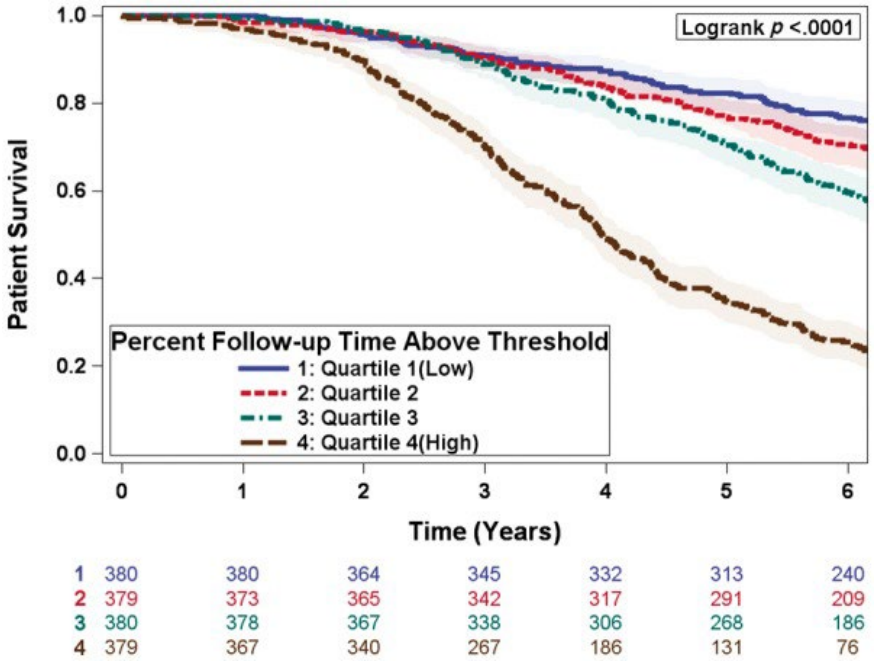
OptiVol and Arrhythmias

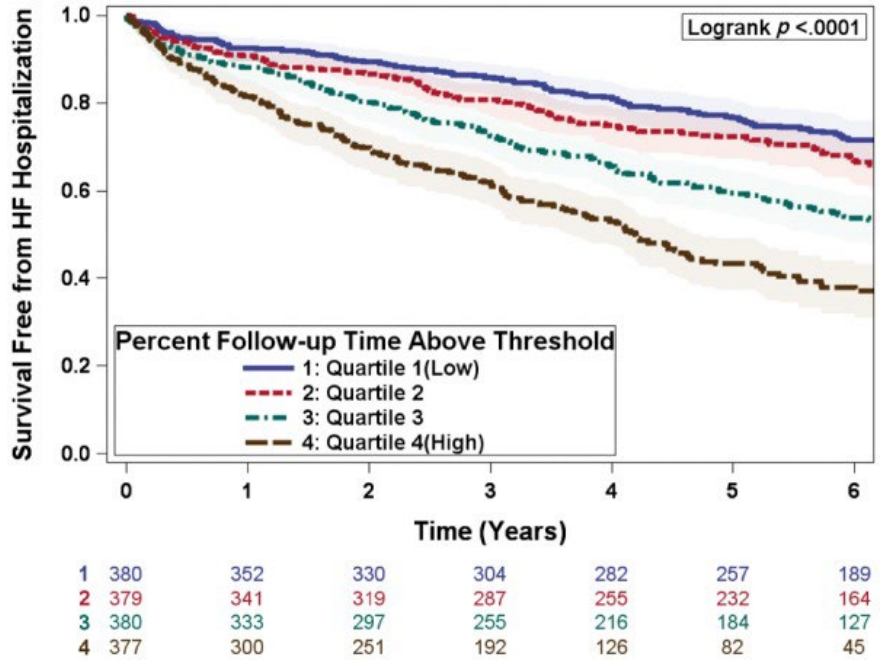
- Intrathoracic impedance changes can precede VT/VF episodes
- Decreases in intrathoracic impedance can precede storms of VT
- AT episodes preceded (43%) or occurred almost simultaneously (22%) with the threshold crossing in greater than half the patients

Moore HJ, et al. *Pacing Clin Electrophysiol*. 2010 33:960-966.
Andriulli J, et al. *Int J Cardiol*. 2008;123:333-334.
Jhanjee R, et al. *Circ Arrhythm Electrophysiol*. 2009;2:488-494.

UVA/UMN/Medtronic Study Integrating National ICD Registry and Medicare Claims Data: OptiVol Fluid Crossings Predict All-Cause Mortality and Survival Free of HFH in CRT

This cohort (N=1565) had OptiVol®-enabled cardiac resynchronization therapy defibrillators (CRT-D) devices from the Implantable Cardioverter Defibrillator Registry with data linked to both Medicare claims/summary data and Medtronic's CareLink® Network data





Brown JR, Alonso A, Warman EN, Bilchick KC. Long-term impact of intrathoracic impedance findings on survival and heart failure hospitalizations after cardiac resynchronization therapy in ICD Registry patients. Europace. 2018 Jul 1;20(7):1138-1145. doi: 10.1093/europace/eux197. PMID: 29016777; PMCID: PMC6041970.

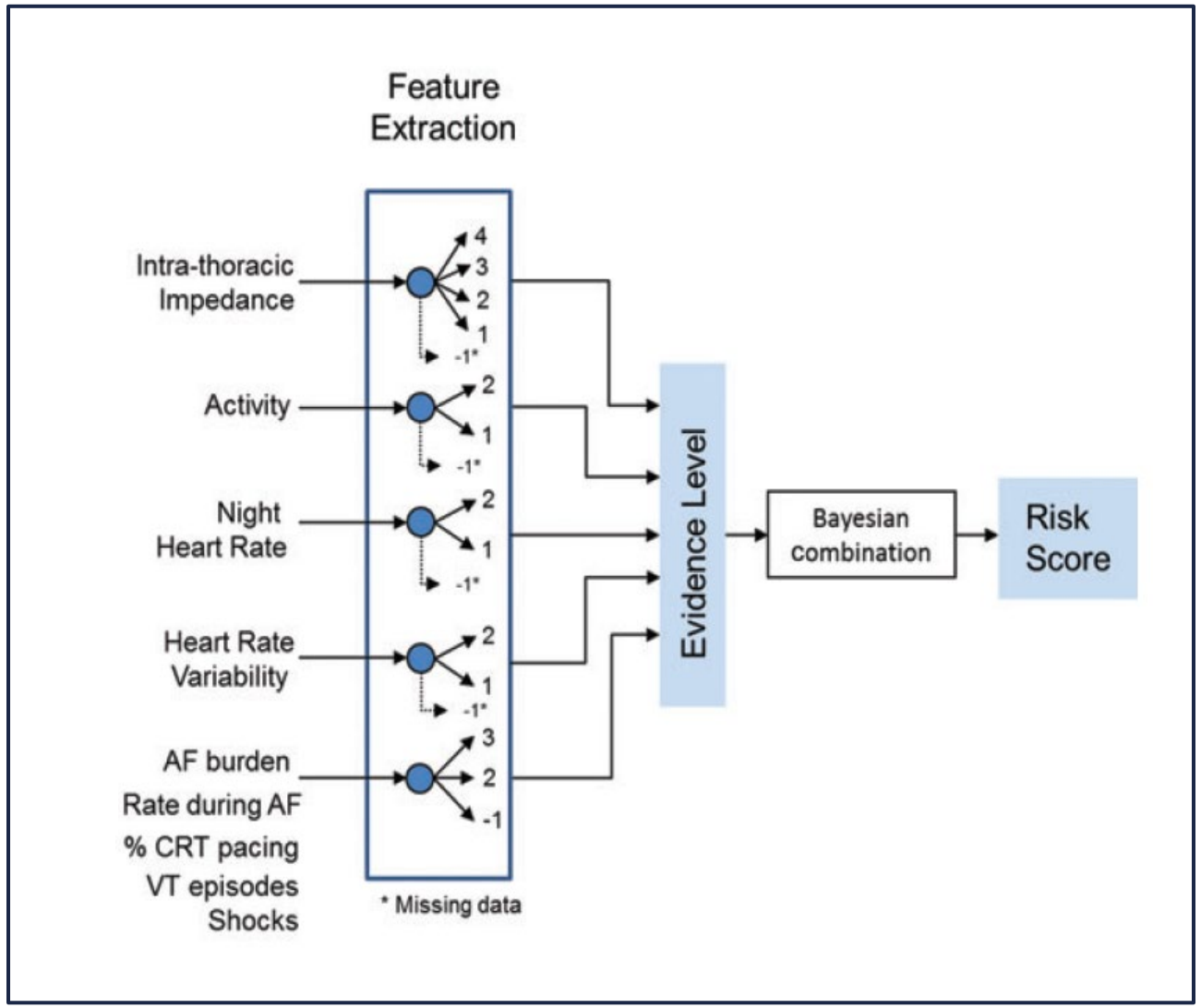
Triage HF – Multiparametric Approach with Impedance

TriageHF Utilizes Device-based Cardiac Compass Heart Failure Diagnostics trends:

- Fluid Status
- HR Variability
- AT/AF Burden
- HR During AF
- CRT % Pacing
- Night HR
- Activity
- VT/VF

Through Carelink, multivariate combination algorithm (TriageHF) determines a combined HF risk score that's translated to an overall patient risk status:

High | Medium | Low



TriageHF Digital Workflow

Cellular or Wi-Fi

MyCareLink Relay™ Home Communicator, MyCareLink Heart™ Mobile App, and MyCareLink™ Patient Monitor

Scheduled transmissions or CareAlert™ notifications automatically sent to clinic.

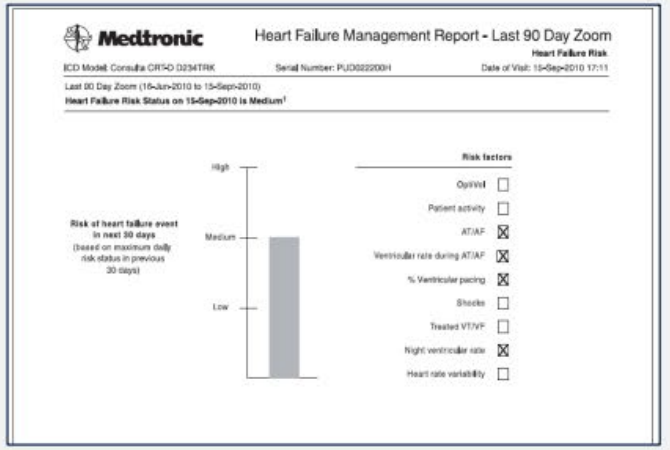
HF Risk	Status
	New
Medium	Viewed
High	New
Low	Viewed
Low	New
Medium	New
High	New

CareLink™ Network

Quickly sort high-, medium-, or low-risk heart failure patients.

or

Review **TriageHF notifications** for high-risk patients.

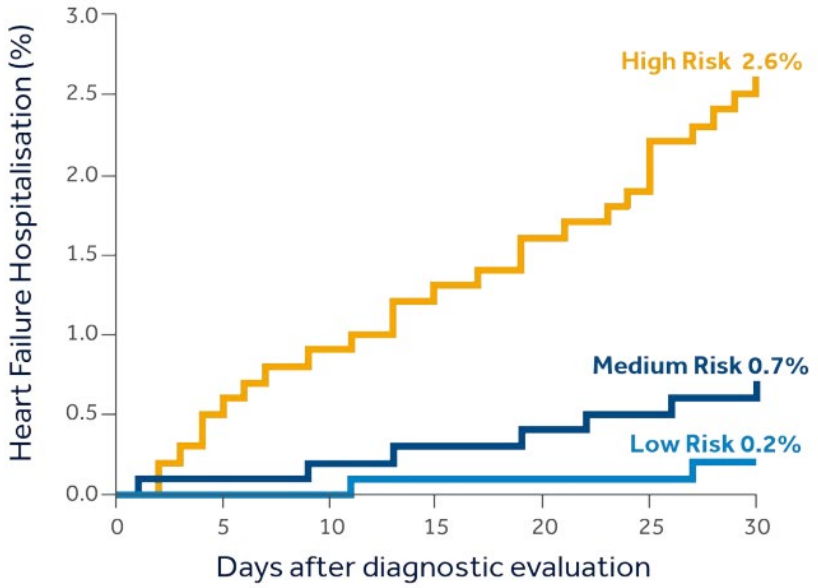


Review an **automated & simple** report displaying factors contributing to risk status.

Validation of TriageHF in RAFT Trial

- 1,224 patients (61% CRT, 39% ICD) with patients followed for 40 ± 20 months.
- Parent Study – RAFT: Multicenter, randomized, controlled study (RAFT) — NYHA Class II/III, LV systolic dysfunction, wide QRS
- End Points
  - Primary end point — death from any cause or hospitalization for HF.
  - Secondary end point — hospitalization for HF alone (> 24 hours of treatment for HF)
- Results
  - Low-risk months — HF hospitalizations were 0.21%
  - Medium-risk months — HF hospitalizations were 0.66%
  - Hhigh-risk months — HF hospitalizations were 2.61%

The risk of HF as determined by the algorithm correlated with HF hospitalizations and several HF signs and symptoms amongst patients in the (RAFT) trial.[1]



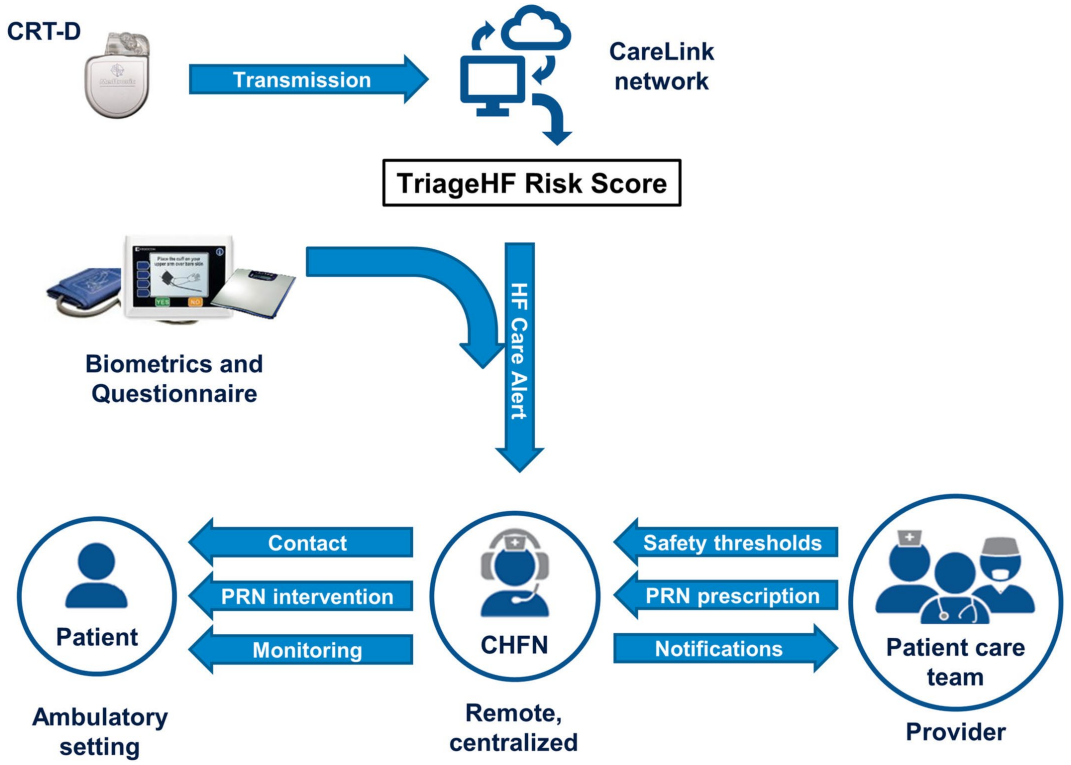
[1] Gula LJ, et al. *Heart Rhythm*. 2014;11:1626-1631.

Gula LJ, Wells GA, Yee R, Koehler J, Sarkar S, Sharma V, Skanes AC, Sapp JL, Redfearn DP, Manlucu J, Tang AS. A novel algorithm to assess risk of heart failure exacerbation using ICD diagnostics: validation from RAFT. Heart Rhythm. 2014 Sep;11(9):1626-31.

Physician-directed, nurse-implemented, ambulatory, medication TriageHF intervention strategy

- Certified HF nurses (CHFN) in the Medtronic Care Management Services Program implemented an ambulatory medication intervention strategy by following a standardized guided action pathway triggered by risk-based alert from Triage-HF
- When CHFN received notification of increased risk score (HF care alert), they implemented a 3 day course of diuretic up-titration (PRN) previously prescribed by a physician

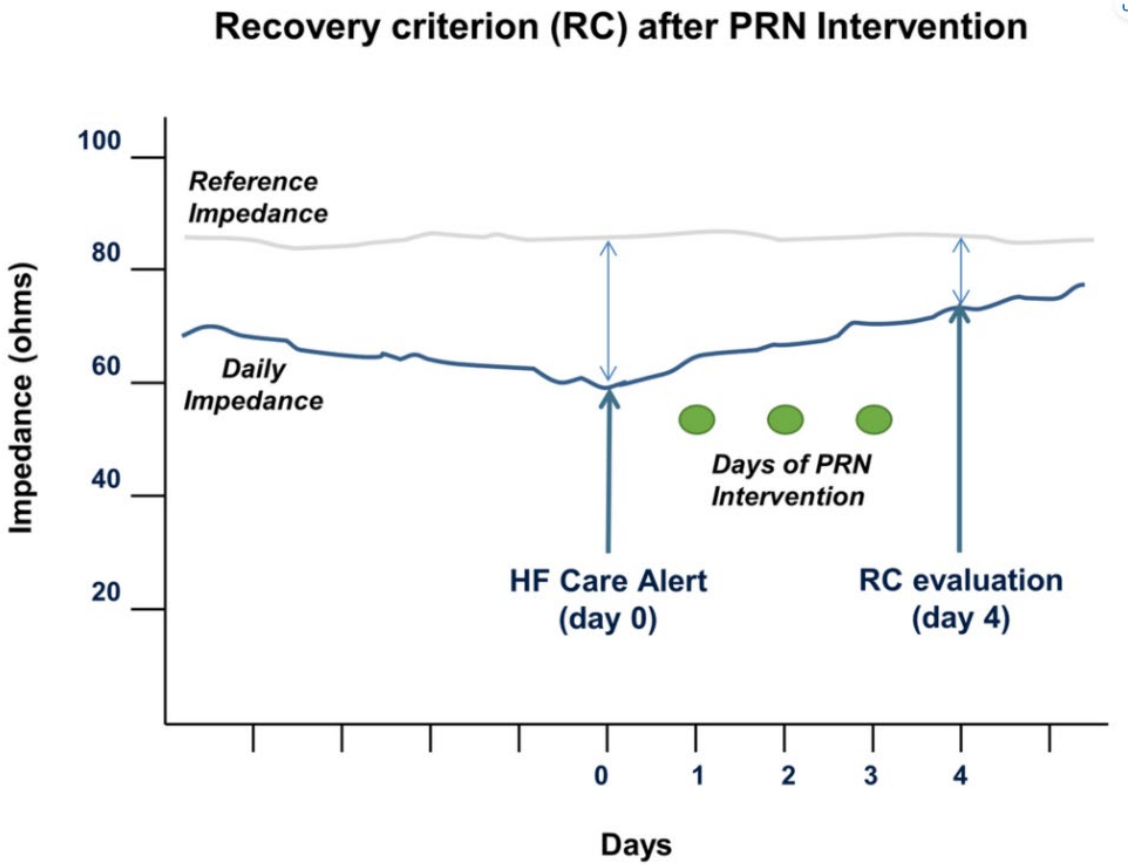
INTERVENE-HF Study based on TriageHF Risk Score



Zile MR, Costanzo MRR, Ippolito EM, Zhang Y, Stapleton R, Sadhu A, Jimenez J, Hobbs J, Sharma V, Warman EN, Streeter L, Butler J. INTERVENE-HF: feasibility study of individualized, risk stratification-based, medication intervention in patients with heart failure with reduced ejection fraction. ESC Heart Fail. 2021 Apr;8(2):849-860.

Impedance-Based Assessment of Recovery in INTERVENE-HF

- After completion of the first round of PRN medications (Day 4 post-initiation), CHFNs evaluated the efficacy of the PRN intervention based on impedance recovery to ≥70% of the baseline value
- If the intrathoracic impedance had recovered by Day 4, the PRN intervention was judged to be successful
- If the recovery was not successful by Day 4 and there were no contraindications (such as excessive weight loss or symptomatic hypotension), a second round of PRN medications was initiated, and the recovery criteria was re-evaluated on Day 8



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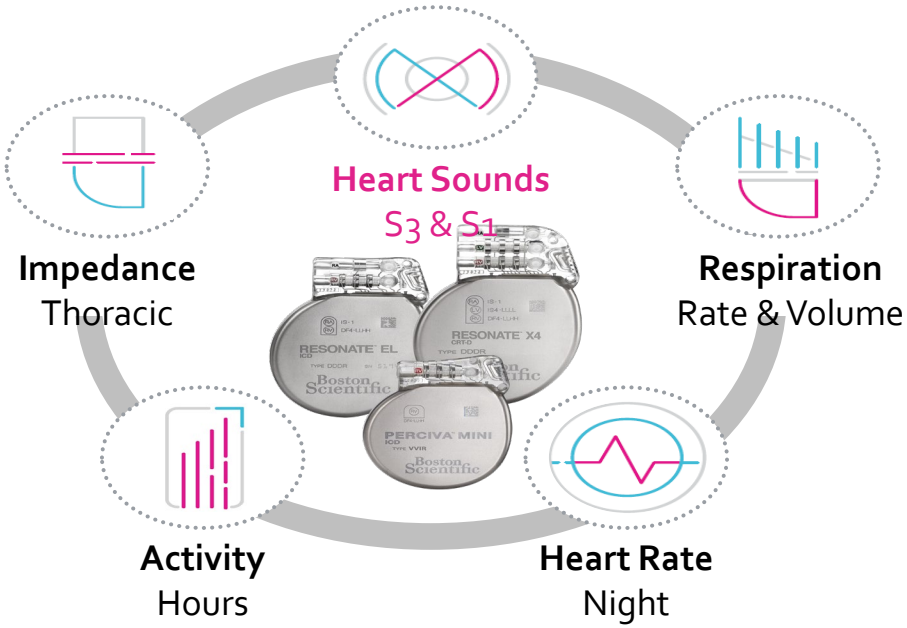
INTERVENE-HF OVERALL FINDINGS

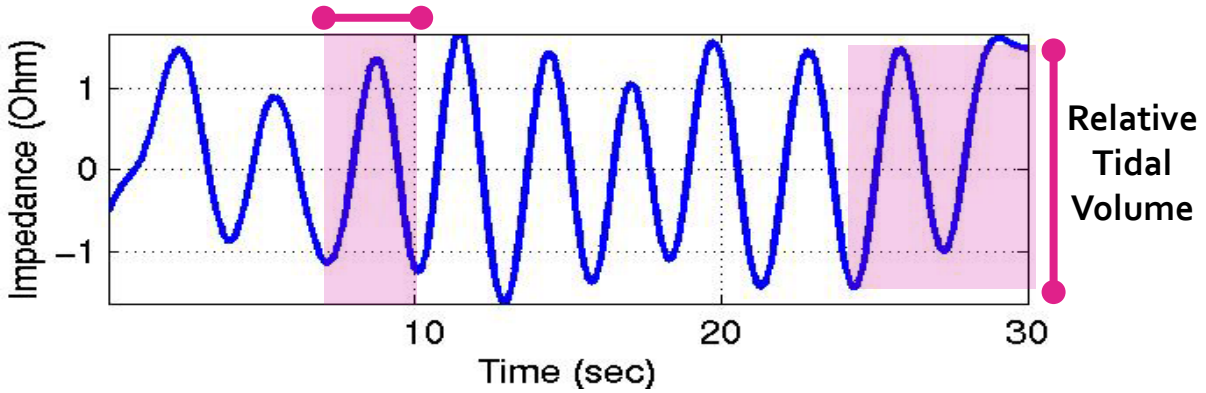
- Sixty-six patients followed for 8.2 ± 3.9 months had 49 HF care alerts
- Twenty-three of 49 alerts did not receive PRN due to protocol-mandated criteria
- Twenty-six of 49 alerts received PRN, 22 were completed, and 19 led to impedance recovery
- Four interventions were stopped for safety without leading to an adverse event (AE). One of 26 PRNs was followed by a HF event
- Eighty-five per cent (22/26) of PRNs were completed without an AE; 69% (18/26) met the recovery criteria.

Zile MR, Costanzo MRR, Ippolito EM, Zhang Y, Stapleton R, Sadhu A, Jimenez J, Hobbs J, Sharma V, Warman EN, Streeter L, Butler J. INTERVENE-HF: feasibility study of individualized, risk stratification-based, medication intervention in patients with heart failure with reduced ejection fraction. ESC Heart Fail. 2021 Apr;8(2):849-860.

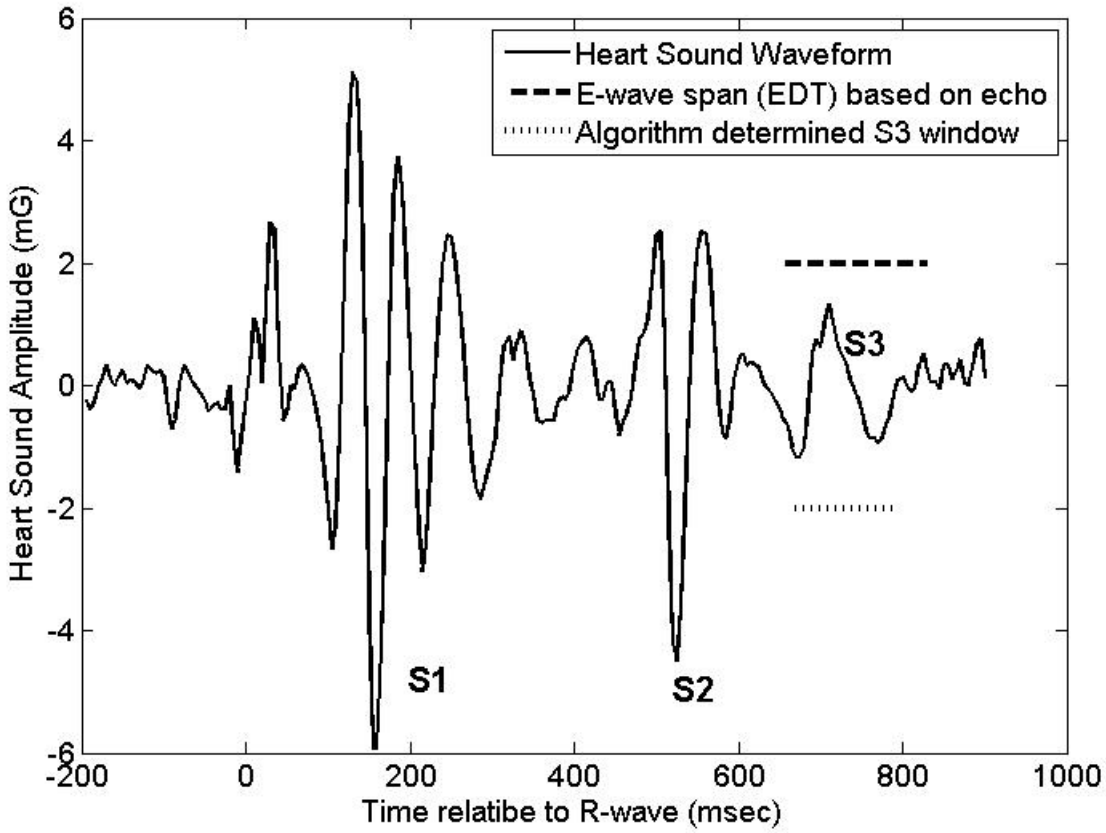
Boston Scientific's Approach to Multiparametric Modeling in HF: HeartLogic

- Worsening heart failure may be associated with an increase in Night Heart Rate
- Device-measured S3: occurs during early diastolic filling, consistent with its known physiologic genesis
- Rapid shallow breathing is a poor prognostic indicator (low tidal volume, increased rate)
- Worsening heart failure may be associated with a decrease in the activity level or a low level of activity





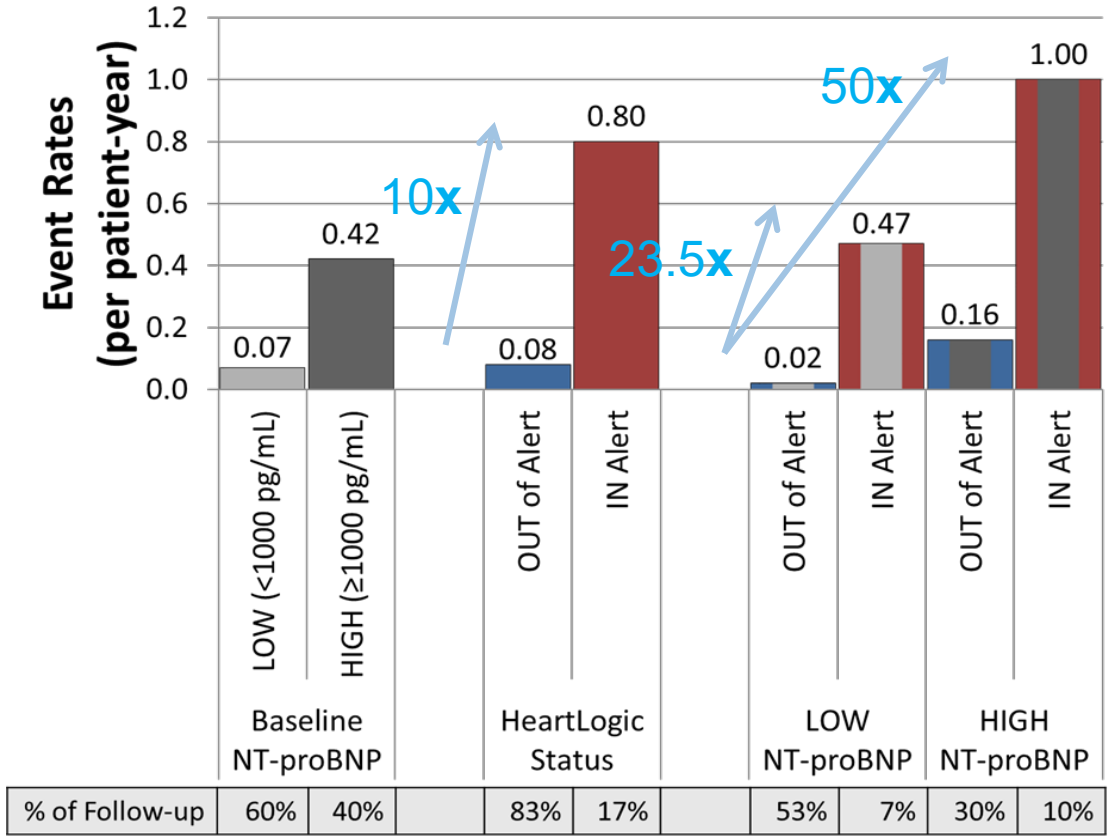
Novel Addition to Modeling: S3 Detection!



Klodas E, Thakur P, An Q, Bank A. Third Heart Sound Measured by Implanted Accelerometer in HeartFailure Patients is Coincident with the Deceleration Phase of Early Diastolic Filling [abstract]. J Card Fail. 2017;23(8):S68-S9.
http://www.onlinejcf.com/article/S1071-9164(17)30412-8/pdf

Combination of HeartLogic and Natriuretic Peptides for Risk Stratification

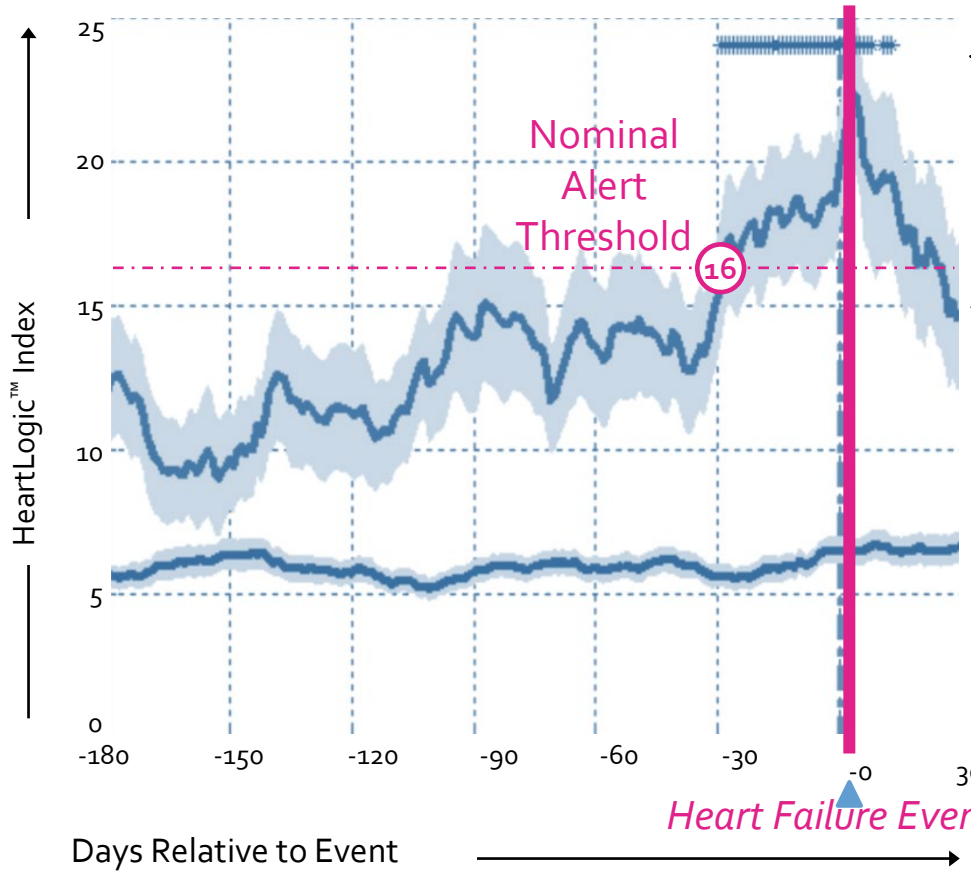
- HeartLogic identified high-risk patients
- 10 x higher heart failure event rate when IN alert than OUT of alert
- 50 x higher heart failure event rate when IN alert and high NT-proBNP
- Very low non-alert event rate of 0.08 per patient year



Gardner et al. Circ-HF 2018;11(7):1-10. https://doi.org/10.1161/CIRCHEARTFAILURE.117.004669

HeartLogic Can Predict a HF Event About a Month Before It Happens

The MultiSENSE Study results showed that it could allow weeks of advanced notice to clinicians to a potential heart failure event



HeartLogic™ Index is significantly elevated about 29 days before a heart failure event as compared to its baseline value during 90-180 days prior

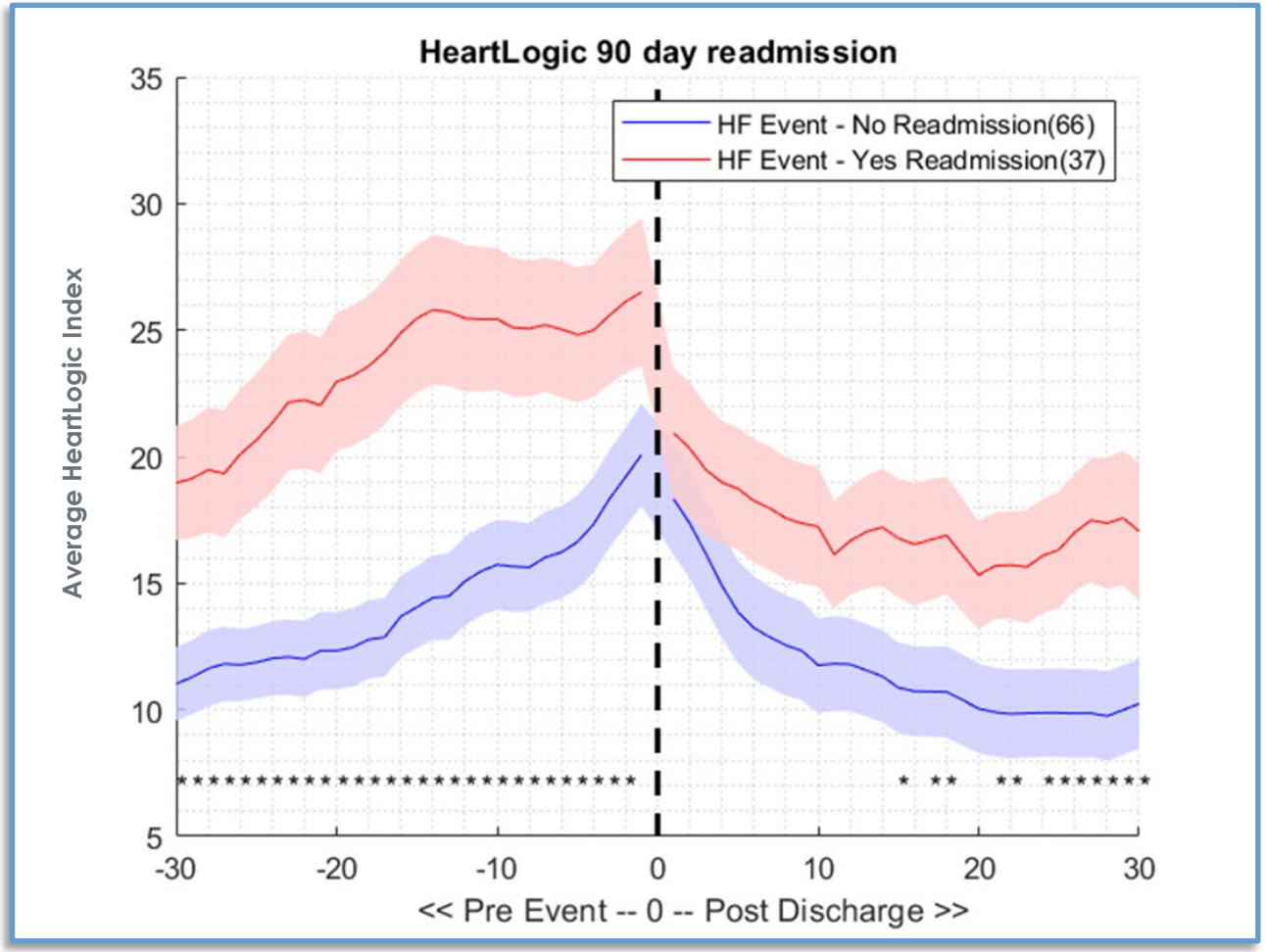
HeartLogic™ Index in patients **with heart failure events**

HeartLogic™ Index in patients **without heart failure events**

Boehmer et al. JACC-HF, 2017;5(3):216-225. http://dx.doi.org/10.1016/j.jchf.2016.12.011

PREEMPT-HF: Rationale for Checking HeartLogic Prior to Discharge from a Heart Failure Admission

- Increased likelihood of 30-Day HF and 30-Day All-cause readmission if IN-ALERT 14 days prior to index HF admission:
  - HF Readmission: OR 3.05, 95% CI [1.02, 9.10]
- Increased likelihood of readmission for primary HF in 90 days if IN-ALERT both 7 days and 14 days post-discharge following index HF admission
  - 7-Days: OR 3.01, 95% CI [1.29, 7.01]
  - 14 days: OR 2.67, 95% CI [1.16, 6.14]



Days where the average HeartLogic index is significantly different with readmissions versus without readmissions are indicated by asterisk (* p < 0.05)

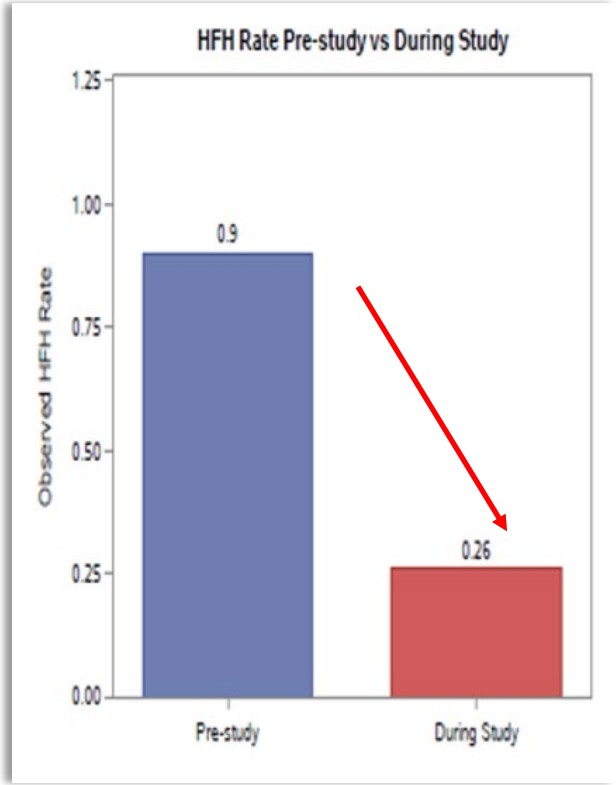
Sauer et al. Primary results of the Precision Event Monitoring for Patients with Heart Failure Using HeartLogic Trial. Abstract and Poster Presentation at HFSA 2023 Annual Scientific Meeting. Oct 2023; Cleveland, OH.

HeartLogic™ was associated with lower rate of HF hospitalizations

Heart Failure Hospitalization Rate*

- Heart Failure Hospitalization (HFH) in-study rates were compared with pre-study 12-month HFH rate.
- **Modeled HFH rate was 67% lower compared to pre-study HFH rate (rate ratio [95% CI]: 0.33 [0.23,0.47])**
- Observed HFH rate was 71% less during study as compared to 12-month pre-study**
  - 0.90 HFH/patient-year pre-study
  - 0.26 HFH/patient-year during study

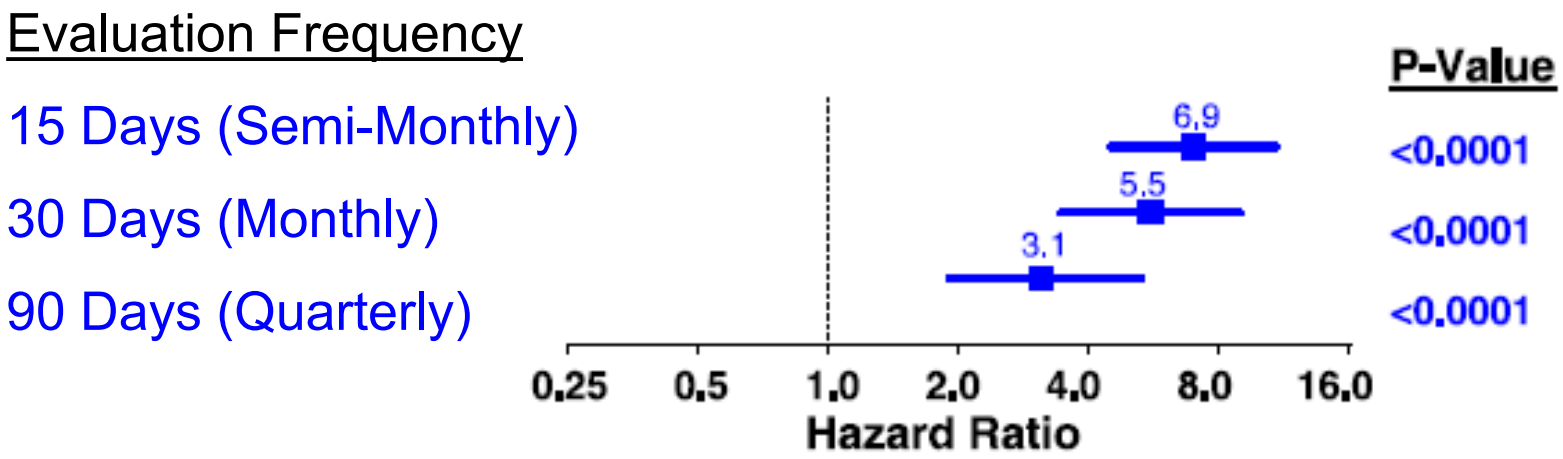
Although noted in context of observational design, this data suggests how HeartLogic may impact HF hospitalizations in real-world clinical practice.



Hernandez AF et al. MANAGE-HF Phase I results. Abstract presented/published at: ESC-HF 2021. June 29-July 1, 2021. Virtual. https://onlinelibrary.wiley.com/doi/epdf/10.1002/ejhf.2297 (Pg 159)

What is the Ideal Monitoring Frequency?

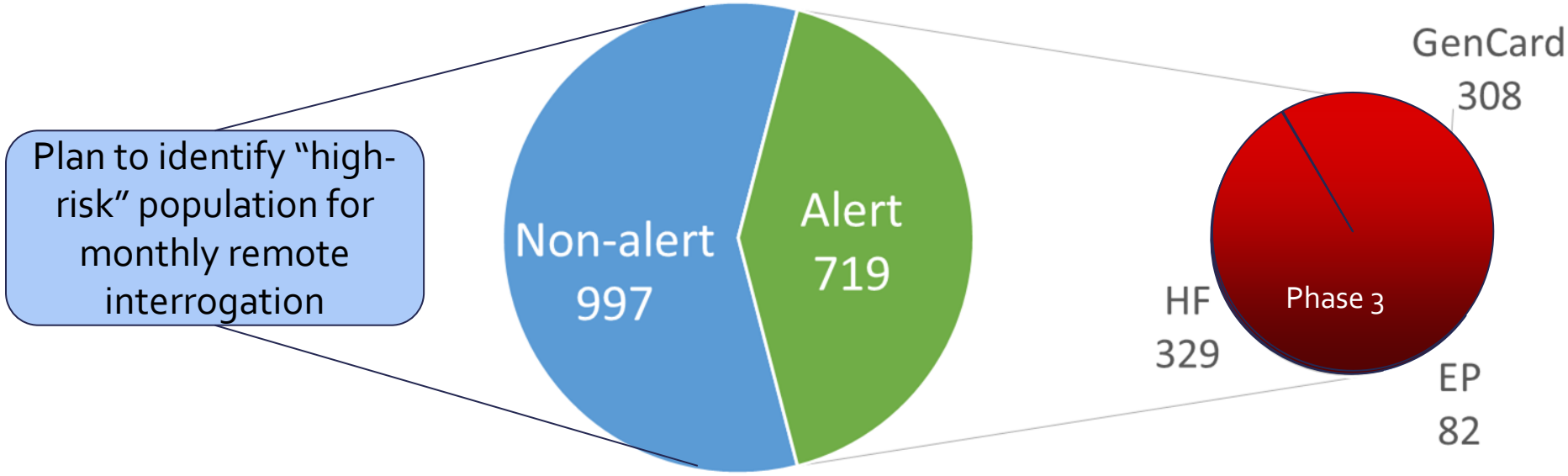
- Remote interrogations may be performed and billed every 3 months
- Increasing the frequency of reviewing the HF device diagnostics from quarterly to monthly will substantially increase the ability to identify patients at higher risk, whereas changing from monthly to semimonthly provides a less notable increase
- In practice, there will be many normal HF results, and these are often discarded rather than billed to patients



Challenges in the Implementation of a HF Monitoring Strategy in EP Clinic

- Staffing is the major issue
- Can EP MDs find the bandwidth to make diuretic and other medication adjustments for their patients?
- Can EP APPs do this work? Some EP APPs have become very specialized with respect to electrophysiology, and they also may not have the time to implement this program.
- A promising approach could be to have HF APP cover the EP clinic

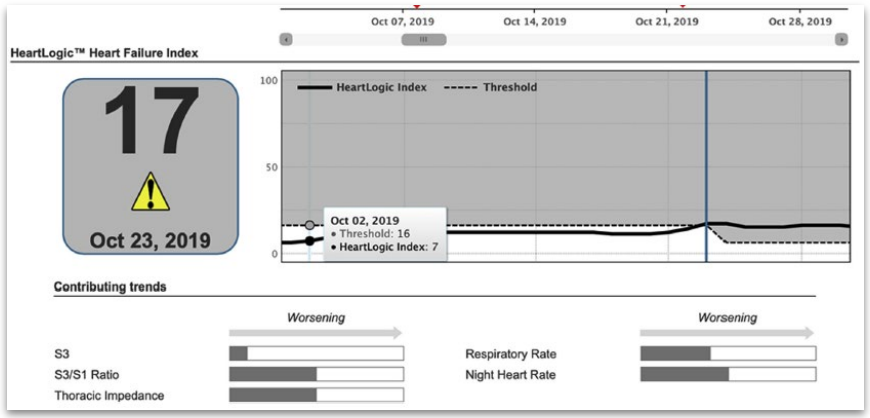
Plan for Implementation of HF Remote Monitoring at the University of Virginia

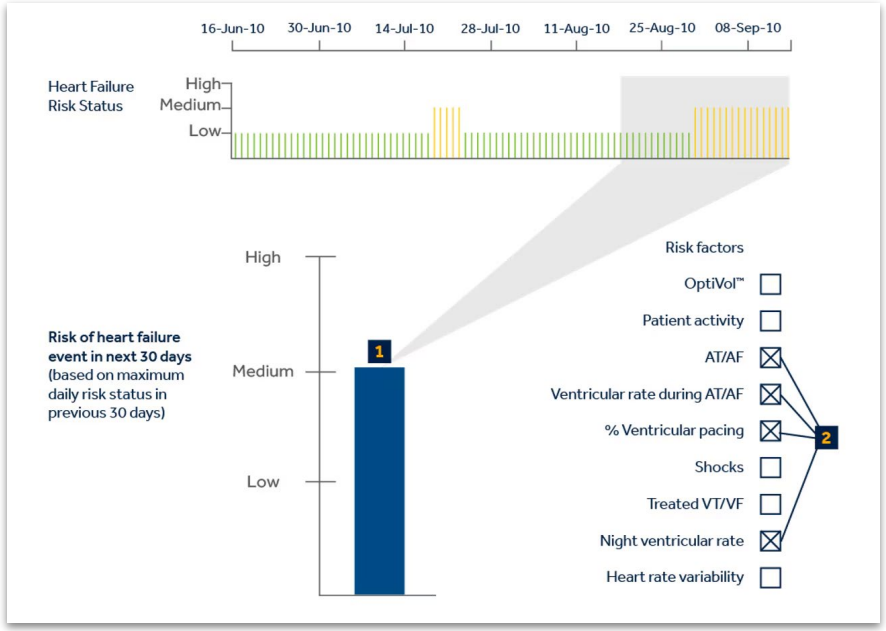


All newly implanted ICD/CRT-D will have HeartLogic or TriageHF enabled

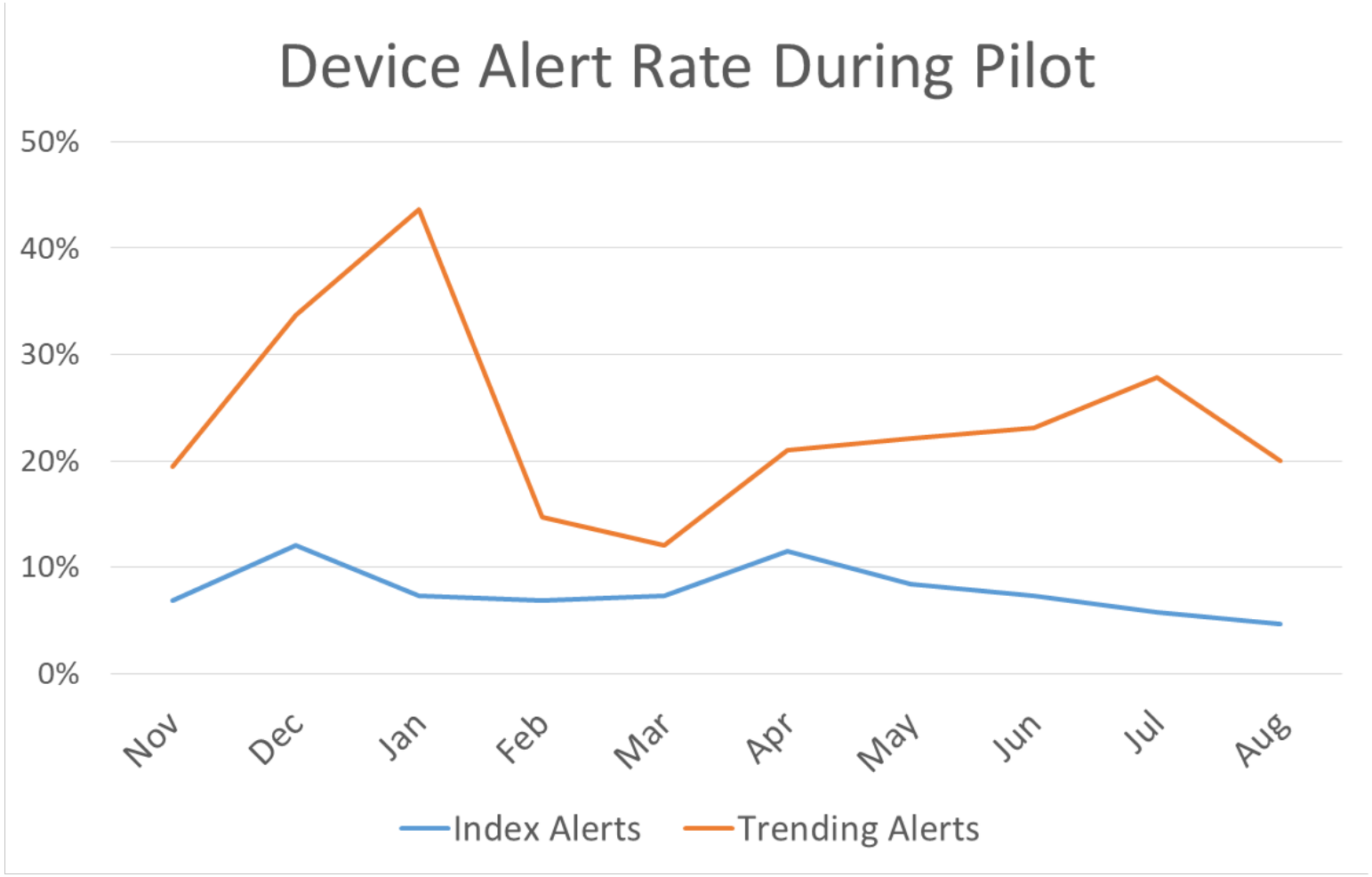
CIED Heart Failure Data

	Trigger	Continued Alerts
Boston Scientific (HeartLogic)	≥16	Until ≤6
Medtronic (TriageHF)	Rolling 30 day risk assessment	Requires re-submission





Manageable Number of Patients "In-Alert"



Conclusions – ICD Remote Monitoring

- Digital data from ICDs and other devices can improve outcomes over prior paradigms by facilitating early adjustment of medications and the need for heart failure hospitalizations
- Thoracic impedance has strong associations with multiple adverse clinical outcomes and prediction can be improved with multiparameter assessments
- The biggest challenge for implementing remote monitoring programs is facilitating translation of the digital health information into communication with patients to improve outcome


Thank You